Guidelines

Japanese Society for Burn Injuries (JSBI) Clinical Practice Guidelines for Management of Burn Care (3rd Edition)

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The Japanese Society for Burn Injuries (JSBI) published the third edition of guidelines to present the standard of care for inpatient treatment of burn injuries in Japan. The guideline is not a mere revision of the first and second editions but has been carefully designed to be user friendly and of high quality for medical professionals engaged in burn care. We think it is important to share these guidelines with other countries to work toward a consensus of burn care, then develop new research to establish evidence for burn care and treatment in the future.

INTRODUCTION

BURN INJURIES ARE highly diverse, with severe burns, in particular, presenting a long and complex pathology. Therefore, it is often difficult to conduct clinical research on this subject with a high level of scientific evidence, and treatment policies vary considerably from one institution to another. In addition, some diagnosis and treatment methods that have been standardized for a long time have insufficient scientific basis. The Japanese Society for Burn Injuries (JSBI), led by its Scientific Committee, published the "Clinical Practice Guidelines for Management of Burn Care"[1] in March 2009. Until then, there were no guidelines for burn care in Japan, and the American Burn Association (ABA) guidelines were released internationally in 1998. However, the ABA guidelines are different from those in Japan, and there are some items that are difficult to apply directly. The "Clinical Practice Guidelines for Management of Burn Care," published under such circumstances, has created a stir in the field of burn care and its academic discipline and is a major step toward the standardization of burn care in Japan.

About 5 years have passed since the first edition was published, and new findings have been added. In addition, the guidelines were revised in March 2015, as planned, to include items such as wound dressings and nutrition that could not be included in the first edition and were published as the "Clinical Practice Guidelines for Management of Burn Care (2nd Edition)".[2] The purpose of the first and second editions of the Guidelines was to present the results (evidence) of clinical research that has been conducted to date on the treatment of burns in order to provide a direction for future clinical research and a basis for the standardization of initial treatment. Internationally, the International Societies of Burn Injuries (ISBI) published the "ISBI Practice Guidelines for Burn Care" in 2016 and 2018.[3,4] However, these guidelines are intended for low- and middle-income countries where adequate medical resources are not available, and many of the contents are not applicable to high-income countries, including Japan, where adequate medical resources are available. The ABA publishes guidelines for each area in its journal (*Journal of Burn Care and Research*), and the guidelines are listed on the journal's website as the "Practice Guidelines Collection".[5]

As it has been approximately 5 years since the release of the "Guidelines for the Treatment of Burns (2nd Edition)," which has been used in the field of burn care, the JSBI decided to release the "Clinical Practice Guidelines for Management of Burn Care (3rd Edition)" under the oversight of the Scientific Committee, as in the past. The purpose of the third edition is to present the standard of care for inpatient treatment of burns in Japan, mainly for burns requiring hospitalization within 4 weeks of injury in high-income countries such as Japan, where adequate medical resources are available. In this revision, new findings since the release of the second edition have been thoroughly reviewed, and new areas that could not be included in the previous editions, such as special burns including electrical and chemical

injuries, analgesia and sedation, blood transfusion, measures against deep vein thrombosis, rehabilitation, liaison, end-of-life care, and family care, have been actively addressed. In addition, the guidelines are based on scientific evidence. Furthermore, considering the fact that medical guidelines are written texts containing recommendations based on scientific evidence and created using a systematic approach, we conducted our work in accordance with the EBM and Guidelines Promoting Project of the Japan Council for Quality Health Care (Medical Information Distribution Service; Minds).[6] As a result, we have included a wide range of items that are inevitable in the treatment of patients with severe burns, including 69 clinical questions (CQs) covering 13 areas. The guideline is not a mere revision of the original guideline but has been carefully designed to be user friendly and of high quality for medical professionals engaged in burn care. In addition, from the perspective of standardizing burn care, the contents of the Advanced Burn Life Support (ABLS) course,[7] a standardization program developed by the ABA that focuses on the initial care of patients with severe burns, were used as a reference. The terminology used in this guideline is based on the glossary of burn terms (2015 revision) published by the JSBI.[8]

The purpose of this guideline is to standardize and improve the quality of burn care in Japan. However, these guidelines are based on the scientific evidence currently available and are not intended to be absolute or universal, nor are they intended to limit individual practice. In future, when important scientific evidence is obtained or additional items are identified, this book will be revised and supplemented successively and will also be fully revised in approximately 5 years.

Disclosure of conflicts of interest and roles of members

Economic conflicts of interest (COIs) and the roles of each member are disclosed at the end of this report. Economic COI was disclosed in accordance with the guidance on eligibility criteria for participation in the COI Management Guidance on Eligibility Criteria for Clinical Practice Guideline Formulation compiled by the Japanese Society of Medical Science in 2017[9] and applied for 3 years, starting in 2018.

Funding

The development of this guideline was funded by the JSBI. The members received no compensation for their work. The intentions and interests of the JSBI and Minds, who collaborated with us in the development of the recommendations, are not reflected in this work.

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OUTLINE OF THE GUIDELINES

Title

THESE PRACTICE GUIDELINES are named the Japanese Society for Burn Injuries (JSBI) Clinical Practice Guidelines for Management of Burn Care (3rd Edition) (hereinafter referred to as the "Guidelines").

Objectives

The objective of the Guidelines is to provide a high standard of care to hospitalized patients with burns in Japan.

Target patient population

The Guidelines are intended for patients of all ages with severe burns that require inpatient treatment in intensive care units, burn care units, or general wards for approximately 4 weeks after injury. We did not include burns that could be

treated only in outpatient clinics. We included burn injuries involving airway, chemical, and electrical injuries.

Target users (users of the Guidelines)

The Guidelines are intended for use by all health-care professionals involved in burn care, including physicians, nurses, pharmacists, and physical therapists. The treatment environment was not limited to specialized burn centers and included centers that provide patients with access to sufficient medical resources for daily care in Japan.

Precautions for use

This guideline describes the standard treatment aimed at improving the overall outcome of patients. Therefore, the decision to follow these Guidelines should be made at the discretion of the physician according to the situation and particularities of each patient. In choosing a treatment, it is important to consider not only the medical evaluation of the patient but also the medical personnel, medical resources, and the patient's wishes.

In view of the nature of these guidelines, the JSBI does not permit them to be used as the basis for judicial decisions. These Guidelines are based on the evidence and consensus of experts in burn care at the time of its development. The Guidelines will need to be revised in response to accumulating evidence and changes in burn care. The JSBI has been publishing a revised edition approximately every 5 years since the first edition was published and plans to continue these revisions.

Organizational structure in the preparation of these Guidelines

The Minds Clinical Practice Guideline Manual 2017, prepared by the Medical Information Service Project of the Japan Council for Quality Health Care, recommends the formation of a guideline supervisory committee, guideline development group, and systematic review team as organizations for the development of clinical practice guidelines.[1]

In these Guidelines, the following organizational structure has been adopted in consideration of the manpower involved in their preparation.

Guideline supervisory committee

The Board of Directors of the JSBI played the role of the supervising committee for these Guidelines. The Board of Directors that was involved in the preparation of the second edition of the Guidelines approved the selection of the members of the guideline development group for the preparation of the third edition. The Board of Directors also discussed and approved the funding needed to produce the Guidelines and played the role of the governing committee, but their intentions were not reflected in the recommendations.

Guideline development group

The Academic Committee of the JSBI functioned as the guideline development group for these Guidelines. The chairperson directed the entire guideline development. In addition to the chair, 13 committee members were in charge of one or two areas. In addition to the committee members, two to three working members were assigned to each area. The list of names, affiliations, and conflicts of interest of all committee members and working members is included in the Appendix section of the Guidelines.

Systematic review team

The systematic review team consisted of members from the guideline development group and some of the working members. At the stage of systematic review (SR), we worked cross-sectionally regardless of the domain to which each member belonged.

Participation of representatives of relevant expert groups and external evaluation by experts

The guideline development group consisted of physicians who are members of the JSBI. In areas where the involvement of multiple professions other than physicians is significant, a physical therapist participated as a working member. In the area of liaison, a psychiatrist also participated as a working member and was involved in the preparation of recommendations. When preparing these Guidelines, we registered our project with the Minds Clinical Guidelines Development Registry and followed the Minds Clinical Guidelines Development Manual 2017 as closely as possible.

Reflecting the values of the target group (patients, general public, etc.)

In order to reflect the values of patients and the public, public comments were solicited twice during the development of this guideline.

Ensuring quality and transparency

Sharing information

In preparing these Guidelines, the discussions of the guideline development group were conducted using the official

mailing system as much as possible. In each area, as appropriate, discussions were sent to the official mailing list to share and solve problems.

Peer review

At each milestone in the development process, the draft prepared for each area was reviewed by all members of the guideline development group. After repeated peer review and revision, the revised draft was approved by the committee.

Voting

In order to avoid interference with each other's academic COIs, the votes of the committee members on the draft recommendations were anonymized, and the result was based on these anonymous votes that were counted by someone other than the committee members.

Scientific meetings and public comments

After soliciting public comments, the CQs were opened at the 45th Annual Meeting of the JSBI, and the opinions of the society members were sought. The revised CQs and answers were also posted on the website of the JSBI and Minds for public comment.

Disclosure of financial COI

The financial COIs of the guideline development group members and working members were disclosed at the end of the report. The financial COIs were disclosed for 3 years from 2018 to 2020 in accordance with the guidance on eligibility criteria for participation in the development of medical guidelines compiled by the Japanese Association of Medical Sciences.[2]

Funding for development

This guideline was developed with funding from the JSBI. The members received no compensation for their work. The intentions and interests of the JSBI and Minds were not reflected in the recommendations.

Measures to disseminate the guidelines

This guideline will be published in *Burn*, the official journal of the JSBI, and on the JSBI website. We will strive to disseminate this guideline at scientific meetings and seminars. In order to convey Japanese burn care standards overseas, we will promote submissions to English journals.

Revision schedule

This guideline is planned to be revised every 5 years. The next revision is scheduled for 2026. If no significant evidence or findings are obtained by then, partial revision will be considered.

HOW THE GUIDELINES WERE DEVELOPED

THE GUIDELINES WERE developed through three processes: CQ formulation, collection and evaluation of evidence through SR, and formulation of recommendations.

Clinical question planning

Process of creating CQs

In addition to the CQs covered in the second edition, drafts of CQs for important clinical issues in daily practice were prepared for each area. The draft CQs, once approved by the guideline development group after peer review and revision by the committee members, were opened for public comment in April 2019, and the opinions of society members were sought at the 45th Annual Meeting of JSBI. The CQs were revised based on the opinions obtained, and 69 CQs in 13 areas were finally determined by the guideline development group.

Types of CQs

The CQs were divided into foreground questions (FQs) and background questions (BQs). An FQ is a CQ on options in clinical practice, and a BQ is a CQ on standard knowledge of diseases, diagnosis, and treatment. To answer the FQs, a PICO (Patients, Intervention, Control, Outcome) model was developed, and an SR was conducted; then, recommendations were made according to the results. Each BQ presented a summary of the evidence on diseases and diagnosis and the variety of treatment and evaluation options.

Collection and evaluation of evidence through SRs

Collection of evidence

To answer the FQs, we conducted an exhaustive literature search based on the PICO model. The evidence included data from randomized controlled trials (RCTs) published in PubMed and SRs published in the Cochrane Library. The target language was English, and the target period was June 1, 1999 to December 31, 2020 (the original period covered was from June 1, 1999 to May 31, 2019, but since the preparation period was extended, the period from June 1, 2019 to December 31, 2020

was added). For RCTs, the systematic review team conducted a primary search of the literature (screening by titles and abstracts) and a secondary search (full text review) in each area. The Cochrane SRs were searched and data were extracted for each area. In each case, two or more experts independently conducted the literature search and evaluation.

Evaluating the evidence

The strength of evidence was determined in accordance with the Guidelines for Burn Care (revised second edition) and the Guidelines for Plastic Surgery as specified below. The levels of evidence included were levels I, II, and VI because only RCTs and SRs were reviewed.

Levels of evidence I: Systematic review or RCT meta-analysis
II: One or more RCTs
III: Non-RCT
IV: Analytical epidemiological studies (cohort studies, case control studies, and cross-sectional studies)
V: Descriptive research (case reports and case-concentration studies)
VI: Reports and opinions of expert committees or clinical experience of experts

Formulate recommendations

Strength of recommendation (degree of recommendation)

The degree of recommendation of each FQ was determined according to the concept of the Minds Clinical Guidelines Development Manual 2017, the Guidelines for Burn Care (2nd revision), Guidelines for Plastic Surgery, and the Japanese Clinical Practice Guidelines for Management of Sepsis and Septic Shock 2016. The balance of the benefits and harms of therapeutic interventions was evaluated according to the evidence, taking into account the patient's preferences and values, medical resources and costs, and feasibility and acceptability factors. The direction and extent of the recommendations were determined as specified below; an asterisk (*) was used for drugs that have not been approved by the pharmaceutical regulatory bodies or those not covered by insurance.

Recommendation grades for FQ Recommendation A: Strong evidence, strongly recommend to do/not to do.
(At least one level I evidence or good quality level II evidence showing efficacy)
Recommendation statement: Do/do not do ◯◯ is strongly recommended.
Recommendation B: There is evidence to support the recommendation to do/not to do.
(At least one level II evidence of inferior quality or good quality level III evidence or very good quality level IV evidence showing efficacy)
Recommendation statement: Do/do not do ◯◯ is weakly recommended.
Recommendation C: No evidence, but recommend to do/not to do.
(Level III–IV evidence of inferior quality or multiple good quality level V or level VI evidence)
Recommendation statement: Do/do not do ◯◯ is recommended.
Recommendation D: Strongly recommend to do/not to do even if the level of evidence is VI; it is established as a standard treatment.
Recommendation statement: Do/do not do ◯◯ is strongly recommended.

Drafting a recommendation proposal

A draft recommendation for the FQ in each area addressed was prepared by describing the background to the recommendation according to the following template.

Template of FQ
1. CQ and answer
2. Background and importance of CQ
3. PICO
4. Summary of evidence (results of SR)
5. Level of evidence
6. Summary of benefits
7. Summary of harms (burden and side effects)
8. Balance between benefits and harms
9. Medical cost of this intervention
10. Feasibility of this intervention
11. Is the intervention evaluated differently by patients, families, medical staff, and physicians?
12. Recommendation decision process
13. Recommendations in other relevant practice guidelines
14. References

The following template was used to create a recommendation for the BQ.

Template of BQ
1. CQ and answer
2. Background and importance of CQ
3. Evidence and commentary
4. Recommendation decision process
5. References

Voting for recommendations

Fourteen members of the guideline development group voted on the draft recommendations for the FQs and BQs prepared by each domain. For the BQs, we did not provide recommendations, but a vote was taken on the appropriateness of the contents. Prior to the vote, the following methods were established.

Voting method

1. Fourteen members of the committee will vote 1 or 0 for the following three items.
   - Are the sentences written in easy-to-understand Japanese?
   - Are there any inconsistencies in the recommendations or their rationale?
   - Are the recommendations appropriate for Japanese practice?
2. The draft recommendation will be adopted if it scores 10 points or more in all three items.
3. If the score is less than 10, the experts in each area will revise the draft recommendation and the committee will re-vote.
4. The results adopted by the committee will be made public at science meetings and through public comments.
5. The results of the voting will be made public at the end of the process.

The results of the voting on the recommendations for each area were entered into an Excel file by the committee members and sent to the secretariat of the JSBI by e-mail. In order to avoid interference with academic COIs of the committee members, voting on the recommendation was conducted anonymously, and the votes were counted and anonymized by the secretariat staff.

After two rounds of voting, seven CQs did not meet the criteria for adoption, but re-voting was decided based on public comments. The results of the voting were reported at the 46th Annual Meeting of JSBI, and all CQs and answers were opened for public comment.

Taking into account public comments and the results of the additional literature search from June 1, 2019 to December 31, 2020, the recommendations were revised in each area. The final recommendation was made after peer review and additional voting by members of the guideline development group, and the full text was published after approval by the Board of Directors.

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CQ1 SEVERITY ASSESSMENT

PROMPTLY ASSESSING THE severity of burns as an acute wound and accurately determining whether treatment at a burn specialty facility are appropriate aspects in the treatment of burns. This knowledge is important not only for burn specialists but also for the general public. How many patients with severe burns can be saved if they receive the best treatment? The findings of the severity assessment should be fed back accurately to the unit providing initial treatment immediately after the onset of burn injury. Hence, three CQs were designed for severity assessment this time.

The CQ format of "What factors are useful?" follows the subclassification of the Burn Treatment Guidelines (1st edition and revised 2nd edition). CQ 1–1: What factors are useful for estimating the prognosis of burns? CQ 1–2: What factors are useful for measuring the burn area and determining the burn depth? CQ 1–3: What factors are useful as a standard of treatment in a burn specialty treatment facility? Review new treatises after the second revised edition for each item. In response to CQ 1–3, we introduced the guidelines of the ABA and the criteria for referral to the burn center of the ABLS course. For each item, standard knowledge was presented using a BQ.

CQ1–1

CQ and answer

CQ: What factors are useful for estimating the prognosis of burn patients?

Answer: Burn area (percentage of the total body surface area: %TBSA) is used as the most basic prognostic factor. In some reports, age, inhalation injury, third-degree burn area, burn index, suicide attempt injury, Revised Trauma Score, and prognostic burn index (PBI) have been used as prognostic factors.

Background and importance of CQs

Estimating the prognosis is important when treating burns as per the treatment policy. As it is difficult to conduct a control test, the level of evidence is still low. However, we answered

this question as a BQ because the content is well established.

Evidence and commentary

A number of studies examined age, inhalation injuries, third-degree burn area, BPI, and suicide attempt injury as prognostic factors. Burn area is the most commonly used basic index. Regarding other factors, no influential papers were found.

Many papers mentioned age and airway burns[1–9] as prognostic factors. Furthermore, in some papers, third-degree burn area,[5] suicide attempt,[10,11] Revised Trauma Score,[12] which is a severity evaluation method calculated from physiological indicators of consciousness level, systolic blood pressure, and respiratory rate were reported to be related to patient outcome.

Regarding the burn index,[6] the level of evidence is low, probably because of the accuracy of the evaluation of the burn depth. The PBI, which is the sum of the burn index and age, is not used in Europe or the United States, but is used in Japan.[13] In some studies, women were at a high risk of burns,[14] but most of the papers reported no significant difference between the sexes.[10,11,15] In addition, the evaluation of the presence or absence of surgery or chronic disease is different from the evaluation of the burn injury and is not used as a predictor of prognosis.

Recommendation decision process

The guideline satisfied the prescribed adoption criteria in the first vote.

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CQ1–2

CQ and answer

CQ: What factors are useful for measuring the area of burns and assessment of the burn depth?

Answer: For measuring the burn area, the rule of 9, the rule of 5, Lund and Browder's law, and the palm method are widely used. Laser Doppler flowmetry, video microscopy, fluorescence method, ultrasonography, near-infrared reflection spectroscopy, and optical coherence tomography are also used to determine burn depth. It has been reported that the system of burn assessment can be improved by using a combination of video microscopy and Doppler flowmetry.

Background and importance of CQ

Measurements of the burn area and burn depth are indispensable for determining the severity of the burn and determining the infusion volume and the treatment policy for the wound surface. In addition, a burn patient requires prompt treatment

when he/she visits the hospital. Therefore, in many burn treatment facilities, a simple method is often used, for example, a diagnostic method not backed by literature or a method selected by the doctor according to his/her experience. There are few papers on the methods for assessing burn depth, and the burn depth determination methods involving complex equipment are not popular. Based on the above, simple methods for the measurement of burn area and evidence-based burn depth assessment were introduced using a BQ.

Evidence and commentary

For measuring the burn area, the rule of 9[1] and the rule of 5[2] are often used in daily medical care and are also recommended in many textbooks and documents. Lund and Browder's law[3] can be used to accurately measure the burn area by age. The palm method[4,5] is used to measure the burn area using the palm, where the total area of a person's palm and all finger pads is considered 1%[4,5] of the area; this method is used for small areas or multiple areas. It has been reported to be useful.

For determining the depth of a burn wound, the wound surface would need to be observed and the blood flow would need to be measured. In many research papers,[6–15] laser Doppler flowmetry was used, and some studies used histological methods.[16] The sensitivity, specificity, and accuracy of Doppler flowmetry are as high as 94–95%,[6–15] similar to the fluorescence method,[1,17] ultrasonography,[1,18] and the reflection-optical multispectral imaging method.[1,19] There is little evidence for the clinical application of optical coherence tomography[20,21] and it is rarely used clinically.

Video microscopy is used in clinics in Japan[22] for observing the blood flow of the burn wound surface, but it is performed in very few clinics. Furthermore, the usefulness of Doppler flowmetry has been confirmed in a prospective controlled trial.[23] However, the burn depth determination method used in daily medical care involves determining the color tone and condition of the wound surface with the naked eye, performed by doctors who are skilled in the treatment of burns, and there is no RCT to support this.

Recommendation decision process

The guideline satisfied the prescribed adoption criteria in the first vote.

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CQ1–3

CQ and answer

CQ: What factors are useful as standards of treatment in a burn specialty treatment facility?

Answer: Artz's criteria[1] and Moylan's criteria,[2] which indicate inpatient treatment at a burn specialty treatment facility with a second-degree burn of 30% TBSA or higher, are widely used clinically. The ABLS course of the ABA recommends that patients with second-degree burns ≥10% of body surface area be treated at a specialized burn treatment facility. In addition, consideration is given to chemical injuries, medical history, pediatric burns, social and mental care, and rehabilitation.[3]

The ABA adds individual factors such as age, comorbid injury, and pre-existing illness to the severity of the burn area and burn depth in the triage at a burn specialty treatment facility or trauma center. Special guidelines are established for dealing with large-scale disasters and wars.[4]

In these Guidelines, "burn center" was defined as a facility that can provide inpatient treatment of burn patients, such as training facilities certified by a burn specialist of the Japan Society for Burns.

Background and importance of CQ

Depending on the severity of the burns, it may be necessary to treat them at an appropriate facility. Since the severity is judged by various factors, such as the extent and depth of burns, comorbid injuries, pre-existing illnesses, and social background, these indicators[1–3] are used accordingly. This CQ was answered as a BQ that introduced the typical indicators used in Japan.

Evidence and commentary

In the United States in the 1970s, some papers[5,6] stated that treatment at a burn specialty treatment facility did not improve the prognosis, as no papers proved that the prognosis improved. However, in recent years, it has been reported that treatment at a burn specialty facility shortens the length of hospital stay and reduces the risk of complications.[7] In 2005, the ABA commented that treatment at a burn center is an efficient and cost-effective treatment strategy.[4] Hence, attention was paid to what level of burns should be treated in a burn specialty facility. However, no paper has verified whether Artz's criteria or Moylan's criteria are appropriate, and their usefulness is not clear. The following are the typical criteria used for transportation to a hospital specializing in burns.

Artz's criteria Severe burns (inpatient treatment in general hospitals and burn center)
- II degree burns 30% TBSA or more
- III degree burns 10% TBSA or more
- III degree burns on the face, hands and feet.
  - o Complications of airway injur
  - o Complications of soft tissue injuries and fractures
  - o Electric injury
- Moderate burns (inpatient care in local general hospitals)
  - a II degree burns 15-30% TBSA
  - b III degree burns 10% TBSA or less (except face, hands and feet)
- Minor burns (can be treated on an outpatient basis)
  - a II degree burns 15% TBSA or less
  - b III degree burns 2% TBSA or less

ABA burn center referral criteria
- Partial thickness burns of greater than 10% TBSA.
- Burns that involve the face, hands, feet, genitalia, perineum, or major joints.
- Third-degree burns in any age group.
- Electrical burns, including lightning injury.
- Chemical burns.
- Inhalation injury.
- Burn injury in patients with pre-existing medical disorders that could complicate management, prolong recovery, or affect mortality.
- Any patient with burns and concomitant trauma (such as fractures) in which the burn injury poses the greatest risk of morbidity or mortality. In such cases, if the trauma poses the greater immediate risk, the patient's condition may be stabilized initially in a trauma center before transfer to a burn center. Physician judgment will be necessary

in such situations and should be in concert with the regional medical control plan and triage protocols.
- Children with burns in hospitals without qualified personnel or equipment for the care of children.
- Burn injury in patients who require special social, emotional, or rehabilitative intervention.

(Excerpt from American Burn Association [2018][3])

Recommendation decision process

The guideline satisfied the prescribed adoption criteria in the third vote.

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CQ2 INHALATION INJURY

INHALATION INJURY REFERS to injury to the respiratory system caused by the inhalation of hot smoke, water vapor, or toxic gases.[1] It is conventionally referred to as inhalation burn, however, because the cause of injury is not limited to heat and the pathogenesis differs from that of skin burns, the JSBI recommends the use of the term "inhalation injury".[2] The diagnosis of airway injury is often made using clinical and bronchoscopy findings, but there is still no international consensus.

In this section, we summarize the current evidence on the diagnosis and severity assessment of inhalation injury (CQ2–1). For the treatment of airway injury, recommendations were made for inhaled heparin (CQ2–2) and inhaled N-acetylcysteine (CQ2–3). There was a lack of evidence to support the recommendations regarding the timing of airway intubation and respiratory management (CQ2–4) and rehabilitation (CQ2–5), so we summarized the current reports and expert opinions.

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CQ2–1

CQ and answer

CQ: How can we diagnose and assess the severity of inhalation injury?

Answer: Bronchofiberscopy and chest computed tomography are used for diagnosis, but there is currently no single definitive indicator of severity.

Background and importance of CQ

Inhalation injuries affect the prognosis of burn patients, but the methods of diagnosis and assessment of the severity of these injuries are still controversial. For this reason, this guideline was designed as a BQ to introduce the current evidence on how to diagnose and assess the severity of inhalation injuries.

Evidence and commentary

For the diagnosis of inhalation injuries, many experts consider the presence or absence of clinical findings as the basis for diagnosis.[1] Patients with positive clinical findings such as oral and pharyngeal soot ($P = 0.02$), hoarseness of voice ($P = 0.05$), and rales ($P = 0.004$) had a significantly longer intensive care unit (ICU) stay than those who did not have these findings. These early clinical findings are more useful in predicting respiratory complications than simple chest radiography.[2]

Bronchofiberscopy is used by many experts as the "gold standard" for the diagnosis of inhalation injuries.[1,3–5] The severity score determined by bronchofiberscopy is significantly associated with mortality ($P = 0.03$),[6] and there is a significant difference in the incidence of acute lung injury (ALI) according

to this severity score ($P = 0.001$).[7] In addition, bronchofiberscopy is clearly more useful in diagnosing the need for airway management than other diagnostic methods.[8–10] However, the degree of respiratory control (positive end-expiratory pressure value required to maintain oxygenation) and the duration of tracheal intubation cannot be predicted from bronchofiberscopy findings in the early stage of injury (on admission).[11] Furthermore, unnecessary diagnostic bronchofiberscopy may increase the risk of mortality, length of hospital stay, and risk of pneumonia complications, so the indications for bronchofiberscopy should be carefully considered.[12]

Gradings based on simple chest radiography findings over time and respiratory function test findings such as extravascular lung water volume ($r = 0.61$), intrapulmonary shunt ratio (Qs/Qt) ($r = 0.65$), static lung compliance ($r = -0.56$), and other respiratory function test findings correlated well.[13] Pathological examination by bronchial mucosal histology or brush biopsy is effective in diagnosing the severity of inhalation injuries ($P < 0.05$),[14] but these methods are invasive and time-consuming. In addition, bronchial mucosal changes are not related to systemic hemodynamics monitored using a pulmonary artery catheter.[15]

In burn cases with suspected inhalation injuries with PaO_2/FiO_2 ratio (P/F ratio) lower than 350 on admission, volume of fluid infusion per body weight per %TBSA is significantly high ($P < 0.03$), which can be a predictive indicator of acute fluid requirements,[6] and P/F ratio at 36–72 h after injury is significantly correlated with the patient's outcome ($P < 0.01$).[16] Furthermore, it has been reported that the P/F ratio alone is not a diagnostic parameter for inhalation injuries, and a diagnostic method based on multifactorial scoring is effective in diagnosing burn severity.[17] Moreover, clinical findings, airway mucosal inflammatory findings, and blood CO-Hb or cyanide levels do not correlate with the development of acute respiratory distress syndrome (ARDS), even if they are scored as criteria for severity.[18]

In one report, bronchial wall thickness at 2 cm below the tracheal bifurcation on chest computed tomography at the time of admission showed a significant correlation with the number of days on a ventilator ($R^2 = 0.56$) and length of stay in the ICU ($R^2 = 0.17$), and is also useful in predicting the onset of pneumonia.[19] Hence, the experts agreed that there is no global standard or method for diagnosing the severity of inhalation injuries.

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CQ2–2

CQ and answer

CQ: Should inhalation of unfractionated heparin be administered as the initial treatment for inhalation injury patients?

Answer: Inhalation of unfractionated heparin for inhalation injury patients as the initial treatment is weakly recommended (evidence level VI, recommendation level C*).

Background and importance of CQ

Acute lung injury due to inhalation injury has been reported to be associated with poor prognosis of burn patients.[1] In the case of inhalation injury, the inflammation increases the vascular permeability of the tracheal and bronchial mucosa, resulting in the formation of a pseudomembrane of exudate mixed with fibrin, blood clots, and necrotic tissue. The pathological condition of inhalation injury is that the peripheral bronchi is obstructed by the pseudomembrane, which decreases the ventilation : perfusion ratio and subsequent progression of lung damage. Patients with inhalation injury are treated with inhalation therapy of heparin or N-acetylcysteine to prevent the formation of pseudomembranes, but the beneficial effects and adverse effects of inhalation therapy are under discussion. Therefore, this CQ was for this guideline.

PICO

Patient: Patient with inhalation injury
Intervention: Treated with heparin inhalation
Control: Treated without heparin inhalation
Outcome: Mortality, respiratory function improvement, complication rate of severe infection, airway bleeding

Summary of evidence (results of SR)

No RCT
No Cochrane SR

Evidence level

Level VI: Expert committee reports and opinions or clinical experience of experts

Summary of benefits

No references were used as evidence. A systematic review examining the effects of heparin inhalation on inhalation injury was reported in 2019;[2] this SR included six observational studies and one RCT, of which two observational studies showed reduced mortality with heparin inhalation, two observational studies showed reduced lung injury score, and one observational study reported shortening of the mechanical ventilation period. The RCT comparing inhaled doses of different heparins reported lower lung injury scores in the high dose (10,000 units every 2 h) group than in the low dose (5,000 units every 2 h) group.

Summary of harms

No references were adopted as evidence. An observational study included in the above systematic review reported that heparin inhalation increased the risk of pneumonia.[2] A protocol of inhaling 5,000 or 10,000 units of heparin every 2 or 4 h has not been shown to increase bleeding complications, but it may prolong activated partial thromboplastin time (APTT) and prothrombin time (PT), and its recommended to monitor these parameters.[2] In one RCT, 25,000 units of heparin was inhaled by the treatment group every 4 h, and the study was suspended after 13 cases were registered.[3] Complications of airway bleeding had been reported in the heparin inhalation group at a low prevalence rate.

Balance between benefits and harms

There was no evidence for heparin inhalation therapy. Based on the above statements, it was determined that the benefits of heparin inhalation therapy would outweigh the harms.

Cost of the intervention

The price of heparin is approximately JPY 150 per 5,000 units (1 V). In the case of the protocol used in the literature (inhalation of 5,000 units of heparin every 4 h), the daily drug cost would be approximately 1,000 yen.

Feasibility

Although this intervention may add to the workload of nurses, heparin inhalation is considered to be acceptable as treatment of patients with inhalation injury. Heparin inhalation therapy is not covered by insurance. Thus, approval from the patients or their family is necessary.

Is the intervention differently evaluated by patients, family, and medical staff?

It is unlikely that the evaluation of heparin inhalation therapy will differ among patients, their family, and medical staff. There may be some resistance to it considering that it is not covered by Japanese insurance.

Recommendations in other clinical practice guidelines

The second edition of the JSBI Clinical Practice Guidelines for Management of Burn Care states that "nebulizer inhalation of heparin and N-acetylcysteine may be considered: Recommendation grade (C)." The ISBI Practice Guidelines for Burn Care (2016) do not provide recommendations for inhalation injury.

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CQ2–3

CQ and answer

CQ: Should N-acetylcysteine inhalation therapy be administered as the initial treatment for inhalation injury patients?

Answer: N-acetylcysteine inhalation therapy for inhalation injury patients as the initial treatment is weakly recommended (evidence level Ⅵ, recommendation level C).

Background and the importance of CQ

Acute lung injury due to inhalation injury is associated with poor prognosis of burn patients.[1] In inhalation injury, the inflammation increases vascular permeability of the tracheal and bronchial mucosa, resulting in the formation of a pseudomembrane of exudate mixed with fibrin, blood clots, and necrotic tissue. The pathological condition of inhalation injury is that the peripheral bronchi is obstructed by the pseudomembrane, which can lead to the ventilation perfusion ratio deteriorating and progression of lung damage. Patients with inhalation injury are treated with inhalation of heparin or N-acetylcysteine to prevent the formation of pseudomembranes, but the benefits and adverse effects of inhalation therapy are under discussion. Therefore, this CQ was important for this guideline.

PICO

Patient: Patient with inhalation injury
Intervention: Treated with N-acetylcysteine inhalation
Control: Treated without N-acetylcysteine inhalation
Outcome: Mortality, respiratory function improvement, complication rate of severe infection, airway bleeding

Summary of evidence (results of SR)

No RCT
No Cochrane SR

Evidence level

Level VI: Expert committee reports and opinions or clinical experience of experts

Summary of benefits

No references were used as evidence. There was no SR examining the effects of N-acetylcysteine alone on inhalation injury. An SR examining the effects of combined use of heparin and N-acetylcysteine inhalation on inhalation injury was published in 2019. This SR included six observational studies, two of which showed reduced mortality, two showed reduced lung injury score, and three reported shortening of the mechanical ventilation period in the treatment group.[1,2]

Summary of harms

No references were used as evidence. N-acetylcysteine inhalation therapy has few side effects and is considered to be safe.[3] The package insert states bronchial obstruction, bronchospasm, nausea, vomiting, stomatitis, rhinorrhea, and bloody sputum (all less than 0.1–5%) as side effects. In addition, there is one case report of drug-induced lung injury.

Balance of benefits and harms

There was no evidence for N-acetylcysteine inhalation therapy. Based on the above statements, it was determined that

the benefits of combined of N-acetylcysteine and heparin inhalation would outweigh the harms.

Cost of intervention

The price of N-acetylcysteine is approximately JPY 56 per 2 mL (1 P). In the case of the protocol used in the literature (inhalation of 3 mL of N-acetylcysteine every 4 h), the daily drug cost would be approximately 500 yen.

Feasibility

Although this may increase the workload of nurses, N-acetylcysteine inhalation is considered to be acceptable as treatment for patients with inhalation injury. N-acetylcysteine inhalation therapy is covered by insurance. It should be noted that the oral solution is used as an antidote for acetaminophen poisoning, and the initial dose is 140 mg/kg, which is different from the dose of 528.6 mg (in 3 mL) used in inhalation therapy.

Is the intervention differently evaluated by patients, family, and medical staff?

It is unlikely that the evaluation of N-acetylcysteine inhalation therapy will differ among patients, their family, and medical staff.

Recommendations in other clinical practice guidelines

The second edition of the JSBI Clinical Practice Guidelines for Management of Burn Care states that "nebulizer inhalation administration of heparin and N-acetylcysteine may be considered: Recommendation grade (C)." The ISBI Practice Guidelines for Burn Care (2016) state that N-acetylcysteine inhalation therapy for inhalation injury may be a useful option. The European Practice Guidelines for Burn Care (2017) do not provide recommendations for inhalation injury.

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CQ2–4

CQ and answer

CQ: How to carry out respiratory management for inhalation injury?

Answer: There are two opinions of airway intubation: (i) prophylactic early intubation, and (ii) intubation when symptoms of upper airway obstruction appear after careful monitoring. Currently, decisions are based on the experience of the responding medical staff and the capacity of the treating facility. There are opinions that ventilation with low tidal volume (LTV) ventilation or high-frequency percussion ventilation should be used for mechanical ventilation, but an effective respiratory therapy for inhalation injury has not been established.

Background and importance of CQ

The timing of tracheal intubation and the optimal method of ventilation for treating inhalation injury are still unclear.[1] Therefore, the CQ on respiratory management of patients with inhalation injury was answered as a BQ to introduce the current evidence.

Evidence and commentary

Regarding the timing of airway intubation in patients with inhalation injury, some reports suggest that prophylactic tracheal intubation is effective. However, in recent years, it has been suggested that inhalation injury alone is not an indication for prophylactic tracheal intubation, and that intubation should be performed when symptoms of upper airway obstruction appear after careful monitoring and successive observations using a bronchofiberscope.[2–4] As the diagnostic criteria for airway injury have not been established, the indications for tracheal intubation are not clear, and decisions are made according to the experience of the medical staff and the environment of the facility.

The ABA Practice Guidelines (2016) provide the following criteria for tracheal intubation in the event of multiple injuries.[5]

1. Decreased level of consciousness (Glasgow Coma Score of <8 points) and findings of inhalation injury (wheezing, edema).
2. Findings of inhalation injury with hypoxemia (SpO_2, <92%) or tachypnea (adhesion of soot to the airway or soot in sputum).

3. Burns that cover more than 30% TBSA and require a large volume of initial resuscitation fluids.
4. When anesthesia or sedation is required for wound care.

As a ventilatory mode, LTV ventilation, which protects the lungs by lowering the maximum airway pressure with a low ventilation volume, has been reported to reduce short-term mortality in cases of ALI or ARDS in a large RCT.[6,7] Although there are no studies on inhalation injury alone, some studies recommended ventilatory management methods for ALI and ARDS due to inhalation injury, and some have recommended LTV.[8] However, whether LTV is appropriate in cases of severe tracheal and bronchial edema due to inhalation injury or reduced thoracic compliance due to thoracic burns or general edema requires further investigation.

Although high-frequency percussive ventilation (HFPV) has been reported to improve oxygenation in the acute phase, RCTs comparing HFPV with LTV have shown no difference in ventilation duration or mortality.[9–11]

Extracorporeal membrane oxygenation (ECMO) has been introduced for severe respiratory failure due to inhalation injury and has been reported to improve survival.[12,13] There are few reports on the effectiveness and indications of ECMO for inhalation injury. Prophylactic tracheostomy for airway injury has been reported on a small scale, but its effect on improving respiratory status and survival is not clear.[14,15]

Recommendation decision process

The guideline met the adoption criteria at the first vote.

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CQ2–5

CQ and answer

CQ: How do you rehabilitate a patient with inhalation injury?

Answer: Rehabilitation includes respiratory physiotherapy, postural drainage, and early mobilization to prevent respiratory complications. However, effective rehabilitation methods have not been established.

Background and importance of CQ

The incidence of respiratory complications due to inhalation injury is high. The respiratory complications influence the

prognosis.[1,2] The purpose of respiratory rehabilitation is to improve respiratory failure caused by inhalation injury and to prevent further respiratory complications, such as pneumonia. Respiratory rehabilitation includes chest physiotherapy, postural drainage, and early mobilization, often used in combination.

The main tools of chest physiotherapy are percussion, expiratory rib cage compression, and active cycle of breathing technique (ACBT). The efficacy of these respiratory rehabilitation techniques has not yet been established, and the evidence is limited. This guideline was presented as a BQ to introduce the current evidence and clinical methods of chest physiotherapy for inhalation injury.

Evidence and explanations

For the rehabilitation of patients with inhalation injuries, the percussion method of tapping the chest wall with the palm in a cupping-like motion, the postural drainage method using gravity, and early mobilization from bed have been reported to be effective in preventing respiratory complications. In recent years, the percussion method has been reported to induce arrhythmia[3,4] and is not performed in Japan.

Expiratory rib cage compression consists of two sequential maneuvers: (i) compressing the patient's chest wall during expiration to decrease the end-expiratory reserve volume, and (ii) releasing the patient's rib cage at the beginning of inspiration to increase the end-inspiratory reserve volume. These techniques reduce dead-space ventilation, increase tidal volume, and support prompt expectoration of sputum.[5,6] The ACBT method combines deep breathing, coughing, and controlled breathing to stimulate sputum production. This technique has been introduced as an expectorant method for patients with chronic obstructive pulmonary disease and those in recovery after surgery; it has been reported to be effective in preventing pneumonia.[7]

Observational studies have shown that these respiratory physiotherapies are also effective in preventing complications of pneumonia in patients with inhalation injuries and may be applied as a technique to promote expectoration in patients with inhalation injuries.[8]

Recommendation decision process

The guideline met the criteria in the first round of voting.

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CQ3 INITIAL FLUID RESUSCITATION

FLUID RESUSCITATION IS provided to burn patients to avoid burn-induced intravascular volume depletion and consequent reduction in tissue-organ perfusion, known as burn shock. Burn shock is reported to occur in patients with burns of more than 15–20% TBSA, and fluid resuscitation has been performed in adults with burns >15% TBSA and in children with burns >10% TBSA (CQ1). The guidelines of the ABA and the International Burn Association state that fluid resuscitation should be initiated when the burn area is approximately 20% or greater (CQ1). The Parkland (Baxter) formula and the modified Brooke formula have long been used to determine the volume of fluid needed for resuscitation (CQ3–9, 10, 11). Urine output in hours has been used as an index of rate adjustment after the start of infusion (CQ3–12). Ringer's lactate solution has been used to prepare the infusion solution (CQ3–3). In 2000, Pruitt proposed the concept of "fluid creep" – excessive fluid infusion based on the Parkland formula can lead to complications such as abdominal compartment syndrome and pulmonary edema. In order to answer the CQ, "What is the optimal fluid therapy?", the use of albumin (CQ3–4), fresh frozen plasma (FFP) (CQ3–5), hydroxyethyl starch (HES)-containing products (CQ3–6), hypertonic lactate saline (HLS) (CQ3–7), high-dose ascorbic acid (CQ3–8), and hemodynamic monitoring systems (CQ3–13) has been discussed. Although a meta-analysis did not show the effectiveness of albumin administration, an RCT reported that early administration of albumin reduced the risk of fluid creep in children. An RCT showed that HES-containing products reduced the amount of fluid infusion, and another RCT

showed that HLS reduced the amount of fluid infusion. However, as HLS products are not commercially available, they must be prepared at each facility. The use of high-dose ascorbic acid has been shown to reduce the total volume of fluid infusion in an RCT, but because the dosage exceeds the limit of health insurance coverage, approval must be obtained from the Institutional Review Board (IRB) of each institution. Fluid management using hemodynamic monitoring systems has not reduced the rate of complications or improved prognosis compared with management using urine output or mean arterial pressure. As described above, the optimal method of fluid resuscitation has not yet been determined, and further investigation is required.

CQ3–1

CQ and answer

CQ: Which patients with burns need initial fluid resuscitation?

Answer:

1. For adult patients with burn area >15% TBSA and children with burn area >10% TBSA.[1]
2. When the burn area is clearly >20% TBSA.[2,3]
3. Adult patients with burn area >20% TBSA and pediatric patients with burn area >10% TBSA should be resuscitated with salt-containing fluid infusion based on weight and percentage burn.[4]

Background and importance of CQ

Although initial fluid resuscitation may affect the prognosis of burn patients, very few clinical trials have focused on the indications for initial fluid resuscitation for burns and the level of evidence is low. Nonetheless, the treatment of fluid resuscitation is well established. In this guideline, the indications for initial fluid resuscitation in burn patients were presented through BQs. The timing of fluid infusion is discussed in CQ3–2, the fluid composition is discussed in CQ3–3, and the infusion rate is discussed in CQ3–9 for adults and CQ3-10 pediatric patients.

Evidence and commentary

It is generally believed that burns greater than 15% TBSA cause systemic inflammatory response and resuscitation with intravenous fluids is necessary to avoid burn shock and subsequent death.[5,6] Traditionally, fluid infusion therapy has been used when the burn area is greater than 15% TBSA in adults and greater than 10% TBSA in children. This was shown by Baker *et al*. in their survey in the UK and Ireland.[1] In a survey of ABA participants and ISBI members, resuscitative fluid infusion was initiated in patients with 10–20% TBSA burns.[7] Resuscitation with intravenous fluids is required when the burn area is >10% TBSA in infants and children and >15% TBSA in teens and in adults.[8]

In regional guidelines, the ABA's ABLS course states that resuscitation infusion should be initiated when the burns are clearly greater than 20% TBSA at the time of prehospital care and primary survey.[2] The ISBI Practice Guideline for Burn Care states that adult patients with burns greater than 20% TBSA and pediatric patients with burns greater than 10% TBSA should be resuscitated with salt-containing infusion based on weight and burn percentage.[4] The European Practice Guidelines for Burn Care of the European Burn Association states that appropriate fluid management is important for extensive burns and that the need for resuscitation fluids is related to the depth and area of the burn.[9] The Japanese Dermatological Association's Guidelines for the Treatment of Burns states in CQ5: "We recommend infusion therapy for burn areas of 15% TBSA or more in adults and 10% TBSA or more in children. However, even if the burns are less than 15% TBSA, initial fluid resuscitation may be started depending on the general condition of the patient."[10]

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CQ3–2

CQ and answer

CQ: When should initial fluid infusion be initiated for burn patients?

Answer: There are no definitive criteria. In pediatric patients with burns, infusion started within 2 h of injury was associated with reduced rates of sepsis, renal injury, and mortality.

Background and importance of CQ

Although a delay in the initiation of fluid infusion affects the prognosis of burn patients, initial fluid infusion has traditionally been started as soon as the patient arrives at the hospital, and there have been no RCTs on the timing of initial fluid infusion. Therefore, this guideline presents the current evidence on the timing of initial fluid infusion in burn patients.

Evidence and commentary

A retrospective study of the comparison of the initiation of fluid resuscitation within 2 h of injury versus 2–12 h in pediatric burn patients showed that delayed initiation of fluid resuscitation was associated with significantly increased rates of sepsis, renal impairment, and mortality[1] in patients aged 6 months to 17 years with burns greater than 80% TBSA (third-degree burns of 70% TBSA or greater). In 103 cases of pediatric burns, a delay in the start of infusion significantly affected mortality (surviving cases: $n = 66$, 0.6 ± 0.2 h; fatal cases: $n = 34$, 2.2 ± 0.5 h).[2] Fluid resuscitation should not be delayed in patients who require initial infusion.

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CQ3–3

CQ and answer

CQ: What is used for the composition of the initial infusion?

Answer: Ringer's lactate solution is widely used, and a 5% dextrose preparation is used for maintenance infusion in children.

Background and importance of CQ

Although the composition of the initial resuscitative fluid influences the prognosis of burn patients, there is no clear evidence. Therefore, this guideline was presented as a BQ to introduce the current evidence on the composition of the initial infusion fluid used for burn patients. The combination of albumin, hypertonic lactate saline, and high-dose ascorbic acid is discussed in a separate section.

Evidence and commentary

In the widely used infusions formula for adults, Parkland (Baxter) formula[1], Modified Brooke formula[2], formula for children, Cincinnati formula[3], Galveston formula[4], Ringer's lactate solution is recommended. The ABA guidelines[5] and the ABLS course[6] state that Ringer's lactate solution should be used. The ISBI practical guideline for burn care[7] states in the FAQ section that many experts believe that Ringer's lactate solution should be used as salt-containing fluid. The European Practice Guidelines for Burn Care developed by the European Burn Association do not mention the composition of the initial fluid, but state that Ringer's lactated solution should be adjusted based on urine output.[8] The Japanese Dermatological Association's Guidelines for Burn Care recommend the use of isotonic electrolyte solutions (e.g., Ringer's lactate, Ringer's acetate) for the initial infusion.[9] Baker *et al*. reported in a survey of burn units in the UK and Ireland that Ringer's lactate solution was widely used (76% of adult burn units and 75% of pediatric burn units).[10] In a survey of ABA participants and ISBI members, Ringer's lactate solution was the most commonly used solution.[11] In children, maintenance fluid infusions are required, and the ABLS course[6] states that 5% dextrose should be used as maintenance fluid for infants and those weighing less than 30 kg. The Cincinnati formula[3] and Galveston formula[4] also state that 5% dextrose should be administered as needed. The European Burn Association guidelines state that maintenance fluids should be administered in young children due to their limited glycogen stores.[8]

The crystalloid solution is used to replenish the functional extracellular fluid volume, and although saline solution was used in the past, there is a risk of acute kidney injury and hyperchloremic metabolic acidosis, and the low-osmolarity Ringer's lactate solution is widely used.[12]However, acetic acid has a vasodilating effect, and some Japanese experts have expressed doubts about the use of Ringer's acetic acid solution for the initial infusion of burn patients.[13]

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CQ3–4

CQ and answer

CQ: Is it useful to use albumin products in the initial fluid resuscitation?

Answer: The use of an albumin product in the initial infusion in patients aged 1–12 years with burns of 15–45% TBSA is weakly recommended (level of evidence I, recommendation B).

Background and importance of CQ

In the Parkland formula[1] and the modified Brooke formula,[2] albumin is not used in the first 24 h but is administered in the following 24 h, and the Cincinnati formula[3] and the Galveston formula,[4] which are used in children, also use albumin. This is an important CQ on the efficacy of using albumin or colloidal solutions in the initial infusion.

PICO

Patient: Patients with burns
Intervention: Use of albumin products
Control: Albumin products were not used
Outcome: Survival rate, rate of respiratory failure/compartmental syndrome, total administered fluid volume

Summary of evidence (results of SR)

References used: Two RCTs

(1) Cooper AB, Cohn SM, Zhang HS *et al.*; ALBUR Investigators. Five percent albumin for adult burn shock resuscitation: Lack of effect on daily multiple organ dysfunction. Transfusion 2006; 46: 80–9.[5]

This multicenter study compared the efficacy of Ringer's lactate solution alone (n = 23) against that of a combination of 5% human albumin (Plasbumin-5) 2 mL/body weight (BW) (kg)/TBSA% and Ringer's lactate solution (n = 19) in patients aged more than 15 years with burns greater than 20% TBSA and within 12 h of injury. The resuscitation goal (mean arterial pressure >70 mmHg and urine output >0.5 mL/kg/h) recommended by the ABA was reached. The results showed that the administration of 5% albumin up to 14 days after injury did not reduce the multiple organ dysfunction score (MODS) in adult patients with burns.

(2) Müller Dittrich MH, Brunow de Carvalho W, Lopes Lavado E. Evaluation of the "early" use of albumin in children with extensive burns: a randomized controlled trial. Pediatr. Crit. Care Med. 2016; 17: e280–6.[6]

This was a single-center study comparing early (n = 23) and late (n = 23) administration of 5% albumin at 8–12 h postinjury in 1–12-year-old patients with a burn area of 15-45% TBSA within 12 h after injury. The rate of infusion was adjusted by urine output; 5% albumin was administered at a dose of 0.5 g/kg over 4 h between 8 and 12 h, once daily for 3 days. The volume of crystalloid fluid during resuscitation, fluid creep, and length of hospital stay were compared. The results showed that the amount of crystalloid required decreased in the early administration group, and the number of fluid creeps and the length of hospital stay were reduced. Fluid creep is a phenomenon reported by Pruitt in 2000, in which excessive fluid infusion exacerbates edema and causes harms such as compartment syndrome, ARDS, and multiple organ failure.[7]

Adopted literature: One Cochrane SR

Roberts I, Blackhall K, Alderson P *et al*. Human albumin solution for resuscitation and volume expansion in critically ill patients. Cochrane Database Syst. Rev. 2011; 2011: CD001208.[8]

This study analyzed the effect of albumin and human plasma protein administration prior to death in critically ill patients with decreased circulating blood volume, burns, and hypoalbuminemia. In the four burn studies (205 patients in total), the relative risk of death with albumin administration was 2.93 (95% confidence interval, 1.28–6.72).

Level of evidence

Level I: SR or meta-analysis of RCTs

Benefits

In patients aged 1–12 years with a burn area of 15–45% TBSA, early use of albumin preparations may reduce fluid volume, prevent fluid creep, and shorten hospital stay. Albumin preparations are less expensive and have a lower risk of transfer of pathogens such as hepatitis virus and ABO compatibility issues than fresh-frozen plasma; albumin preparations have no risk of transfusion-related ALI (TRALI).

Harms

As albumin is a blood product, there is a risk of viral infection. It should be noted that the use of isotonic albumin preparations in large quantities may result in sodium overload.

Balance between benefits and harms

Although no systematic review has demonstrated the efficacy of albumin administration, one RCT reported that early administration (within 12 h of injury) reduced fluid volume, fluid creep, and length of hospital stay in patients aged 1–12 years with a burn area of 15–45% TBSA. Therefore, the use of albumin products may be considered to be more beneficial than harmful, provided that the adverse drug reaction of blood products are carefully monitored.

Cost of the intervention

Albumin preparations are sold by several pharmaceutical companies in Japan.

1. Albuminar 5% intravenous injection, 12.5 g/250 mL, JPY 4,082/bottle.
2. Blood donation albumin 5% intravenous injection, 12.5 g/250 mL (Nichiyaku), JPY 4,603/bottle.
3. Blood donor albumin 5% intravenous injection, 12.5 g/250 mL (JB), JPY 4,791/bottle.

Feasibility of this intervention

The use of albumin products for patients with severe burns is covered by health insurance in Japan, and it is assumed that facilities treating burn patients who require hospitalization have enough experience in albumin product administration. Therefore, the feasibility of this intervention (administration of an isotonic albumin preparation, 5% albumin preparation) is considered to be high.

Are the interventions evaluated differently by patients, families, medical staff, and/or physicians?

It is assumed that there is little variation in the evaluations of patients, families, medical staff, physicians, and surgeons. However, there are differences in attitudes toward human blood-derived products.

Recommendations in other relevant practice guidelines

The Japanese Dermatological Association guidelines state that "the use of colloids and hypertonic lactated saline (HLS) is recommended as one of the initial fluid resuscitation options."[9] The ABA Practice Guidelines for Burn Shock Resuscitation mentions that the addition of colloid fluid 12–24 h after injury may reduce the total volume of fluid infusion required.[10]

In the ISBI Practice Guidelines for Burn Care, the expert opinion is that resuscitation of very large injuries (e.g., >70% TBSA) proceeds smoothly with the inclusion of colloids. Others believe that fluid creep (very large volumes of salt solutions that can be dangerous and sometimes lethal) is less likely to develop with colloid administration.[11]

The Guideline for the Use of Blood Products (Pharmaceutical Safety and Environmental Health Bureau, Ministry of Health, Labor and Welfare, Japan, March 2019) states that "in cases of severe burns, the superiority of colloid infusion containing albumin products for acute phase infusion against complications such as life prognosis and multiple organ damage is not clear compared with extracellular fluid replacement solutions, and it is recommended to reduce the total infusion volume, temporarily. The administration of an isotonic albumin preparation is recommended for the purpose of reducing the total fluid volume, maintaining collagen osmolarity, and suppressing the increase in intra-abdominal pressure."

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CQ3–5

CQ and answer

CQ: Is it useful to administer FFP during the initial infusion of fluids for burns?

Answer: The use of FFP is weakly recommended (level of evidence II, recommendation grade B).

Background and importance of CQ

In 2005, O'Mara *et al*.[1] reported that FFP use reduced total fluid volume and intra-abdominal pressure elevation in patients with burns. This is a CQ on the efficacy of FFP use in burns and is of great importance.

PICO

Patient: Patients with burns
Intervention: Use of FFP in the initial fluid resuscitation
Control: FFP was not used in the initial fluid resuscitation
Outcome: Survival rate, rate of respiratory failure/compartmental syndrome, total administered fluid volume

Evidence summaries (results of systematic reviews)

Referenced literature: One RCT

O'Mara MS, Slater H, Goldfarb IW *et al*. A prospective, randomized evaluation of intra-abdominal pressures with crystalloid and colloid resuscitation in burn patients. J. Trauma 2005; 58: 1011–8.[1]

Thirty-one patients aged 17 years or older with a burn area of >40% TBSA or with a burn area of >25% TBSA and airway injury were randomized to receive FFP or crystalloid solution. The FFP-treated patients received 2,000 mL Ringer's lactate solution and 75 mL/kg FFP over 24 h to achieve a urine output of 0.5–1.0 mL/kg/h. The crystalloid group was treated with Ringer's lactate solution to achieve a urine output of 0.5–1.0 mL/kg/h. Intra-abdominal pressure was measured by intravesical pressure. Bladder pressure was measured as intra-abdominal pressure. The FFP group required 0.14 L/kg of fluid, whereas the crystalloid group required 0.26 L/kg (P = 0.005). The intra-abdominal pressure increased to 32.5 ± 9.5 mmHg in the crystalloid group, whereas it was 16.4 ± 7.4 mmHg in the FFP group. There was a correlation between the volume of fluid infusion and intra-abdominal pressure in both groups.

Adopted literature (Cochrane SR): None

Level of evidence

Level II: One or more RCTs

Benefits

The administration of FFP is expected to decrease the total volume of fluid infusion and reduce the risk of complications due to fluid creep.

Harms

In the Guidelines for the Use of Blood Products (Pharmaceutical Safety and Environmental Health Bureau, Ministry of Health, Labor and Welfare, Japan, March 2019), it is stated that "Compared with plasma-fractionated products, fresh-frozen plasma has a risk of transmitting transfusion-

transmitted infections because it has not been inactivated against infectious pathogens, and the plasma protein concentration is diluted by the blood preservation solution." The guidelines also state that "Traditionally, fresh frozen plasma has been used alone or in combination with erythrocyte solution to replenish circulating plasma volume. However, safer extracellular fluid replacement solutions (e.g., Ringer's solution – lactate/acetate), artificial collagen solutions (e.g., HES, dextran), or isotonic albumin preparations are recommended for this purpose." Other known harms of blood transfusion include citrate poisoning (hypocalcemia), transfusion-related circulatory overload, sodium overload, anaphylactic reactions, blood group incompatibility, and TRALI. Transfusion-related ALI is known to occur in the course of resuscitation by transfusion.

Balance between benefits and harms

The reduction of total fluid volume by administration of FFP may reduce the risk of fluid creep. However, as FFP is not allowed to be administered as a collagen solution in Japan, the harm (burden) of using FFP may outweigh the benefit.

Cost of intervention

The trade names and drug prices of FFP are as follows.
Fresh frozen plasma-LR (JRC) 120, JPY 9,160
Fresh frozen plasma-LR (JRC) 240, JPY 18,322
Fresh frozen plasma-LR (JRC) 480, JPY 24,210

Feasibility of this intervention

The Guidelines for the Use of Blood Products state that the administration of FFP is "primarily intended for therapeutic administration by simultaneous replacement of multiple deficient coagulation factors" and does not allow administration as a colloid solution, making this intervention less feasible than other options.

Are the interventions evaluated differently by patients, families, medical staff, and/or physicians?

It is assumed that there is little variation in the values of patients, families, medical staff, and physicians. However, there are differences in attitudes toward human blood-derived products (blood transfusions).

Recommendation decision process

The recommendation was adopted in the second vote.

Recommendations in other relevant practice guidelines

The Japanese Dermatological Association's Guidelines for the Treatment of Burns states that "the use of colloids and hypertonic lactated saline (HLS) is recommended as one of the initial fluid resuscitation options."[2] The ABA Practice Guidelines for Burn Shock Resuscitation states that the addition of colloid fluid 12–24 h after injury may reduce the total volume of fluid infusion.[3]

In the ISBI Practice Guidelines for Burn Care, the expert opinion in the Q&A section is that several burn experts believe that resuscitation of very large injuries (e.g., >70% TBSA) proceeds smoothly with the inclusion of colloids. Others believe that fluid creep (very large volumes of salt solutions that can be dangerous and sometimes lethal) is less likely to develop with colloid administration.[4] There is no statement on this in the European Burn Association guidelines.

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CQ3–6

CQ and answer

CQ: Should a preparation containing HES be administered for fluid resuscitation?

Answer: It is suggested that a part of the crystalloids used for fluid resuscitation be replaced with a preparation containing HES (evidence level II, recommendation level B).

Background of CQ

The amount of fluid resuscitation for severe burns is calculated using the Parkland (Baxter) formula and has been performed with crystalloids such as Ringer's lactate. As a result of adjusting the infusion volume using the urine volume as

an index, a larger infusion volume than the initially predicted infusion volume may be required, causing abdominal compartment syndrome and pulmonary edema, known as "fluid creep." Substitution with colloids is being investigated as a means of reducing total fluid volume and infusion-related complications. This is a CQ regarding the efficacy of an artificially adjustable 6% HES-containing colloids preparation.

PICO

Patient: Patients with burns
Intervention: Administration of HES-containing products
Control: No use of HES-containing products
Outcome: Total administered fluid volume, survival rate

Summary of evidence (results of SR)

References used: Two RCTs

(1) Vachou E, Gosling P, Moiemen NS. Hydroxyethylstarch supplementation in burn resuscitation – a prospective randomized controlled trial. Burns 2010; 36: 984–91.[1]

Twenty-six patients with burns of 15% TBSA or higher were randomly assigned to receive all initial fluids as crystalline fluid (Hartmann's fluid) or replace one-third of the predicted fluid volume with 6% HES. The fluid volume required in the first 24 h was 307 mL versus 263 mL, respectively, which was significantly lower in the HES group ($P = 0.0234$). In addition, the HES group gained less weight at 24 h (2.5 kg versus 1.4 kg, $P = 0.0039$), C-reactive protein (CRP) level at 48 h was low (21.0 mg/dL versus 12.8 mg/dL, $P = 0.0001$), and the albumin-creatinine ratio, which is an index of capillary leak at 12 h, was low ($P = 0.0310$). There were no significant differences in serum creatinine levels or mean hourly urine volume 24 h after injury, and no renal damage was observed as an adverse event. We conclude that replacing one-third of the predicted fluid volume with HES reduces the total fluid volume, reduces interstitial edema, and suppresses the inflammatory response.

(2) Béchir M, Puhan MA, Fasshauer M *et al*. Early fluid resuscitation with hydroxyethyl starch 130/0.4 (6%) in severe burn injury: A randomized, controlled, double-blind clinical trial. Crit. Care 2013; 17: R299.[2]

Forty-eight burn patients with 15% TBSA or higher were given a double-blind, randomized infusion up to 72 h after injury, and divided into a Ringer's lactate solution plus 6% HES 130/0.4 in a ratio of 2:1 group, and a Ringer's lactate solution only group. There was no significant difference in the total fluid volume for 3 days ($P = 0.39$), and there was no significant difference in creatinine level ($P = 0.97$) or urine volume ($P = 0.90$), ARDS incidence ($P = 0.95$), ICU length of stay ($P = 0.80$), length of hospital stay ($P = 0.57$), 28-day survival ($P = 0.95$), or in-hospital mortality ($P = 0.31$). We conclude that there is no benefit of adding 6% HES to the initial fluid for burns.

Literature references: No SR

Level of evidence

Level II: More than one RCT

Benefits

By substituting a part of the initial infusion solution for burns with a preparation containing 6% HES, it is possible to reduce the total infusion volume, weight gain, and inflammatory reaction.

Harms

There were no adverse events that required special attention with regard to the crystalline liquid alone. Kidney injuries were not reported in the referenced literature.

Balance between benefits and harms

If it reduces total fluid volume and does not affect mortality or complication rates, the benefit may outweigh the harm.

Cost of the intervention

Voluven 6% solution for infusion, JPY 936/500 mL
Salinhes fluid solution 6%, JPY 752/500 mL
Hespander fluid solution, JPY 746/500 mL

Feasibility of this intervention

The 6% HES-containing preparation is used in many facilities, and it is easy and feasible to replace a part of the crystalloids with it.

Is the intervention differently evaluated by the patients, families, medical staff, and/or physicians?

It is assumed that there is little variation in the values of patients, families, medical staff, or physicians.

Recommendation decision process

The guideline met the stipulated adoption criteria at the first vote.

Recommendations in other relevant clinical practice guidelines

The Japanese Dermatological Association's Burn Treatment Guidelines (2017 edition) mentions colloids (albumin preparation) but does not mention the 6% HES preparation. The ABA Practice Guidelines state that the addition of colloids may reduce the total fluid volume, especially 12–24 h after injury.[3] The ISBI Practice Guidelines for Burn Care (2016) states that no conclusions have been reached regarding the use of colloids.[4] The European Practice Guidelines for Burn Care (2017) states that colloids should not be administered within 8 h after injury.[5]

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CQ3–7

CQ and answer

CQ: Is it useful to administer HLS as an initial infusion?

Answer: The use of HLS as the initial fluid is weakly recommended (level of evidence I, recommendation B).

Background and importance of CQ

The use of HLS to improve the circulating blood volume was reported by Monafo in 1970.[1] In a 2004 Cochrane SR, the use of HLS was associated with a relative risk of death of 1.49 (95% confidence interval, 0.56–3.95) in burn patients.[2] The authors stated that they did not have sufficient data to say that hypertonic crystalloid was superior to isotonic crystalloid, but the confidence interval was wide enough to rule out a clinically significant difference. Subsequently, in 2009, Belba *et al*. reported a reduction in the amount of fluid and cumulative infusion required in the first 24 h.[3] This was an important CQ on the effectiveness of the use of HLS in the initial infusion of fluids in burn patients.

PICO

Patient: Patient with burns
Intervention: Administer HLS
Control: No HLS administered
Outcome: Survival rate, rate of respiratory failure/compartmental syndrome, total fluid volume

Evidence (results of SR)

Adopted literature: One RCT

Belba MK, Petrela EY, Belba GP. Comparison of hypertonic versus isotonic fluids during resuscitation of severely burned patients. Am. J. Emerg. Med. 2009; 27: 1091–96.[3]

Fifty-five adult patients with burns greater than 20% TBSA or pediatric patients with burns greater 15% TBSA admitted to the ICU within 24 h of injury were randomly assigned to receive HLS or not. The HLS group received HLS containing 250 mEq/L sodium and 120 mEq/L lactate at a dose of 0.5mL/kg/%TBSA in the first hour that was adjusted for urine output of 0.5–1 mL/kg/h in subsequent hours. Ringer's lactate solution was used in the nontreated group and was administered according to the Parkland formula for adults and the Shriner formula for pediatric patients. The results showed that HLS administration resulted in more fluid ($P = 0.001$) and sodium loading ($P = 0.0025$) in the first hour after injury and reduced plasma sodium ($P = 0.003$), plasma osmolality ($P = 0.002$), and amount of fluid required and total fluid infusion in the first 24 h of burn shock. The authors also reported that the amount of sodium administered ($P = 0.001$) and excreted in urine ($P = 0.001$) was higher in the HLS group.

Adopted literature: Cochrane SR

Bunn F, Roberts I, Tasker R *et al*. Hypertonic versus near isotonic crystalloid for fluid resuscitation in critically ill patients. Cochrane Database Syst Rev 2008; 2008: CD002045.[2]

The use of HLS had a relative risk of death of 1.49 (95% confidence interval, 0.56–3.95) in burn patients. In all, 14 trials analyzed the use of HLS, and burn patients were included in three of them ($n = 72$; Bortolani 1996; Caldwell 1979; Jelenko 1978). They also noted that all of the adopted

trials were conducted more than 20 years ago and that treatment protocols may be different from those used currently.

Level of evidence

Level I: SRs or meta-analyses of RCTs

Benefits

In one RCT,[3] HLS administration reduced total fluid volume.

Harms

The Cochrane SR showed a relative risk of death of 1.49, although the confidence interval was large (adverse effect). There is no commercially available formulation of HLS, so it needs to be prepared at each institution (burden).

Balance of benefits and harms

The harm exceeds the benefit.

Cost of this intervention

Currently, HLS products are not commercially available.

Feasibility of this intervention

It is assumed that there are barriers to the preparation and administration of the HLS unless the facility has experience, and the feasibility is low.

Are the interventions evaluated differently by patients, families, medical staff, and/or physicians?

It is presumed that the HLS needs to be formulated at each facility, and this intervention may cause variation in the values held by health-care providers.

Decision process

The guideline met the stipulated adoption criteria at the first vote.

Recommendations in other relevant practice guidelines

The Japanese Dermatological Association guidelines for burn care recommend HLS as one of the initial fluid resuscitation options.[4] The ABA guidelines state that it should only be used by experienced clinicians under strict blood sodium concentration monitoring.[5] There is no statement in the ISBI or European Burn Association guidelines.

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CQ3–8

CQ and answer

CQ: Should high-dose ascorbic acid (vitamin C) be administered with the initial fluid?

Answer: Administration of high-dose ascorbic acid in combination with the initial fluid weakly recommended (level of evidence II, grade of recommendation B) (*).

Background and importance of CQ

Ascorbic acid has been studied because it has antioxidant effects and is expected to reduce lipid peroxidation reactions and increased vascular permeability that can be caused by the free radicals generated by the burns.

In 1997, Mann *et al.*[1] reported that there was no difference in fluid balance at 72 h between patients with greater than 30% TBSA burns treated with ascorbic acid at 1 g/h and those treated with saline. In 2000, Tanaka *et al.*[2] compared 37 patients with thermal burns with greater than 30% TBSA within 2 h of injury using a control group treated with Ringer's lactate solution based on the Parkland formula to maintain circulatory dynamics and urine output of 0.5–1.0 mL/kg/h and a treatment group treated with high-dose ascorbic acid (66 mg/kg/h) during the first 24 h. In 2011, Kahn *et al.*[3] reported in a retrospective study that the ascorbic

acid group (66 mg/kg/h) had lower fluid requirements and higher urine output in the first 24 h. This was an important CQ on the efficacy of the combination of high-dose ascorbic acid in the initial fluid resuscitation in burn patients.

PICO

Patient: Initial fluid resuscitation of burn patients
Intervention: Concomitant administration of high-dose ascorbic acid (66 mg/kg/h)
Control: No administration of high-dose ascorbic acid
Outcome: Survival, rate of respiratory failure/compartment syndrome, total fluid volume

Summary of evidence (results of SRs)

References used: One RCT

Tanaka H, Matsuda T, Miyagantani Y *et al*. Reduction of resuscitation fluid volumes in severely burned patients using ascorbic acid administration. A randomized, prospective study. Arch. Surg. 2000; 135: 326–31.[2]

Thirty-seven patients with burns greater than 30% TBSA who were hospitalized within 2 h of injury were randomly assigned to receive ascorbic acid (66 mg/kg/h for the first 24 h) or not. In both groups, Ringer's lactate solution was used as the initial fluid to maintain circulatory balance and urine output (0.5–1.0 mL/kg/h). The results showed that the volume of fluid infusion and the burned tissue water content were lower in the ascorbic acid group during the first 24 h ($P < 0.01$). The P/F ratios at 18, 24, 36, and 48 h after injury were significantly lower in the control group ($P < 0.01$). Serum malondialdehyde (antioxidant stress marker) levels at 18, 24, and 36 h after injury were lower in the ascorbic acid group ($P < 0.05$). The length of mechanical ventilation was shorter in the ascorbic acid group ($P < 0.05$).

Adopted literature: No Cochrane SR

Level of evidence

Level II: One or more RCTs

Benefits

The total volume of fluid infusion may decrease, and the risk of complications such as duration of ventilation and wound edema may be reduced.

Harms

No harm such as acute kidney injury was reported in the above two clinical studies.[2,3] However, because treatment with high-dose administration is not covered by health insurance, it must be approved by the IRB of each institution, which may be a burden.

Balance of benefits and harms

It is thought that the benefits outweigh the harms.

Cost of the intervention

Ascorbic acid injection is available in a number of generic forms, including 100 mg, 500 mg, 1,000 mg, and 2,000 mg, and most pharmaceutical companies charge 84 yen per tube for any volume.

Feasibility of this intervention

The use of ascorbic acid injection is not covered by health insurance for burns.

Are the interventions evaluated differently by patients, families, medical staff, and physicians?

Although vitamin C is a well-known nutrient, its use for burn treatment is not covered by health insurance, and it is likely that the attitudes toward vitamin C administration for burn treatment of health-care providers are different.

Decision process

The guideline met the stipulated adoption criteria at the first vote.

Recommendations in other relevant practice guidelines

There is no statement on this topic in the guidelines of the Japanese Dermatological Association, the ISBI, or the European Burn Association. The ABA guideline states that "administration of high-dose ascorbic acid may decrease the overall fluid requirements, and is worthy of further study."[4]

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CQ3–9

CQ and answer

CQ: How do you set the initial infusion rate for an adult burn patient?

Answer: The appropriate initial infusion rate has not been established. The Parkland formula, modified Brooke formula, and the method of the ABLS are commonly used (see Table 1).

Background and importance of CQ

Initial fluid management affects the respiratory and circulatory dynamics, risk of tissue edema, and organ damage in burn patients, but the rate of initial infusion remains controversial. Therefore, this guideline was presented as a BQ to introduce the current reports on the initial infusion rate in adult burn patients.

Evidence and commentary

The Parkland (Baxter and Shires) formula[1] reported by Baxter and Shires in 1968, which calculates the total fluid infusion for first 24 h as 4 mL/kg/% TBSA burn, is now widely known. However, in some cases, more fluid than that specified by the Parkland (Baxter) formula is administered, and complications such as abdominal compartment syndrome and pulmonary edema have been observed due to excessive fluid infusion, which is called "fluid creep."[2–4]

An increase in fluid volume has been observed in cases of inhalation injury, electrical injury, or delayed initial infusion;[3] recently, an increase in the use of narcotics ("opioid creep") has been observed, which could be one of the causes of excessive fluid in patients who are on narcotics at the time of admission.[3,5] Because excessive fluid infusion can induce abdominal and limb compartment syndrome,[3,6,7] cause organ damage,[7,8] and worsen the prognosis, previous studies examined the appropriate amount of initial fluid, but there is no high-level evidence. In order to avoid excessive fluid infusion, the ABLS proposes an initial fluid infusion therapy with a total fluid volume of 2 mL/kg/%TBSA burn for 24 h based on the modified Brooke formula, and infusion therapy at 500 mL/h before the calculation of the initial infusion volume is needed to avoid harm caused by a delay in the start of initial infusion.[8] However, the response to infusion varies greatly among individuals, no matter which guidelines are followed, and although indices for adjusting the infusion volume are being studied, the infusion volume is generally adjusted based on circulatory dynamics and urine output.[9] The details are described in another section (CQ3–12).

Recommendation determination process

The guideline met the criteria for adoption as specified at the first vote.

Table 1. Initial infusion methods for adult burn patients (initial 24 h infusion)

Formula	Method
Parkland (Baxter)	Total fluid infusion of Ringer's lactate solution for first 24 h at 4 mL/kg/% TBSA burn, with half of the total dose given in the first 8 h and the remainder in the next 16 h
Modified Brooke	Total fluid infusion of Ringer's lactate solution for first 24 h at 2 mL/kg/% TBSA burn, with half of the total dose given in the first 8 h and the remainder in the next 16 h
Evans	Saline at 1 mL/kg/% burn + colloid at 1 mL/kg/% burn + 5% glucose solution at 2,000 mL
Brooke	Saline at 1.5 mL/kg/% burn + colloid at 0.5 mL/kg/% burn + 5% glucose solution at 2,000 mL
ABLS	Initial infusion rate before calculation of burn area: 500 mL/h After calculation of burn area: half of Ringer's at 2 mL/kg/% burn (4 mL/kg/%burn for high-voltage electrical injury) should be administered in the first 8 h, and the other half should be administered in the next 16 h. However, if the hourly urine output is greater/less than the target urine output (0.5 mL/kg/h, 1 mL/kg/h for high-voltage electrical injuries) for 2 consecutive hours, the infusion rate should be reduced/increased, respectively, by one-third

ABLS, Advanced Burn Life Support; TBSA, total body surface area.

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CQ3–10

CQ and answer

CQ: How do you set initial infusion rate for a pediatric burn patient?

Answer: The appropriate initial infusion rate for children has not been established. The rate of infusion is usually higher per body weight and burn area than that used for adults, and the initial infusion is administered based on the Cincinnati formula,[1] the Galveston formula,[1] and ABLS formula,[2] which are based on the Parkland (Baxter) formula[2] (see Table 2).

Background and importance of CQ

Initial fluid management influences the respiratory and circulatory dynamics of burn patients and the development of tissue edema and organ damage, but the rate of infusion remains controversial. Therefore, this guideline was presented as a BQ to introduce current data on the rate of initial fluid infusion in pediatric burn patients.

Table 2. Initial infusion methods for child burn patients (initial 24-h infusion)

Formula	Method
Cincinnati formula[1]	Older children: Ringer's lactate solution at 4 mL/kg/%TBSA burn + 1,500 mL/m^2 BSA. Half the dose should be administered for the first 8 h, and the other half for the next 16 h. Younger children: Ringer's lactate solution at 4 mL/kg/%TBSA burn + 1,500 mL/m^2 BSA. In the first 8 h, half of the dose should be administered with 50 mEq/L of sodium bicarbonate; in the next 8 h, one-fourth dose should be administered, and in the last 8 h, the next fourth dose should be administered with 5% albumin.
Galveston formula[1]	Ringer's lactate solution at 5,000 mL/m^2 BSA burn (resuscitation infusion) + 2,000 mL/m^2 (maintenance infusion) to be administered. Half dose should be administered for the first 8 h, and the other half for the next 16 h. Administer 5% albumin and 5% dextrose as needed
ABLS[2]	Initial infusion rate before calculation of burn area: 5 years or younger: 125 mL/h, 6–13 years old: 250 mL/h, 14 years old or older: 500 mL/h. After calculation of burn area: 3 mL/kg/%TBSA burn for 13 years or younger, 4 mL/kg/%TBSA burn for electrical injury; half dose in the first 8 h, the other half in the next 16 h. After the start, the infusion rate is adjusted hourly so that the hourly urine output is 1 mL/kg for children weighing <30 kg and 0.5 mL/kg for children weighing >30 kg. Infants and children weighing <30 kg: Administered maintenance fluid containing 5% dextrose. The infusion dose is 4 mL/kg/h for the first 10 kg of body weight, 2 mL/kg/h for the next 10 kg of body weight, and 1 mL/kg/h for the remaining body weight

ABLS, Advanced Burn Life Support; BSA, body surface area; TBSA, total body surface area.

Evidence and commentary

There are no clear evidence-based guidelines on the appropriate initial fluid volume for children. Although it is necessary to avoid excessive fluid infusion while maintaining circulatory dynamics and tissue return, it has been reported that the volume of fluid infused per body weight and burn area[3] and that the target urine volume, which is used as an index for adjusting the amount of infusion,[2] is higher than that in adults.

In infants and children, the glycogen stores are low and they are prone to hypoglycemia, so some formulas include maintenance infusion with dextrose in the predicted fluid requirements. However, the Cincinnati formula and the Galveston formula are currently used as so-called "two figure formulas," which consider the need for resuscitation infusions in addition to maintenance infusions; there are no studies comparing the superiority of the two formulas.[4] Both formulas include albumin administration. On the other hand, the ABLS formula is also considered to be based on the two-figure formula, but it does not include albumin.

In the Cincinnati formula,[1] older children receive Ringer's lactate solution at 4 mL/kg/%TBSA burn + 1,500 mL/m^2 body surface area Body surface area (BSA) over 24 h, with half of the total dose given in the first 8 h and the remainder in the next 16 h. Younger children also receive a Ringer's lactate solution at 4 mL/kg/%TBSA burn + 1,500 mL/m^2 BSA in the first 24 h, but half of the total volume is given in the first 8 h, with 50 mEq sodium bicarbonate per liter of Ringer's lactate solution. In the next 8 h, quarter of the total volume of Ringer's lactate solution alone and in the last 8 h, quarter of the total volume of Ringer's lactate solution with 5% albumin is administered. In the Galveston formula,[1] the total volume of Ringer's lactate solution at 5,000 mL/m^2 BSA burn as a resuscitation infusion and 2,000 mL/m^2 BSA burn as a maintenance infusion is administered. Half of the total dose is administered in the first 8 h, and the rest in the next 16 h, 5% albumin and 5% dextrose are added if needed.

In the ABLS formula,[2] if infusion is considered to be necessary (see CQ3–1), Ringer's lactate solution should be administered before the burn area is calculated at a rate of 125 mL/h for patients aged 5 years or younger, 250 mL/h for patients aged 6–13 years, and 500 mL/h for patients aged 14 years or older. After calculating the patient's weight and burn area, the expected 24-h infusion requirement of 3 mL/kg/%TBSA burn is administered to patients under 13 years of age and 4 mL/kg/%TBSA burn, to patients with electrical injuries; half of the infusion is administered in the first 8 h, and the other half in the next 16 h. After the initial infusion, the infusion rate should be adjusted hourly to achieve a urine output of 1 mL/kg for children who weigh less than 30 kg and 0.5 mL/kg for children who weigh more than 30 kg. In addition to these infusion rates, infants and children weighing less than 30 kg should receive a maintenance infusion containing 5% dextrose. The maintenance infusion rate is based on the so-called "4-2-1 formula": 4 mL/kg/h for the first 10 kg of body weight, 2 mL/kg/h for the next 10 kg of body weight, and 1 mL/kg/h for the remainder of the body weight. The rate of this maintenance infusion is not adjusted according to urine output.

Recommendation determination process

The first ballot met the specified criteria for adoption.

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CQ3–11

CQ and answer

CQ: What is the initial infusion rate in patients with inhalation injury or electrical injury?

Answer: No conclusions has been obtained about the initial infusion rate in the patients with inhalation injury or electrical injury. The infusion should be started with the Parkland (Baxter) or ABLS formula, but more infusions are required subsequently.

Background and importance of CQ

Initial infusion in patients with inhalation injury requires more fluid volume than in patients without inhalation injury; there is no quantitative method for determining the rate of initial fluid infusion in patients with inhalation injury. We presented this CQ as a BQ on the initial infusion rate in patients with airway injury.

Reports and commentary

In 1985, Navar *et al*.[1] retrospectively reviewed 171 burn patients and reported that the volume of fluid infusion in patients with inhalation injury was 5.76 mL/kg/% burn at 24 h, which was significantly higher than 3.98 mL/kg/% burn in patients without inhalation injury. In 1998, Dai *et al*. retrospectively reviewed 62 patients and reported that the initial fluid volume at 24 h was 3.1 and 2.3 mL/kg/% burn in patients with and without inhalation injury, respectively.[2] In a retrospective study of 131 patients, Inoue *et al*.,[3] in 2002, reported that the volume of fluid infusion increased by approximately 30 mL/kg at 24 h in patients with inhalation injury.

Patients with electrical injury require a large amount of infusion due to deep tissue damage and for renal protection compared to patients without electrical injury.[4] In 1982, Holliman *et al*.[5] reported in a retrospective study that, on average, 12 mL/kg/%TBSA burn was required in the first 24 h. The ABLS states that in the case of electrical injuries, half of 4 mL/kg/%TBSA burn should be administered in the first 8 h, and the other half in the next 16 h, and if the hourly urine output is higher or lower than the target urine output for 2 consecutive hours, the infusion rate should be decreased or increased, respectively, by one-third.[6]

At present, it is difficult to quantify the severity of inhalation injury and electrical injury, and the effect of these injuries on fluid requirements is unclear, but it is commonly reported that inhalation injury and electrical injury increase the initial fluid requirement.

Recommendation determination process

The guideline met the specified criteria for adoption at the first vote.

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CQ3–12

CQ and answer

CQ: Are there any indicators to determine if the initial infusion rate is appropriate?

Answer: There are no established indicators of the appropriate rate of initial infusion. Respiratory and circulatory monitoring and hourly urine output have been used.

Background and importance of CQ

The appropriate initial infusion rate is still under discussion and many methods have been investigated, but no conclusions have been made. Therefore, this guideline is presented as a BQ to introduce the current reports on the appropriate infusion rate index.

Evidence and commentary

Even if infusion is performed according to the commonly proposed method, it must be adjusted and the index of adjustment must be studied. Respiratory and circulatory monitoring and hourly urine output have been traditionally used, but it has been reported that it is not appropriate to use only hourly urine output.[1] It has been reported that blood lactate and invasive monitoring can be used as indicators to prevent excessive fluid infusion,[2] but the efficacy of lactate alone as an indicator in burn treatment has not yet been demonstrated (see CQ3–13). Although many studies have been conducted, the volume of fluid infusion is generally adjusted according to circulatory dynamics and urine output.[3] It is desirable to adjust the hourly urine output to 0.5 mL/kg or higher in adults and 1.0 mL/kg or higher in children,[4] but there is no high-level evidence on the appropriate value. When myoglobinuria or hemoglobinuria occur, the hourly urine output should be doubled until the color tone improves visually to avoid acute kidney injury.

Recommendation of this determination process

The guideline met the specified criteria for adoption at the first ballot.

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3 Paratz JD, Stockton K, Paratz ED *et al*. Burn resuscitation-hourly urine output versus alternative endpoints: a systematic review. Shock 2014; 42: 295–306.
4 American Burn Association. Advanced Burn Life Support Course Provider Manual 2018 Update. Chicago, IL: American Burn Association, 2018.

CQ3–13

CQ and answer

CQ: Is the transpulmonary thermodilution technique (TPTD) or arterial pulse contour analysis useful as an index of infusion rate in the initial infusion of burn patients?

Answer: TPTD or arterial pulse contour analysis can be used as an indicator of fluid rate in the initial resuscitation of burn patients with a TBSA of approximately 10% or more (evidence level II, recommendation level B).

Background and importance of CQ

The infusion rate of initial fluid therapy for widespread burns has traditionally been calculated using the Parkland (Baxter) formula,[1] and hourly urine volume has been used as an index to adjust the infusion rate after the start of infusion.[2] In recent years, TPTD using a central venous catheter and a dedicated arterial catheter has made it possible to easily measure the intrathoracic blood volume index (ITBVI) and the extrapulmonary water content. In addition, by analyzing the waveform obtained by invasive arterial pressure measurement, it has become possible to monitor indexes such as pulse pressure variation and stroke volume variation. This is a CQ on the usefulness of adjusting the infusion rate using the data obtained from these indices. It is considered that these new technologies are widely applied in daily clinical practice in Japan and are used for patient assessment together with classical indicators. This CQ presented new evidence on this aspect.

PICO

Patient: Burn patient requiring initial infusion
Intervention: TPTD or arterial pressure waveform analysis is used
Control: TPTD or arterial pressure waveform analysis is not used
Outcome: Survival rate, respiratory failure/compartment syndrome complication rate, total fluid volume

Summary of evidence (results of SR)

References used: Two RCTs

(1) Csontos C, Foldi V, Fischer T *et al*. Arterial thermodilution in burn patients suggests a more rapid fluid administration during early resuscitation. Acta Anaesthesiol. Scand. 2008; 52: 742–9.[3]

Initial fluid therapy was initiated for 24 burn patients with >15% TBSA within 3 h of injury according to the Parkland (Baxter) formula. These patients were randomly assigned to two groups, defined by the metric used to determine infusion rate: hourly urine volume (10% increase in fluid rate if less than 0.5 mL/kg/h, 10% decrease if 1.0 mL/kg/h or more) or ITBVI (if <750 mL/m^2). Five hundred mL of Ringer's lactate bolus was administered (if 750–800 mL/m^2, the infusion rate is increased by 10%, and if 850 mL/m^2 or more, the dose is decreased by 10%). MODS and central venous oxygen saturation ($ScvO_2$) were compared between these groups until 3 days after the injury. In the group using ITBVI as an index, the $ScvO_2$ was significantly higher on day 1 ($P = 0.024$), and the MODS was significantly lower on days 2 and 3 ($P = 0.024$, $P = 0.014$). There was no significant difference in survival rate. This suggests the advantage of adjusting the infusion rate using ITBVI as an index.

(2) Tokarik M, Sjöberg F, Balik M *et al*. Fluid therapy LiDCO controlled trial – optimization of volume resuscitation of extensively burned patients through noninvasive continuous real-time hemodynamic monitoring LiDCO. J. Burn Care Res. 2013; 34: 537–42.[4]

In one study using initial fluid therapy calculated as per the Parkland (Baxter) formula, the patients was randomly assigned to the nontreatment group controlled by hourly urine volume and mean arterial blood pressure and to the treatment group managed by arterial pressure waveform analysis. This study compared the total infusion volume up to 24 h after the injury. The total infused fluid volume was significantly reduced by 10% in the group managed by arterial pressure waveform analysis, and the urine volume was similar in both groups. This suggests the value of regulating infusion volume by arterial pressure waveform analysis.

Level of evidence

Level II: One or more RCTs

Benefits

Adjusting the administration rate of initial fluid therapy using TPTD or arterial pressure waveform analysis as an index may stabilize the hemodynamics, suppress the onset of organ damage, and reduce the total fluid volume. However, there is no evidence that it contributes to improved survival.

Harms

A dedicated catheter insertion procedure is required, and there is a risk of catheter-related bloodstream infection.

Balance between benefits and harms

Initial fluid therapy using TPTD and arterial pressure waveform analysis are equivalent to or greater than the Parkland (Baxter) formula and infusion volume regulation by hourly urine volume and average blood pressure, and the benefits are considered to outweigh the harms.

Cost of the intervention

There are costs associated with various catheters and monitoring equipment. The points required for central venous catheter insertion (1,400 points) and open arterial pressure measurement (260 points/day) can be calculated.

Feasibility of this intervention

Transpulmonary thermodilution technique and arterial pressure waveform analysis are widely applied in intensive care target diseases such as sepsis and are considered to be feasible as long as there is no burn at the catheter insertion site.

Is the intervention differently evaluated by the patients, families, medical staff, and/or physicians?

It is assumed that there is little variation in the evaluations of patients, families, medical staff, and physicians.

Recommendation of decision process

The guideline met the stipulated adoption criteria at the first vote.

Recommendations in other relevant clinical practice guidelines

There is no mention in the guidelines of the Japanese Dermatological Association. The ABA Practice Guidelines (2016) do not recommend preload-enhancing treatment strategies, but invasive monitoring should be used for older patients and patients who do not respond adequately to standard treatment.[5] There is no mention in the ISBI Practice Guidelines for Burn Care (2016) or the European Practice Guidelines for Burn Care (2017).

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1 Baxter CR, Shires T. Physiological response to crystalloid resuscitation of severe burns. Ann. N. Y. Acad. Sci. 1968; 150: 874–94.
2 American Burn Association. Advanced Burn Life Support Course PROVIDER MANUAL 2018 UPDATE. Chicago, IL: American Burn Association, 2018.
3 Csontos C, Foldi V, Fischer T, Bogar L. Arterial thermodilution in burn patients suggests a more rapid fluid administration during early resuscitation. Acta Anaesthesiol. Scand. 2008; 52: 742–9.
4 Tokarik M, Sjöberg F, Balik M, Pafcuga I, Broz L. Fluid therapy LiDCO controlled trial-optimization of volume resuscitation of extensively burned patients through noninvasive continuous real-time hemodynamic monitoring LiDCO. J. Burn Care Res. 2013; 34: 537–42.
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CQ4 INITIAL TOPICAL TREATMENT

TOPICAL TREATMENT IS a critical and full-length management and operation modality in burn injury treatment. The methods are applied for wide-ranging depths of burn injury and the purpose is to manage infections and facilitate the acceleration of wound recovery. Therefore, we decided to establish the CQ setting with a focus on the depth of the burn injury. The previous edition considered external medicine and wound dressing for burns; however, this edition converted the contents into CQs. The guideline focuses on inpatients, but includes CQs for outpatients because topical treatment is considered the foundation of the burn injury treatment. In particular, the aspects such as the use of steroid, disinfectant, and base material for external medicine have been explored in this new attempt. In addition, we examined CQs on polyhexanide/betaine gel, which was

newly approved by the Japanese government after the second edition. We also established CQs for silver sulfadiazine (SSD), which has been used popularly for third-degree burn injury. Furthermore, we addressed CQs related to the limited range of dermal burns (DB) in outpatients.

Topical treatment is a mix of traditional and new treatments for burn injuries. The Guidelines use data from Japanese research because of the difference in approved materials for wound dressing and external medicine between Japan and other countries.

CQ4–1

CQ and answer

CQ: Are topical steroids effective in treating epidermal burns (EB) and second-degree DB within 1 week of injury?

Answer: There is a lack of evidence to support the efficacy of topical steroids, and some argue that they should not be used casually. However, there are opinions that recommend their use at signs of local inflammation. When specialists use steroids for their anti-inflammatory effects, it is advisable to use them in the early stage of injury (approximately 2 days) while paying close attention to the side effects of steroids.

Background and importance of CQ

Topical steroids with anti-inflammatory effects have been used for EB (e.g., sunburns) and superficial dermal burn (SDB) for many years in Japan. For this reason, this guideline is a BQ to introduce the current evidence on the usefulness of topical steroids.

Evidence and commentary

Expert opinions recommend the use of topical steroids for local inflammatory signs such as pain and erythema in EB and SDB.[1–4]

In their RCT, Pedersen *et al*.[5] compared the effects of clobetasol propionate (strongest) or placebo on artificially created EB or SDB in 12 healthy volunteers and found that there was no significant difference in the anti-inflammatory effect on pain and erythema. Similarly, Faurschou *et al*. conducted an RCT to examine the effect of topical steroids on EB caused by UVB irradiation in 20 healthy volunteers, but found no significant difference in the outcomes with and without topical steroids.[6] In addition, Matsumura *et al*. conducted a double-blind study using betamethasone valerate and gentamicin sulfate ointment for fresh grade II burns, and found no difference in the reduction of swelling or pain among the signs of inflammation between the groups. Only redness was reduced with both ointments, but epithelialization was delayed to the fourth day after injury.[7]

Recommendation decision process

The criteria for adoption were met in the first round of voting.

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1 Yamanaka K1 & Mizutani H Principles of initial treatment of burn wounds. Monthly Book Derma 2008; 146: 16–20. (in Japanese).
2 Takuma K, Sasaki J. Wound treatment and local therapy. Initial treatment of burns and indices for local and antimicrobial chemotherapy. Iyaku J. Sha, Osaka 2008; 129–56. (in Japanese).
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4 Toh T, Okano Z, Moriuchi H. From daily inquiry - adrenocortical hormone. Pharmacy 1988; 39: 1085–93.
5 Pedersen JL, Møiniche S, Kehlet H. Topical glucocorticoid has no anti-nociceptive or anti-inflammatory effect in thermal injury. Br. J. Anaesth. 1994; 72: 379–82.
6 Faurschou A, Wulf HC. Topical corticosteroids in the treatment of acute sunburn: a randomized, double-blind clinical trial. Arch. Dermatol. 2008; 144: 620–4.
7 Muramatsu M, Sekiguchi T. Experience with steroid ointment for fresh grade II burn wounds. Plast. Surg. 1972; 15: 318.

RECOMMENDATIONS IN OTHER RELEVANT MEDICAL GUIDELINES

THE JAPANESE DERMATOLOGICAL Association's Guidelines for the Treatment of Burns (2017 Edition):

Are topical steroids useful in the treatment of EB and SDB?

Recommendation statement: The anti-inflammatory effect of topical steroids is expected, and their use is suggested as an option in the early stages of injury.

Recommendation level: 2D

On the usefulness of topical steroids for burns, there are only expert opinions, at evidence level VI, and

recommendation level 2D. On the other hand, there are three RCTs (including double-blind studies) that show no anti-inflammatory effect of topical steroids on physically injured skin, including burns. However, we took into consideration the fact that many expert opinions point out the usefulness of topical steroids for EB and SDB, and that many topical steroids have been used for burns in Japan.

Guidelines for the Treatment of Burns (Revised 2nd Edition):

(1) For grade II burns, Vaseline ointment base is recommended to maintain a moist environment, and the main agent (antibiotic, steroid, etc.) should be selected according to the size and depth of the burn (C).

There is no study comparing steroid ointments in burns, but case reports (level IV) and expert opinions (level IV) suggest that steroid ointments can be used to reduce inflammation in the early stages of SDB, and oily ointments can be used to speed healing in a moist environment. Similarly, antibiotic ointment can be recommended to protect the wound surface with oleophilic ointments, as per expert opinion (level IV) for SDB wounds. As some topical steroids are covered by health insurance and others are not, the drugs that are covered for burns are listed in the reference section.

CQ4–2

CQ and answer

CQ: Is a silver-containing wound dressing effective for local treatment of partial thickness burns within 1 week after injury?

Answer: We strongly recommend the use of silver-containing Hydrofiber wound dressings (evidence level I, recommendation level A).

We strongly recommend the use of silver-containing polyurethane foam/soft silicone wound dressing (evidence level II, recommendation level B) (*).

The use of silver-containing alginate wound dressings is weakly recommended (evidence level II, recommendation level B) (*).

Background and importance of CQ

Various topical therapies have been used for partial thickness burns within 1 week after injury, and past guidelines have also described the usefulness of each. Among these, silver-containing wound dressings occupy a large position as a local treatment option, and there are various silver-containing wound dressings in Japan, each of which has its own characteristics. Therefore, this CQ is important for the purpose of reconfirming the usefulness of each wound dressing.

PICO

Patient: Patients with partial thickness burns within 1 week
Intervention: Silver-containing wound dressing is used as topical therapy
Control: This treatment is not used
Outcome: Degree of pain, time to healing, scar formation

Summary of evidence (results of SR)

References used: Five RCTs

(1) Muangman P, Pundee C, Opasanon S. A prospective, randomized trial of silver containing Hydrofiber dressing versus 1% silver sulfadiazine for the treatment of partial thickness burns. Int. Wound J. 2010; 7: 271–6.

In outpatients with partial thickness burn wounds with a body surface area of <15%, silver-containing Hydrofiber wound dressings are more useful than SSDs in terms of cost, time to healing, pain, number of treatments, and content.

(2) Yarboro DD. A comparative study of the dressings silver sulfadiazine and Aquacel Ag in the management of superficial partial-thickness burns. Adv. Skin Wound Care 2013; 26: 259–62.

(3) Caruso DM, Foster KN, Blome-Eberwein SA *et al*. Randomized clinical study of Hydrofiber dressing with silver or silver sulfadiazine in the management of partial-thickness burns. J. Burn Care Res. 2006; 27: 298–309.

(4) Tang H, Lv G, Fu J *et al*. Randomized controlled trial of polyhexanide/betaine gel versus silver sulfadiazine for partial-thickness burn treatment. J. Trauma Acute Care Surg. 2015; 78: 1000–7.

(5) Silverstein P, Heimbach D, Meites H *et al*. An open, parallel, randomized, comparative, multicenter study to evaluate the cost-effectiveness, performance, tolerance, and safety of a silver-containing soft silicone foam dressing (intervention) versus silver sulfadiazine cream. J. Burn Care Res. 2010; 32: 617–26.

Silver-containing silicone foam was superior to SSD in terms of cost, cure rate, and number of replacements.

(6) Opasanon S, Muangman P, Namviriyachote N. Clinical effectiveness of alginate silver dressing in outpatient management of partial-thickness burns. Int. Wound J. 2010; 7: 467–71.

References: Two Cochrane SRs

(7) Wasiak J, Cleland H, Campbell F *et al*. Dressings for superficial and partial thickness burns. Cochrane Database Syst. Rev. 2013; 3 :CD002106. doi: 10.1002/14651858.CD002106.pub4.PMID: 23543513

A comparison of silver-containing Hydrofiber wound dressings with SSDs showed a significant reduction in treatment duration, pain relief, and number of replacements.

(8) Storm-Versloot MN, Vos CG, Ubbink DT *et al*. Topical silver for preventing wound infection. Cochrane Database Syst. Rev. 17;3:CD006478.doi: 10.1002/14651858.CD006478.pub2.

Evidence level

Regarding silver-containing Hydrofibers, the evidence level was set to I because there was one systematic review and two RCTs. The evidence level for silver-containing polyurethane foam/soft silicone was set to II because there were two RCTs. The evidence level for silver-containing alginate was set to II because there was one RCT.

Summary of benefits

Three RCTs[1–3] and two SRs[7,8] compared silver-containing Hydrofiber wound dressings to SSDs. In all cases, silver-containing Hydrofiber significantly reduced pain, shortened wound healing period, and reduced the cost compared to SSD. Two RCTs[4,5] compared silver-containing polyurethane foam/soft silicone with SSD. There was no difference in the duration of wound healing in either case, but the frequency of replacement was reduced with the Hydrofiber. In the first volume, pain reduction and cost reduction were observed. One RCT[6] compared silver-containing alginate with SDD, which shortened the wound healing period.

Summary of harms

Regarding the use of local silver, Aziz *et al*.[8] reported that the wound healing was significantly worse with silver-based dressings than without such dressings, and there was no evidence that it was effective in preventing infection.

Balance between benefits and harms

Aziz *et al*.[9] concludes that the use of silver-containing wound dressings was neither good nor bad in preventing infection and promoting wound healing. However, regarding silver-containing Hydrofiber wound dressings, other SRs and RCTs have shown superiority in pain reduction, replacement frequency reduction, shortening of wound healing period, and reduction of cost compared to conventional treatments. On the other hand, silver-containing polyurethane foam/soft silicone wound dressing showed no difference in wound healing time, but led to reduced pain and cost. Silver-containing alginate wound dressing was found to shorten the wound healing period.

Medical costs of this intervention

The frequency of replacement of the wound dressing changes depending on the amount of exudate, but the overall medical cost and burden on the patient will be reduced with the reduction in the frequency of replacement. The price of the dressing for wounds leading to the dermis is 6 yen per cm (as of March 2020). In Japan, there is no price difference between silver-containing wound dressing and silver-free wound dressing per area.

Feasibility of this intervention

If the frequency of replacement is reduced by using this material, the burden on medical staff will also be reduced. Silver-containing polyurethane foam/soft silicone and silver-containing alginate are not covered by insurance for partial-thickness burns as wound dressings or for wounds leading to the subcutaneous tissue. Silver-containing Hydrofiber is covered by insurance as a wound dressing for wounds leading to the dermis.

Is the intervention differently evaluated by the patients, family, medical personnel, and physicians?

Regarding wound dressings, Selig *et al*.[10] surveyed 121 burn facilities in 39 countries and found that the selection criteria for ideal burn dressing were nonstickiness, absorbency, ease of removal, and frequency of replacement. For the patient, reducing the frequency of replacement is useful because it reduces the risk of pain.

Duteille *et al*.[11] used a glove-shaped silver-containing Hydrofiber wound dressing for partial-thickness burns on the fingers, which was good for compatibility, overall glove role, and pain during rest and finger movement. It was also easy to wear and take off.

Recommendation decision process

Regarding the silver-containing Hydrofiber wound dressing, the SRs and RCTs showed its superiority to other options in terms of reduction of pain, replacement frequency, wound healing period, and cost, and it is also covered by insurance. It should also be noted that there is no difference in the cost of silver-containing and silver-free wound dressings in Japan.

On the other hand, the silver-containing polyurethane foam/soft silicone wound dressing did not improve the wound healing period, but it was found to reduce pain and cost, so its use is weakly recommended. We weakly recommended the use of silver-containing alginate wound dressing because it only shortened the wound healing period. The latter two types of wound dressings are not covered by insurance as wound dressings for wounds that reach the subcutaneous tissue, so (*) is added.

Recommendations in other relevant clinical practice guidelines

Recommended by the Japanese Society of Burns (A) (*) and the Japanese Dermatological Association (1A and 2B).

REFERENCES

1 Muangman P, Pundee C, Opasanon S, Muangman S. A prospective, randomized trial of silver containing hydrofiber dressing versus 1% silver sulfadiazine for the treatment of partial thickness burns. Int. Wound J. 2010; 7: 271–6.
2 Yarboro DD. A comparative study of the dressings silver sulfadiazine and Aquacel Ag in the management of superficial partial-thickness burns. Adv. Skin Wound Care 2013; 26: 259–62.
3 Caruso DM, Foster KN, Blome-Eberwein SA *et al*. Randomized clinical study of hydrofiber dressing with silver or silver sulfadiazine in the management of partial-thickness burns. J. Burn Care Res. 2006; 27: 298–309.
4 Tang H, Lv G, Fu J *et al*. Randomized controlled trial of polyhexanide/betaine gel versus silver sulfadiazine for partial-thickness burn treatment. J. Trauma Acute Care Surg. 2015; 78: 1000–7.
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8 Storm-Versloot MN, Vos CG, Ubbink DT, Vermeulen H. Topical silver for preventing wound infection. Cochrane Database Syst. Rev. 2010; 3: CD006478.
9 Aziz Z, Abu SF, Chong NJ. A systematic review of silver-containing dressings and topical silver agents (used with dressings) for burns wounds. Burns 2012; 38: 307–18.
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11 Duteille F, Jeffery SLA. A phase II prospective, non-comparative assessment of a new silver sodium carboxymethylcellulose (Aquacel Ag burn) glove in the management of partial thickness hand burns. Burns 2012; 38: 1041–50.

CQ4–3

CQ and answer

CQ: Is polyhexanide/betaine gel effective for local treatment of partial thickness burns within 1 week of injury?

Answer: We strongly recommend the use of polyhexanide/betaine gel (evidence level II, recommendation level B) (*).

Background and importance of CQ

Various topical therapies have been used for partial-thickness burns within 1 week after injury, and past guidelines have also described the usefulness of each. Recently, polyhexanide/betaine gel has become newly available in Japan, so this CQ is important for the purpose of confirming the usefulness of this material.

PICO

Patient: Patients with partial thickness burns treated within 1 week of injury
Intervention: Polyhexanide/betaine gel is used as topical therapy
Control: This treatment is not used
Outcome: Degree of pain, infection rate, time to cure, cost

Summary of evidence (results of SR)

References used: One RCT

(1) Wattanoploy S, Chinaroonchai K, Namviriyachote N *et al*. Randomized controlled trail of polyhexanide/betaine gel versus silver sulfadiazine for partial thickness burn treatment. Int. J. Low. Extrem. Wounds 2017; 16: 45–50.

Polyhexanide/betaine gel was not significantly different from SSD in wound healing time, infection rate, or cost, but was superior in pain relief.

Referenced Cochrane SR: None

Evidence level

There was one RCT and the evidence level was II.

Summary of benefits

One RCT compared polyhexanide/betaine gel with SSD. There were no significant differences in wound healing time, infection rate, or cost, but the former led to superior pain relief.

Summary of harms

None reported.

Balance between benefits and harms

Polyhexanide/betaine gel was not significantly different from SSD in terms of wound healing time, infection rate, or cost, but was superior in terms of pain relief.

Medical cost of this intervention

The insurance reimbursement price is JPY 37/g (as of March 2020).

Feasibility of this intervention

In Japan, it is classified as an atypical type of wound dressing for wounds that extend to the subcutaneous tissue, so there is no insurance coverage for partial thickness burns.

Is the intervention differently evaluated by the patients, families, medical staff, and physicians?

Wattanaploy *et al.*[1] reported that this material is easy to remove from the wound surface and causes little pain, so the satisfaction of medical staff and patients is high.

Recommendation decision process

Regarding polyhexanide/betaine gel, the RCT showed no significant difference in wound healing period, infection rate, or cost compared with SDD, but the degree of pain was alleviated. However, since it is classified as an atypical type of wound dressing for wounds that extend to the subcutaneous tissue, it is not covered by insurance for partial-thickness burns, so (*) is added, and its use is weakly recommended.

Recommendations in other relevant clinical practice guidelines

There is no mention in the guidelines of the Japanese Society of Burns or the Japanese Dermatological Association.

REFERENCE

1 Wattanoploy S, Chinaroonchai K, Namviriyachote N *et al*. Randomized controlled trail of polyhexanide/betaine gel versus silver sulfadiazine for partial thickness burn treatment. Int. J. Low Extrem. Wounds 2017; 16: 45–50.

CQ4–4

CQ and answer

CQ: Is trafermin (basic fibroblast growth factor [bFGF]) effective for topical treatment of partial thickness burns within 1 week after injury?

Answer: We strongly recommend the use of trafermin (evidence level II, recommendation A) (*).

Background and importance of CQ

In recent years, there have been many reports on the use of trafermin for partial thickness burns treated within 1 week after injury. Although its usefulness has been mentioned in past guidelines, this CQ is important for the purpose of confirming the usefulness of this drug.

PICO

Patient: Patients with second-degree burns treated within 1 week
Intervention: Trafermin is used as a topical therapy
Control: Trafermin is not used
Outcome: Degree of pain, infection rate, time to healing, scar properties, cost

Summary of evidence (results of SR)

References used: Two RCTs

(1) Akita S, Akino K, Imaizumi T *et al*. Basic fibroblast growth factor accelerates and improves second-degree burn wound healing. Wound Repair Regen. 2008; 16: 635–41.

In adults with partial thickness burns, objective scar evaluation, scar progression, viscoelasticity, hardness, and keratin function evaluation were performed in the bFGF group

and the control group, and all items were significantly improved in the bFGF-administered group.

(2) Hayashida K, Akita S. Quality of pediatric second-degree burn wound scars following the application of basic fibroblast growth factor: Results of a randomized, controlled pilot study? Ostomy Wound Manage. 2012; 58: 32–6.

In pediatric patients with partial thickness burns, the effect of suppressing hypertrophic scars was examined using the Vancouver scar scale, keratin pressure/moisture meter, and spectrocolorimeter in the bFGF-administered group and control group. The scars were suppressed in the bFGF group and the color tone of the skin graft was significantly improved in the bFGF-administered group.

References adopted: No Cochrane SR

Evidence level

There were two RCTs and the evidence level was II.

Summary of benefits

Two RCTs[1,2] compared the trafermin-treated group and the control group. Akita *et al*.[1] reported that in adult patients with partial thickness burns, wound healing period, scar elasticity, hardness, and water retention ability were excellent in the trafermin group. Hayashida *et al*.[2] examined partial thickness burns in children, and the trafermin group showed superior results in terms of wound healing period and scar improvement. In a report comparing the trafermin group and control group for partial thickness burns diagnosed with deep dermal burn (DDB), it was reported that the number of days until epithelialization was significantly shorter in the trafermin group;[3] period until epithelialization was predominantly shorter in the group treated within 3 days than in the group treated after 4 days.[4]

Summary of harms

As side effects, irritation, pain, redness, rash, contact dermatitis, elevated AST/ALT, and excess granulation tissue have been reported. In addition, its use on the site of a malignant tumor is contraindicated.

Balance between benefits and harms

The use of this drug shortened the wound healing period and showed excellent scar healing. No major side effects were observed.

Medical costs of this intervention

The price is JPY 7295.7/bottle of 250 μg spray and JPY 9,010.4/bottle of 500 μg spray; 30 μg is sprayed once a day within an ulcer diameter of 6 cm (as of March 2020).

Feasibility of this intervention

As this agent is a spray and a moist environment cannot be obtained with its use alone, there is no evidence as to which one should be selected for the combined use of multiple layers of external preparations and wound dressings. There is also a report of intrablister injection[5] regarding the administration method.

Is the intervention differently evaluated by the patient, family, medical staff, and physician?

The use of this drug may cause irritation and pain. In addition, it is necessary to use it in combination with an external preparation or a wound dressing to maintain a moist environment.

Recommendation decision process

The use of this drug shortened the wound healing period, and the scar properties after healing were significantly excellent. However, it was more effective when used earlier after the occurrence of injury than when used later. Although there is insurance coverage for burn ulcers, the definitions of burn ulcers and fresh burns are ambiguous, and partial thickness burns treated within 1 week of injury may not be covered by insurance.

Recommendations in other relevant clinical practice guidelines

Recommended by the Japanese Society of Burns (A) (*) and the Japanese Dermatological Association guidelines (1A).

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1 Akita S, Akino K, Imaizumi T *et al*. Basic fibroblast growth factor accelerate and improves second-degree burn wound healing. Wound Repair Regen. 2008; 16: 635–41.
2 Hayashida K, Akita S. Quality of pediatric second-degree burn wound scars following the application of basic fibroblast growth factor: results of a randomized, controlled pilot study? Ostomy Wound Manage. 2012; 58: 32–6.

3 Fujiwara O, Soejima K, Nozaki M *et al*. Experience of local treatment with bFGF preparation for fresh second-degree burn wounds. Jpn. J. Burn Inj. 2008; 34: 71–9. (In Japanese).
4 Komuro A, Kishibe M, Yamamoto Y *et al*. Treatment of second-degree burn wounds using trafermin (Fiblast® spray). Jpn. J. Burn Inj. 2009; 35: 27–39. (In Japanese).
5 Kurokawa M, Morooka H, Kamino C. Benefits of intra-blister bFGF injection therapy and hydrogel coating therapy after bFGF spraying for partial thickness burns. Jpn. J. Burn Inj. 2009; 35: 21–6. (In Japanese).

CQ4–5

CQ and answer

CQ: Are disinfectants effective for local treatment of partial thickness burns treated within 1 week of injury?

Answer: We strongly recommend the use of disinfectants for the topical treatment of partial thickness burns within 1 week of injury (evidence level VI, recommendation level C).

Background and importance of CQ

Considering the different types of wounds and disinfectants, this CQ is important for confirming the usefulness of iodine-based preparations (povidone iodine, iodine tincture, iodoform, etc.), sodium hypochlorite, and chlorhexidine gluconate in the context of medical care in Japan.

Evidence and commentary

Regarding the sterilization of burns, there are opinions[1] that burns should be cleaned with iodine preparations and chlorhexidine gluconate, that they should be used for disinfection,[2,3] and that sterilization is not necessary and cleaning with physiological saline or tap water is recommended.[4,5]

In an SR of disinfectants for burns,[6] iodine preparations were compared with SSDs in two RCTs, but the effectiveness of iodine agents in terms of wound healing time was unclear. One RCT compared sodium hypochlorite with SDD, which showed a slight reduction in wound healing time, but did not analyze the infection rate.

Although various disinfectants are covered by insurance, all of them may cause contact dermatitis, so caution is required when using them. In particular, it has been reported that iodine preparations are cytotoxic.[7] In addition, when used for a wide range of burns, absorption from the wound surface may cause renal dysfunction and thyroid dysfunction.[8]

There was no evidence of the efficacy of a general disinfectant for partial thickness burns treated within 1 week of injury. On the other hand, in many RCTs, comparison with disinfectants is performed using SDD, so it is necessary to compare with those without antibacterial agents. Currently, there is an opinion[5] that disinfectants may be used when there is a clear infection, so its use is weakly recommended.

Recommendations in other relevant clinical practice guidelines

There is no mention in the guidelines of the Japanese Society of Burns. The guideline (2B) of the Japanese Dermatological Association proposes it as one of the options.

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CQ4–6

CQ and answer

CQ: Should blisters be deroofed early in second-degree burns?

Answer: It is recommended that the blisters not be deroofed early while considering the risk of infection (level of evidence II, recommendation grade B).

Background and importance of CQ

Although blisters are often seen in second-degree burns, there is no consensus on whether they should be deroofed or preserved, and if so, when they should be deroofed.

PICO

Patient: Patients with second-degree burns with blistering
Intervention: Early deroof of blisters
Control: Preserve blisters
Outcome: Healing time, pain, infection, scarring

Summary of evidence (results of SR)

References used: RCT

(1) Ro HS, Shin JY, Sabbagh MD *et al*. Effectiveness of aspiration or deroofing for blister management in patients with burns: A prospective randomized controlled trial. Medicine (Baltimore) 2018; 97: e0563.

When comparing the two groups of blister preservation (blister fluid aspiration) and blister deroofing, blister preservation (blister fluid aspiration) was slightly more effective in terms of bacterial infection, pain, and scarring.

Level of evidence

Level II

Summary of benefits

The adopted evidence did not show any benefit of deroofing the blisters. However, in some areas, such as the joints of the extremities, the waist where the belt touches, and the neck, the blister contents may interfere with movement. When the blisters interfere with movement and the blister content fluid coagulates and cannot be aspirated, deroof of the blister is considered to be useful. Deroof of the blisters is also necessary when infection is observed in the blisters.

Summary of harms

When comparing the two groups of blister preservation (blister fluid aspiration) and blister deroofing, blister preservation (blister fluid aspiration) was slightly more effective in terms of bacterial infection, pain, and scarring.[1] In addition, the rate of bacterial infection increases in the order of blister fluid content, blister fluid aspiration, and blister deroofing, and preserving the blister is beneficial for preventing bacterial infection.[2]

Balance between benefits and harms

There is no benefit in deroofing blisters. Preservation of the blisters may prevent bacterial infection, may be effective in relieving pain, and may reduce the possibility of hypertrophic scarring. Because the blisters may interfere with movement, depending on the age of the patient, the location of the burn, and blister size, it is necessary to consider whether to preserve, deroof, or aspirate the blister fluid, depending on each patient's situation. For example, in areas where pressure is likely to be applied, such as exposed areas, lumbar region, and back, blister fluid aspiration can be considered. If the blister is damaged and bacterial infection is suspected, it is necessary to deroof the blister as soon as possible. It has been reported that the time for epithelialization is shorter with fluid aspiration than with fluid preservation.[3]

Medical cost of the intervention

Deroofing of blisters can be done with procedure fee for wound care. The cost of ointment and wound dressings will be incurred after deroofing.

Feasibility of the intervention

Aspiration of blister contents and deroofing of blisters are easy to perform.

Is this an intervention that is evaluated differently by patients, families, healthcare providers, and physicians?

As there may be differences in the financial abilities and wishes of the patients and their families, the physicians should consult with the patients.

Recommendation decision process

The criteria for adoption were met in the first round of voting.

Recommendations in other relevant medical guidelines

There is no mention in the Japanese Burn Association or the Japanese Dermatological Association.

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CQ4–7

CQ and answer

CQ: Do we use SSD for initial DB?

Using SSD for initial DB is strongly recommended (evidence level VI, recommendation degree D).

Background and importance of CQ

Silver sulfadiazine has been used frequently for topical treatment of initial DB and it showed a high success rate based on the previous guideline. On the other hand, the wide range of DBs that require inpatient treatment has been changing since the evidence of effectiveness was published, and early removal of necrosis is the major treatment today. Thus, this CQ presented important evidence on this medicine.

PICO

Patient: Initial DB patient
Intervention: Use SSD as topical treatment
Control: SSD was not used
Outcome: Frequency of infection, period of full recovery, period of inpatient treatment

Summary of evidence (results of SR)

No RCT
No Cochrane SR

Level of evidence

Level VI: Report, opinion of advisory committee, or experience of clinical study of experts

Summary of benefits

Silver sulfadiazine has been frequently used in burn injury and reported as a comparison to other medicines or materials. There was no paper found on the evidence of DB after the appointed paper in the second edition of the Burn Injury Treatment Guidelines of the Japan Society for Burn Injuries Members. The report of Pegg *et al*.[1] stated that SSD was effective in reducing the risk of bacterial infections and the mortality rate in their research of 645 burn injury patients (SSD, 314 patients; maphenide, 156 patients; existing treatment, e.g., gentamicin ointment, 175 patients). Furthermore, Oyama *et al*.[2] and Ono *et al*.[3] reported the effectiveness of SSD in reducing bacterial infections.

Summary of harms

Antibiotic-resistant bacteria[4] and leukopenia[5] have been reported. There is an opposite viewpoint[6] that suggests avoiding SSD treatment for SDB injury, considering the risk of epidermal tissue formation due to the existence of toxic cells.

Balance between benefits and harms

There is a benefit of using this medicine for DB, which is applicable to the inpatient-wide area of burn treatment, because the primary care strategy is to control bacterial infections. However, careful observation is required to monitor the appearance of antibiotic-resistant bacteria and/or leukopenia.

Medical cost of this treatment

The cost of this medicine is JPY 12.8/g (as of March 2020).

Possibility of recommendation of this medicine

It is covered by medical insurance for burn injury, so it can be used in daily treatment.

Are the evaluations of patients, families, medical staffs, and doctors different?

The evaluations are not different; this medicine is well-known with a high frequency of use in the past.

Recommendation decision process

The guideline cleared the standard adoption criteria at the first round of voting.

Recommendation of treatment guideline

It is recommended by the Japan Society for Burn Injuries Members (B#) and Japanese Dermatological Association (1B). The ISBI Practice Guidelines for Burn Care (2016) mentioned the usefulness of SSD to control bacterial infections with materials that contain silver, but there is no statement on the level of recommendation.

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CQ4–8

CQ and answer

WHICH TOPICAL TREATMENT is effective for a limited DB in outpatient care?

There are opinions on the use of necrosis removal medicines, such as bromelain ointment and/or solcoseryl, in preservative treatment.

BACKGROUND AND IMPORTANCE OF CQ

THIS GUIDELINE RECOMMENDS inpatient burn care, but the majority of the clinical treatment is usually executed as outpatient care. Burn injuries with limited areas caused by a portable electric heater or handwarmer are often encountered. This BQ presented evidence on limited DB.

Evidence and comments

There is no specific paper on topical treatment for limited DQ in outpatient care and general burn injury treatment guidelines mention this. The second edition of the Burn Injury Treatment Guidelines used data from two double-blind trials of bromelain or solcoseryl ointment, but these were published more than 20 years ago.[1,2] Both showed effective necrosis removal. Patients often do not prefer surgical treatment for DB, although it is considered a preferred method of necrosis removal, and no clear recommendation is established yet. The guidelines of the Japan Dermatological Association provide a description of cadexomer iodine, dextranomer, and SSD.

Recommendation decision process

The guideline cleared the standard adoption criteria at the first round of voting.

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CQ5 SURGICAL MANAGEMENT OF BURN WOUNDS

SURGICAL MANAGEMENT OF burn wounds is key to saving lives and treating extensive burns. In extensive burns, debridement of necrotic tissue and wound closure should be performed as soon as possible. However, in extensive burns, it is often difficult to cover the burn area early with autologous skin, because the donor sites for the autologous skin graft are limited. Therefore, it is necessary to utilize allogeneic skin, artificial dermis, or cultured epidermal autografts to address the lack of autologous skin needed after debridement.

Early excision and skin grafting is very important in the treatment of extensive burns. After 1 week of injury, local infection develops in the burn wound. This can lead to various infections, and these infections have a significant impact on prognosis. In the JSBI's Burn In-patient Registry (JSBI Burn Registry [JBR]), the most common cause of death was infection-related disease beginning in the second week of hospitalization.[1]

Allogeneic skin grafting is considered to be the gold standard for the treatment of extensive burns worldwide. In Japan, the Japan Skin Bank Network (JSBN) provides cryopreserved allogeneic skin grafts, and the surgical procedure is now covered by insurance. At present, allogeneic skin grafting over high-magnification mesh autologous skin graft as well as autologous patch skin graft are the most commonly used methods.[2]

Cultured epidermal autografts have been commonly used in the treatment of extensive burns in Japan for more than

10 years and are now becoming an indispensable part of the treatment. The procedure has been improved in many ways, and nowadays, the combination with high-magnification autologous mesh grafts is becoming popular.

There have been various opinions on the use of artificial dermis for extensive burns. Some argue that it is an artificial product that does not lead to viable skin formation and promotes wound infection when used on burn wounds. On the other hand, there is an opinion that the successful use of artificial dermis not only temporarily avoids the shortage of donor sites, but also improves the quality of scars.[3]

In the second edition, topics of "early surgery," "allogeneic skin grafting," and "cultured autologous skin grafting" were included. In the third edition, when formulating the CQ on early surgery, evidence on the use of cryopreserved allogeneic skin, autologous epidermis, and artificial dermis in extensive burns was reviewed. We added a section on "regenerative epidermal suspension" in addition to "hydrosurgical debridement."

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CQ5–1

CQ and answer

CQ: Is early excision of necrotic tissue within 1 week after injuries useful for extensive burns (>30% TBSA)?

Answer: Early excision of necrotic tissue at the early stage of injury is recommended for extensive burns (evidence level VI, recommendation grade C).

Background and importance of CQ

Burn wounds without blood flow can be a source of infection, and inflammatory mediators released from burn wounds can cause sepsis and organ failure, which can be fatal in extensive burns.

Early excision to remove necrotic tissue after injury may reduce the incidence of sepsis and organ failure and may contribute to the survival of patients with extensive burns. In this guideline, we designed a CQ to evaluate the effectiveness of early excision for extensive burns.

PICO

Patient: Patients with fresh burns (TBSA >30%)
Intervention: Early excision of necrotic tissue
Control: Early excision of necrotic tissue was not performed
Outcome: Survival (or mortality), hospital days, and blood transfusion volume

Summary of evidence (results of SR)

No RCT
No Cochrane SR

Level of evidence

Level VI: Reports and opinions of expert committees or clinical experience of experts

Summary of benefits

A review on surgical excision in severe burns was published in 2017.[1] Four observational studies reported that early excision within 24–48 h was associated with low mortality and short hospital stay.[2–5] On the other hand, two observational studies found that mortality was reduced in patients without inhalation injury.[6,7]

Summary of harms

In four observational studies, it was reported that early excision increased the amount of blood transfusion.[8–11]

Balance between benefits and harms

Although we could not find evidence on the efficacy of early excision, we believe that the benefits outweigh the harms. However, based on the above evaluation, we believe that the benefits outweigh the harms if treatment is performed with attention to the harms of early excision.

Medical cost of this intervention

Debridement of necrotic tissue has the following cost for a maximum of five times: 1,020 points (less than 100 cm^2),

3,580 points (100 cm^2 and greater than 3,000 cm^2), and 10,030 points (3,000 cm^2 and greater than 3,000 cm^2).

Post-debridement autologous partial thickness skin grafting has the following cost: 3,520 points (less than 25 cm^2), 6,270 points (25 cm^2 to 100 cm^2), and 25,820 points (more than 200 cm^2).

Allogenic cadaver skin for covering the wound has the following cost: 8,000 points (less than 200 cm^2), 16,000 points (200–500 cm^2), 32,000 points (500–1,000 cm^2), 80,000 points (1,000–3,000 cm^2), and 95,000 points (more than 3,000 cm^2).

The procedure fee is not calculated when the dermis is covered with an artificial dermis and costs approximately JPY 450 per cm^2 of artificial dermis.

Feasibility of this intervention

Early excision is usually carried out urgently, and although it is expected to add to the workload of medical personnel, it is acceptable considering the benefit to patients with extensive burns.

Is the intervention evaluated differently by patients, families, medical staff, and physicians?

Depending on the patient's general condition, the evaluation of early surgery is likely to vary among medical professionals.

Recommendation decision process

The guideline met the specified criteria for adoption after the first round of voting.

Recommendations in other relevant practice guidelines

The second edition of the JSBI guideline states, "Early surgery to remove necrotic tissue and close the wound early after injury is recommended for extensive burns (B)."

The ISBI Practice Guidelines for Burn Care (2016) mentions the benefits of early excision and recommends early surgery for burns with less than 20% TBSA, but does not provide recommendations for extensive burns.

The Surgical Management of the Burn Wound and Use of Skin Substitutes: An Expert Panel White Paper in the ABA Practice Guidelines Collection states that early excision may increase survival and not only excision but also wound coverage is necessary, but no recommendation is given.

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CQ5–2

CQ and answer

CQ: Is cryopreserved allogeneic skin grafting useful at the time of surgery for extensive burns?

Answer: Cryopreserved allogeneic skin grafting is recommended at the time of surgery for extensive burns (level of evidence VI, recommendation grade C).

Background and importance of CQ

Since Girdner[1] performed the first allogeneic skin graft in 1981, aspects such as development of a skin bank network and the collection, storage, distribution, and safety of use of allogeneic skin have been discussed. Allogeneic skin is generally considered to be effective in promoting epithelialization in DDB wounds and in preparing the wound bed for skin graft after debridement of the burn eschar.[2]

The use of cryopreserved allogeneic skin grafts for primary wound closure at the time of early excision in cases of extensive burns with more than 50% TBSA is expected to reduce pain, maintain fluid and body temperature, and prepare the graft bed, and thus contribute to improved survival.[3–5] However, some reports suggest that this technique should be used with caution in patients with moderate burns of less than 50% TBSA.[1,6,7] This is a CQ on the efficacy of cryopreserved allogeneic skin grafting in extensive burns, which is of great importance.

PICO

Patient: Patients with fresh burns (>30% TBSA)
Intervention: Use of cryopreserved allogeneic skin graft at the time of surgery
Control: Cryopreserved allogeneic skin graft not used at the time of surgery
Outcome: Survival, number of operations, hospital days, and medical cost

Summary of evidence (results of SR)

No RCT
No Cochrane SR

Level of evidence

Level VI: Reports and opinions of expert committees, or clinical experience of experts

Summary of benefits

Outcomes were analyzed for 18 references (12 RCTs and 6 non-RCTs) from among 142 references on burn treatment using allogeneic skin grafts, published up to May 2018.[1] Of the 18 references, 13 used skin grafts for graft beds or for autologous transplants (sandwich technique), and five used grafts to promote wound healing of DDB.

The results of the analysis did not show the superiority of allogeneic skin grafting in terms of any of the evaluation factors, such as promotion of wound healing, graft take rate, scar appearance, and mortality. The reasons for this were that the sample size of most of the studies was less than 50 patients, the burn area of the target patients varied widely from 0.5% to 95%, and patients with both DDB and DB were included.

As this CQ is meant for patients with fresh extensive burns greater than 30% TBSA, evidence from the above-mentioned studies cannot be adopted directly. However, epidemiological studies have shown that the treatment of extensive burns with allogeneic skin graft can improve survival.[8] These results suggest that the use of cryopreserved allogeneic skin for the treatment of extensive burns improves the survival rates.

Summary of harms

The use of cryopreserved allogeneic skin grafts in the treatment of patients with medium-range burns of 20–50% TBSA has been reported to increase the number of surgeries, prolong hospitalization, increase medical costs, and decrease survival. The survival rate of patients with medium-range burns of 20–50% TBSA has been reported to decrease.[6,7]

Balance between benefits and harms

The benefit of allogeneic skin graft is superior when used for the treatment of patients with extensive burns greater than 50% TBSA. There is a cautious balance of benefit and harm when it is used for patients with burns of 30–50% TBSA.

Medical costs required for this intervention

Cryopreserved allogeneic skin in Japan will be supplied by JSBN. In order to use cryopreserved allogeneic skin, it is necessary to register as a member of JSBN, and a basic annual membership fee of 100,000 yen is required regardless of usage. For adult patient usage, the fee is 700,000 yen per transplant (maximum 10 units, each unit is approximately 100 cm^2), and for pediatric patient usage (under 16 years of age), the fee is 70,000 yen per unit.

The cryopreserved allogeneic skin graft cost will be reimbursed under the K014-2 Skin Grafting (cadaver) Program, depending on the graft area: 8,000 points (less than 200 cm^2), 16,000 points (200–500 cm^2), 32,000 points (500–1,000 cm^2), 80,000 points (1,000–3,000 cm^2), and 96,000 points (more than 3,000 cm^2).

Feasibility of this intervention

JSBN recommendation level BI: 10 or higher, or DDB: 15% TBSA or higher is the limit for the use of cryopreserved

allogeneic skin. In addition, insurance covers the use of cryopreserved allogeneic skin in the treatment of burns, which is highly practicable.

Is the intervention evaluated differently by patients, families, medical staff, and physicians?

It is assumed that there is little variation in the evaluations of patients, families, medical staff, and doctors.

Recommendation decision process

The guideline met the specified criteria for adoption at the first ballot.

Recommendations in other relevant practice guidelines

The second edition of the JSBI Guidelines states that "(1) For extensive burns, allogeneic skin grafting is recommended at the time of early surgery (B). (2) Allogeneic skin may be applied to the surface of a second-degree burn wound as a biological dressing to promote early wound healing (B)." The Japanese Society of Dermatology's Guidelines for the Treatment of Burns (2017 edition) does not mention this guideline.

The ISBI Practice Guidelines for Burn Care (2016) states (in chapter 8, surgical management of the burn wound) that "After excision or debridement of the deep burn wound, it is essential that the wound is covered with autograft skin or an appropriate skin substitute" (recommendation 7). Cryopreserved allogeneic skin is widely used and is suitable for temporary wound coverage for several weeks before rejection, but no recommendation is given.

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CQ5–3

CQ and answer

CQ: Is cultured epidermal autograft useful in extensive burns?

Answer: Cultured epidermal autografts are weakly recommended for extensive burns (level of evidence II, recommendation B).

Background and importance of CQ

Cultured epidermal autograft has been used since the 1980s and its usefulness has been reported.[1–3] In other countries, autologous cultured epidermal grafts have been used in graft beds constructed from allogeneic skin, and good take rates have been reported.[4,5]

In Japan, cultured epidermal autografts have been covered by insurance since 2009, and clinical results have been collected. In a 6-year multicenter post-use study, it was observed that cultured epidermal autografting on artificial dermis was successful and that the combination of cultured epidermal autograft and autologous skin graft had a high take rate. Cultured epidermal autografts may have a lifesaving effect in extensive burns.[6]

However, the ways to prepare the graft bed and use it in combination with autologous skin are unclear. This CQ focused on the efficacy of cultured epidermal autograft in extensive burns, which is of great importance.

PICO

Patient: Patients with extensive burns (>30% TBSA)

Intervention: Cultured epidermal autografting (any method) was performed
Control: Cultured epidermal autografting was not performed
Outcome: Survival (or mortality), wound closure time, scar quality, scarring, and medical costs

Summary of evidence (results of SR)

References used: One RCT

Gardien KL, Marck RE, Bloemen MC *et al*. Outcome of burns treated with autologous cultured proliferating epidermal cells: A prospective randomized multicenter intrapatient comparative trial. Cell Transplant. 2015; 25: 437–48.[7]

Patients with burns of 6–51% TBSA were treated with cultured epidermal autografts cultured on a collagen scaffold, in combination with a 3:1 mesh graft. There was no difference in the take rate compared with 3:1 mesh alone graft. Epithelialization after 5–7 days and the long-term scar quality were better with cultured epidermal autograft. The survival rate was not studied.

Adopted literature: No Cochrane SR

Level of evidence

Level II: One or more RCTs

Summary of benefits

Since the patients included in the study had burns ranging from 6 to 51% TBSA (average 24%), early epithelialization was obtained by using cultured epidermal autograft in combination with 3:1 mesh skin grafts. The long-term scar quality was better than that with the conventional method. Although survival rates have not been reported in RCTs, a 6-year multicenter postoperative study in Japan showed that the use of cultured epidermal autograft contributed to improved survival.[6]

Summary of harms

In patients with extensive burns, it takes approximately 3 weeks to prepare and use the cultured epidermal autograft, and additional costs are incurred.

Balance between benefits and harms

If early epithelialization is achieved, the length of hospitalization may be shortened and total hospitalization costs may be reduced. The benefits of using cultured epidermal autografts may outweigh the harms if the surgery is planned well.

Medical cost of this intervention

Conventional partial thickness skin grafts have the following point distribution: 3,520 points for <25 cm^2, 6,270 points for 25 cm^2 to 100 cm^2, and 25,820 points for >200 cm^2.

In addition, if a cultured epidermal autograft is used, the cost of tissue sampling and culturing the skin is JPY 4,460,000, and the cost of one cultured epidermal autograft sheet (10 × 8 cm) is JPY 154,000. Up to 40 sheets can be used for extensive burns for over 30% of the body surface area.

Feasibility of this intervention

As the cost of cultured epidermal autografts is reimbursed, the practicability of this intervention is high. Extensive burns >30% TBSA are usually treated in specialized burn centers, and although there is a learning curve in surgery and wound management with the use of a cultured epidermal autograft, it seems feasible.

Is the intervention evaluated differently by patients, families, medical staff, and physicians?

There is little variation in the evaluations of patients, families, medical staff, and physicians.

Recommendation decision process

The guideline met the specified criteria for adoption at the first ballot.

Recommendations in other relevant practice guidelines

The JSBI guidelines (2nd edition) state that "In severe burns with a TBSA of 50–60% or more, the use of a cultured epidermal autograft may be considered, as it may improve survival by allowing epithelialization of the wound with a smaller area of skin than a conventional autologous graft" (B). The ISBI Practice Guidelines for Burn Care (2016) describes it as cell-based therapy, but there is no recommendation.

In the ABA's Practice Guidelines Collection, Surgical Management of the Burn Wound and Use of Skin Substitutes: An Expert Panel White Paper, it is stated that cultured epidermal autografts are susceptible to infection and have no dermis, which limits their ability to heal wounds that, once healed, can quickly detach and lead to hypertrophic scars; however, it is stated that the combination of artificial dermis

and allogeneic skin grafting can improve their effectiveness. No recommendation is given.

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CQ5–4

CQ and answer

CQ: Is the application of artificial dermis useful during early excision of extensive burns?

Answer: It is weakly recommended for the use of artificial dermis when performing early excision (evidence level II, recommendation grade B).

Background and importance of CQ

Four products of artificial dermis are reimbursed by insurance in Japan and are used in clinical practice for full thickness skin defects. It has been used in Japan for extensive burns since the late 1990s, but its effectiveness is controversial.[1–3] Its use may be limited, especially in cases of complications such as infection. Allogeneic skin is said to be the gold standard for temporary wound closure in extensive burns, but the supply of allogeneic skin is not sufficient in Japan, and it is not used in low-magnification mesh skin grafts like in the United States and Europe; usually 1:3–6 mesh is used in Japan. In addition, there is a potential risk of donor-induced viral infections in allogenic skin. This is a CQ on the effectiveness of the use of artificial dermis in extensive burns and is of considerable importance.

PICO

Patient: Patients with fresh burns (>30% TBSA) who are undergoing early excision
Intervention: Application of artificial dermis
Control: No application of artificial dermis
Outcome: Days of hospitalization, survival rate, the rate of epithelialization, hypertrophic scarring, incidence of wound infection, and sepsis

Summary of evidence (results of SR)

References used: One RCT

Branski LK, Herndon DN, Pereira C *et al*. Longitudinal assessment of Integra in primary burn management: A randomized pediatric clinical trial. Crit. Care Med. 2007; 35: 2615–23.[4]

There is no difference in the rate of complications such as graft failure or bacterial infections when artificial dermis is used at the time of early excision in patients with extensive burns compared to conventional skin closure methods, including allogeneic skin. It is beneficial for acute phase metabolism, such as reduced resting energy expenditure. In addition, the split-thickness skin graft used for wound closure is thinner than conventional grafts, so epithelialization of the donor site does not take a long time, and long-term scarring is also less.

In addition, in a multicenter RCT in the United States, the take rate of the artificial dermis was 80%, and the shallow donor site was closed early, with good aesthetic results.[5]

Level of evidence

Level II: One or more RCTs

Summary of benefits

The use of artificial dermis results in early metabolic stabilization. With artificial dermis, the split thickness skin graft, which is grafted after application of the artificial dermis, is thin and results in rapid epithelialization of the donor site. In

the long-term results, the scarring is better than that with conventional methods.

Summary of harms

If wound infection occurs after artificial dermis application, it could be detected late underneath the artificial dermis. In patients for whom the wound can be closed by a single skin graft, the use of artificial dermis may require a second operation, which may prolong the hospital stay.

Balance between benefits and harms

It is as effective as allogeneic skin grafts, and since the skin graft for final wound closure is thin, the donor site heals quickly. With careful attention to the side effects of wound infection, the use of artificial dermis is considered to be beneficial.

Medical cost of this intervention

The procedure fee associated with the application of the artificial dermis is not calculated. The price of the artificial dermis itself is approximately JPY 450 per cm^2.

If 30% of the body surface area is covered by the artificial dermis (17,000 cm^2 × 0.3), and the expansion rate of the artificial dermis is 1:1.5, 3,400 cm^2 of artificial dermis is needed, which is equivalent to approximately JPY 1.5 million.

Feasibility of this intervention

Since four products of artificial dermis are currently approved by the pharmaceutical authorities in Japan and reimbursement prices have been set, the feasibility of this intervention is high. As extensive burns over 30% TBSA or more are usually treated at a burn center, wound management with artificial dermis likely to be feasible, despite the learning curve.

Is the intervention evaluated differently by patients, families, medical staff, and physicians?

There is little variation in their evaluations because the artificial dermis itself is composed of collagen of animal origin.

Recommendation decision process

The guideline met the specified criteria for adoption at the first ballot.

Recommendations in other relevant practice guidelines

There is no mention of it in the guidelines of the Japanese Burn Association or the Japanese Dermatological Association. The ISBI Practice Guidelines for Burn Care mentions the artificial dermis (dermal regeneration template), but there are no recommendations in the Management of the Burn Wound and Use of Skin Substitutes: An Expert Panel White Paper. The ISBI Practice Guidelines for Burn Care states that artificial dermis may save lives and contribute to skin quality.

Supplementary

In recent years, many techniques have been introduced, such as the sandwich method, in which an artificial dermis is used on top of an autologous high-magnification mesh/patch skin graft in a single operation,[6] autologous skin graft performed simultaneously on top of a thin artificial dermis without a silicon layer,[7,8] and artificial dermis impregnated with bFGF.[9]

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HYDROSURGERY SYSTEM

THE VERSAJET HYDROSURGERY system has been shown to be useful in burn wound excision.[1] It is a promising, safe, and effective alternative for conventional debridement of burns, allowing immediate skin grafting, high selectivity for healthy and necrotic tissue, high skin graft viability, and rapid healing. The advantages are particularly significant for wounds with complex geometries.

(1) Kakagia DD, Karadimas EJ. The efficacy of Versajet hydrosurgery system in burn surgery. A systematic review. J. Burn Care Res. 2018; 39: 188–200.

REGENERATIVE EPIDERMAL SUSPENSION

REGENERATIVE EPIDERMAL SUSPENSION (RECELL) is a technique of harvesting healthy skin tissue, separating it to the cellular level, creating an autologous cell suspension, and spraying or applying it to the wound after debridement with/without meshed skin graft, allowing it to grow like a colony and achieve epidermalization.

The cells from 1 cm^2 of skin strip can be applied to an 80-cm^2 wound. It has shown good results in terms of accelerated healing and holds great promise as a complementary therapy to conventional burn treatment with skin grafting.

(2) Gravante G, Di Fede MC, Araco A *et al*. A randomized trial comparing ReCell system of epidermal cells delivery versus classic skin grafts for the treatment of deep partial thickness burns. Burns 2007; 33: 966–72.

CQ6 BURN INFECTION

THE MAJOR CAUSES of death in burn patients are shock, organ failure, and infection in the early stages of injury according to major national and international reports.[1] In the JBR, the second most common cause of death was infection-related conditions, accounting for 30% of all cases.[2]

When the skin is damaged by physical factors such as heat injury, it is exposed to a wide variety of microorganisms from the outside world, and bacteria invade the damaged area. Whether or not the damage progresses to bacteremia or sepsis depends not only on the amount of bacteria, but also on the pathogenicity and protective capacity of systemic immunity.[3,4]

Systemic immunity is known to be affected in more than 15–20% TBSA, and the presence of diseases such as diabetes mellitus, advanced liver cirrhosis, and cancer further contributes to immunodeficiency.[5] Infection-related deaths also occurred in JBR from the third day of injury, and infection became the major cause of death from 7 to 10 days.

Pathogenic microorganisms that cause infection are present on the skin and droplets of patients, contaminated materials from the field to the hospital, instruments and floating objects in hospital facilities, feces and nasal passages of patients, or hands and droplets of health-care workers, and exposure to pathogenic microorganisms can trigger infection.[6]

Based on these considerations, infection control measures for patients with extensive burns should be implemented from the time of injury, taking into account contamination and the type and virulence of pathogenic microorganisms.

In this section on infection, "Characteristics of conditions caused by infection in burn patients in JBR" is described, followed by "Standard precautions for burn patients," "Private room management and isolation for burn patients," and "Defecation management for burn patients" as infection prevention.

In addition, hydrotherapy for burn patients, which has recently become a problem as a cause of nosocomial infection, and prophylactic crobial agents for burn patients were discussed.

antimiIn the case of burn infection, RCTs under certain conditions, such as degree of invasiveness, individual differences, and drugs administered, are often difficult to conduct because of the unique nature of severe burns with the possibility of death. In addition, as there were no appropriate study designs, the items in this section are listed as BQ.

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CQ6–1

CQ and answer

CQ: How does infection affect patient mortality in burn patients?

Answer: Infection-related conditions have been reported to influence the mortality of burn patients, followed by early shock/organ failure.

Background and importance of CQ

It has been reported in many papers that mortality increases with the increase in burn area. This is an important issue because infections in burn patients have a significant impact on the course of treatment, and we have presented this as a BQ.

Evidence and commentary

According to JBR statistics, the most common cause of acute mortality in burn patients was "early shock/organ failure" (46%), and "infection-related conditions" was the second most common cause (27%).[1]

Infection-related deaths were observed on the third day of injury and were most common after the second week, when deaths due to "early shock/organ failure" decreased. In addition, deaths in burn patients increased with increasing burn area, and "death due to infection" was the most common cause of death in cases of burns of 11–40% TBSA.

Several experts have reported that burns of 20–30% TBSA or more can cause severe sepsis and multiple organ failure.[2,3] The most common causes of infection are infection of necrotic tissue due to burns and catheter infection.[4]

The causative microorganisms are often indigenous skin bacteria, but infections with toxin-producing organisms such as *Clostridium perfringens*, *Staphylococcus aureus*, and Group A streptococcus can cause fulminant sepsis and be fatal, even if the burn area is small. In addition, infections caused by multidrug-resistant bacteria such as methicillin-resistant *Staphylococcus aureus* (MRSA), multidrug-resistant *Pseudomonas aeruginosa*, and multidrug-resistant *Acinetobacter baumannii*, and other multidrug-resistant bacteria can easily lead to sepsis and become severe.[5] It is important to take measures to prevent infection in burn patients.

Recommendation decision process

The guideline met the specified criteria for adoption at the fifth ballot.

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CQ6–2

CQ and answer

CQ: How do you implement standard precautions for burn patients?

Answer: Standard precautions should be taken with sterile gloves for patients with a burn area of 20% TBSA or greater.

Background and importance of CQ

Patients with extensive burns are more likely to be exposed to various microorganisms, which can enter the body and cause sepsis. Therefore, it is important to use standard precautions to reduce the chance of exposure to new pathogens. The use of standard precautions in burn patients is considered a matter of course, but there is much debate about the content of these precautions. In this section, we present the evidence on standard precautions for burn patients using a BQ.

Evidence and commentary

Patients with burns greater than 25–30% TBSA are more likely to progress from bacteremia to sepsis due to decreased cellular immunity from excessive invasion.[1] In a JBR report, infection was the main cause of death in burn patients with a burn area of 11–40% TBSA (see CQ6–1). However, there were many cases of infection-related deaths in patients with less than 30% TBSA, suggesting that standard prophylaxis should be applied in patients with 20% TBSA or more, taking into account the risk of serious infection, including age and underlying disease, and efficiency.

Wearing sterile gloves, gowns, and masks during bandage changes is effective in preventing infection.[2–4] In a clinical study in a burn unit (BU), the number of MRSA infections decreased with the use of sterile gloves.[5] It was also reported that when disposable gloves and gowns were worn, the MRSA colonization and infection rate decreased from 34.8% to 4.3%.[6]

There was no difference in infection rates with the use of sterile and nonsterile gloves in a clinical study of minor skin surgeries, but sterile gloves and gowns should be used when exposing burn wound surfaces and performing wound care on patients with severe burns who are immunocompromised.

Recommendation decision process

The guideline met the specified criteria for adoption at the fourth ballot.

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CQ6–3

CQ and answer

CQ: How do you provide private room management and isolation for burn patients?

Answer: Patients with burns greater than 20% TBSA should be isolated in a private room to prevent infection.

Background and importance of CQ

Private room management and isolation of burn patients are considered important for infection control, but there is much debate about how to do this. In this section, we present the evidence for private room management and isolation for burn patients using a BQ.

Evidence and commentary

There are two types of isolation methods for burn patients: (i) prophylactic isolation, burn patients are regarded as easily infected patients with impaired immunity and are protected from nosocomial infection, and (ii) source isolation, burn patients are treated as a source of infection after infection with multidrug-resistant bacteria.

Preventive isolation has been reported to have the potential to reduce the risk of microbial colonization and infection in burn patients.[1] Thompson *et al*.[1] compared the management of burn patients in a BU with isolation and a trauma unit (TU) without isolation and reported that the infection rate was 10.8% in the BU and 47.1% in the TU ($P = 0.005$).

McManus *et al*.[2] compared a single-bed isolation (IW) with an open ward (OW) and found that in IW, gram-negative bacteria from blood culture tests were undetectable for a longer period (IW: 28.9 days, OW: 11.8 days) and patient mortality was lower (mortality rate 1.61 in OW $P<0.001$), and patient mortality was also lower (mortality rate of 1.61% in OW, $P<0.001$). Furthermore, Klein *et al*.[3] reported that the incidence of infectious diseases after 7 days was reduced when private rooms and clean gloves were used in a pediatric ICUs.

At present, there is no consensus on whether or not to use high-efficiency particulate air filtration to control airborne infection when managing burn patients in private rooms.[4,5] As described above, isolation and private room management are considered to be important means of infection control,

but in addition, environmental maintenance such as cleaning of medical equipment is also necessary.

In addition to restricting the patient's own behavior, it is also important for health-care workers to be careful not to come into contact with the patient or the environment.

Recommendation decision process

The guideline met the specified criteria for adoption at the fourth ballot.

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CQ6–4

CQ and answer

CQ: Is hydrotherapy effective for burn patients?

Answer: Hydrotherapy is effective in removing residual tissue from burn wounds and improving blood flow to promote wound healing.

Background and importance of CQ

Hydrotherapy has been used for a long time to promote healing of burn wounds, but in recent years, there have been reports of nosocomial infections caused by multidrug-resistant bacteria, and there is much controversy about its use. In this article, we present the evidence on hydrotherapy for burn patients as a BQ.

Evidence and commentary

Hydrotherapy refers to two types of treatment: soaking the body in hot water in a bathtub (bath therapy) and pouring hot water over the body (shower therapy). Hydrotherapy is said to have numerous effects, including improvement of the wound surface (removal of necrotic tissue and pus), promotion of wound healing by improving blood flow, support for physical therapy, and comforting the patient. In Japan, this has been done for many injuries and diseases since the Heian period.[1]

Recently, however, an outbreak of multidrug-resistant bacteria was reported after hydrotherapy was administered to burn patients, indicating that hydrotherapy can be a source of infection.[2] According to a multicenter study in the United States and Canada, hydrotherapy is used in 94.8% of burn centers in North America, and nosocomial infections occurred in many patients treated with hydrotherapy, with isolates of *P. aeruginosa* (52.9%), *S. aureus* (25.5%), and *Candida* sp.[3] In addition, several outbreaks caused by Gram-negative rods such as *P. aeruginosa*, *A. baumannii*, MRSA, and *Candida* sp. that are thought to be caused by hydrotherapy have been reported.[4,5]

For this reason, the following points should be considered when administering hydrotherapy to burn patients who require hospitalization:[6]

1. Do not administer hydrotherapy to patients with severe or extensive burns in the early stages of injury or when their general condition is unstable.
2. Avoid the use of shared showers and bathtubs.
3. Thoroughly clean and dry hydrotherapy equipment that may come into contact with wounds, such as showers, bathtubs, and stretchers. It is difficult to remove microorganisms lodged in plaque stuck in the joints of equipment even with disinfectant.

In addition, the effectiveness of disposable plastic sheets and steam cleaners has also been reported.[7–9] For patients with small burns who can be treated in the outpatient clinic, there are no reports of infection caused by hydrotherapy, and many specialists recommend it for the removal of necrotic tissue from the burn wound surface and for wound healing by improving blood flow.[10]

Recommendation decision process

The guideline met the specified criteria for adoption at the fourth ballot.

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CQ6–5

CQ and answer

CQ: How should defecation management be performed in burn patients?

Answer: In patients with extensive burns who have perianal wounds, intrarectal catheter is effective in preventing perianal wound infection.

BACKGROUND AND IMPORTANCE OF CQ

IN PATIENTS WITH extensive burns who have perianal wounds, fecal management is often difficult because stool and rectal discharge adhere to the burn wounds and grafts. Colostomy or fasting and antidiarrheal agents have been used in the past. However, colostomy is an additional invasive procedure for burn patients, and fasting is not used nowadays because of the risk of complications such as bacterial translocation. In this paper, we present evidence on intrarectal catheters used in recent years in burn patients as BQ.

Evidence and commentary

The intrarectal catheter is a medical device that is inserted through the anus, and the tip is placed in the rectum to guide stool in the rectum into the tube, and then excreted from the other side of the tube into the back. The device had been studied in artificial anus,[1] but from around 1979, implantation in the anus such as "rectal balloons" and "continuous anal plug" was studied.[2,3] The intrarectal catheter for anal implantation has been produced since around 2007, and several products are currently in use.

The use of intrarectal catheters in patients with extensive burns has been reported to be useful.[4] In a prospective cohort study by Keshava *et al*., intrarectal catheter was used in 20 patients (7 with perianal burns and 13 with severe perianal epidermal sequestration); the average number of linen changes decreased from 9.3 per day to 1.2 per day, especially in incontinent patients.[5] In a retrospective study of hospitalized burn patients, Echols *et al*.[6] compared 106 patients each with and without intrarectal catheter and found that urinary tract infection and skin and soft tissue infection were reduced with the use of intrarectal catheter and that defecation management tubes were safe and cost-effective.

In patients with inflammatory bowel disease or anorectal disease, the implantation of tubing may aggravate the disease condition, so its use should be carefully considered. In addition, as complications include anal ulceration, bleeding, and anal laxity, prolonged implantation should be avoided and signs of complications should be checked periodically during insertion.[7]

Recommendation decision process

The guideline met the specified criteria for adoption at the fourth ballot.

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INTRARECTAL CATHETERS ARE indicated for a wide range of patients and are used in the following cases.

1. Prevention of fecal contamination and infection of perianal wounds in patients who are critically ill, bedridden, unconscious, or otherwise unable to defecate on their own: patients with severe burns, Fournier gangrene, or other perianal wounds or surgical sites.
2. Prevention of fecal contamination and infection of perianal wounds in patients with incontinence-related skin disorders.
3. Prevention of catheter contamination.

The indwelling period is limited to 28 days. Contraindications are postoperative wounds in lower colon or rectum or anus, stricture and rectal mucosal disorders (severe proctitis, ischemic proctitis, mucosal ulcer), tumors, severe hemorrhoids, and fecal impaction.

Insurance coverage

If certain conditions are met, 50 points can be calculated for "persistent refractory diarrhea fecal drainage" only on the day of initiation.

CQ6–6

CQ and answer

CQ: How should prophylactic antimicrobial agents be administered to burn patients?

Answer: There is insufficient evidence on the efficacy of prophylactic (systemic) administration of antimicrobial agents immediately after burn injury or in the perioperative period.

On the other hand, some experts recommend systemic administration of prophylactic antimicrobial agents in the presence of toxic shock syndrome (TSS) and toxic shock-like syndrome (TSLS), in the presence of easily infected hosts or sites, in extensive burns, in burns with contaminated wounds, and in complicated cases of respiratory tract burns.

Background and importance of CQ

In 2013, the Cochrane SR of burn patients was published, and it showed a negative view of prophylactic antimicrobial administration in burn patients.[1] However, this SR used an intervention method in which a predetermined antimicrobial agent was uniformly administered to burn patients, and no intervention method was used that limited the target patients to whom prophylaxis should be administered.

In actual burn care, prophylactic administration of antimicrobial agents is often considered for patients with contaminated burn wounds immediately after injury or for those with underlying easily infectious diseases such as diabetes mellitus. Here, we present the evidence and expert opinions on the administration of prophylactic antimicrobial agents to burn patients as a BQ.

Evidence and commentary

According to the 2013 Cochrane SR, the incidence of burn wound infection was not inhibited by antimicrobial agents in three RCTs (119 patients) in which antimicrobial agents were administered systemically and prophylactically.[1]

In only one RCT, in 40 patients who received prophylactic trimethoprim-sulfamethoxazole systemically, there was a significant reduction in the rate of pneumonia. Perioperative prophylactic systemic antimicrobial therapy was evaluated in four RCTs, and no reduction in the incidence of infection was observed.

Selective digestive decontamination (SDD) with nonabsorbable antimicrobial agents was evaluated in two RCTs (140 patients), and it did not significantly reduce the incidence of infection.

Furthermore, there was a significant increase in the detection of MRSA when nonabsorbable antimicrobials were combined with cefotaxime compared to the use of placebo. Selective oropharyngeal decontamination was examined in one RCT (30 patients) and no difference in mortality or sepsis was observed as compared with placebo.

The results of the SR concluded that prophylactic administration of predetermined antimicrobial agents to burn patients is not effective in preventing infection and should not be used. On the other hand, there is very little evidence on how to administer prophylaxis to patients with burns, but by limiting the types of pathogenic microorganisms and the target patients, such as children and the elderly, no practical

conclusion can be reached. Regarding prophylactic administration of antimicrobial agents against TSS and TSLS, for example, there are several opinions, such as prophylactic administration is not necessary because of the low incidence of TSS and TSLS, or that prophylactic administration is recommended because the incidence of TSS and TSLS increases in areas where the proportion of toxin-producing strains is high. Practically, it is necessary to decide whether to administer antimicrobial agents or not, taking into account the region, age, contamination status, severity of illness, and underlying diseases.[2–6]

The term "compromised host" is used to refer to a patient who has a systemic immune compromise (metabolic diseases such as diabetes or cirrhosis; congenital or acquired immunodeficiency syndromes; hematologic diseases such as leukemia; advanced malignancies; use of steroids, immunosuppressive agents, or anticancer drugs; or the elderly) or a local immune deficiency (patients with osteoporosis, artificial valves, artificial blood vessels, arteriovenous shunts for dialysis, cardiac valvular disease, vascular malformations, etc.). Patients with osteoporosis, artificial valves, artificial blood vessels, arteriovenous shunts for dialysis, valvular heart disease, vascular malformations, etc. are prone to infectious thrombosis in conditions that cause nonphysiological blood flow.[7–10]

In such patients with severe burns, some recommend prophylactic administration of antimicrobial agents depending on the risk of infection. In the case of extensive burns, systemic immunocompetence is also reduced, and the patient becomes a susceptible host. In addition to bacteremia and sepsis resulting from infection of the necrotic tissue of burns, infection through intravascular catheters and urinary catheters can easily occur; therefore, prophylactic administration of antimicrobial agents is recommended for compromised hosts with extensive burns.

For inhalation injuries, an RCT found a significant reduction in mortality with a combination of: (i) systemic administration of cefotaxime, (ii) application of polymyxin B, tobramycin, and amphotericin B to the nasopharynx, and (iii) oral administration of SDD.[11] As for prophylactic systemic administration of antimicrobial agents when burns are complicated by inhalation injuries, some reports showed that it is not effective in preventing the onset of pneumonia, but it helped reduce mortality.[12,13]

When administering prophylactic antimicrobial agents, the method of administration has not been established, but some opinions of experts are listed below.

1. Gram staining and bacterial culture of wounds, sputum, urine, etc., should be performed at the time of initial treatment to estimate the microorganisms that have already taken root, and antimicrobial agents should be administered accordingly for 1–2 days and discontinued if no microorganisms are detected in the culture specimen at the time of initial treatment.
2. If necrotic tissue is present, topical antibacterial agents such as sulfadiazine silver should be used topically until the necrotic tissue is removed.

There are few studies on the prophylactic administration of antifungal agents to burn patients. However, it should be noted that there are studies that recommend early administration of empiric antifungals because they progress rapidly and cause endophthalmitis, osteomyelitis, embolism, and deep abscesses.[14,15]

As for recommendations in other practice guidelines, the Guidelines for Burn Care published by the Japanese Dermatological Association state that "uniform prophylactic systemic administration of antimicrobial agents cannot be clearly recommended at this time because there is insufficient evidence to demonstrate efficacy."[16]

The ISBI Practice Guidelines for Burn Care (2018) also state that "prophylactic systemic administration of antimicrobial agents has no evidence of efficacy and should not be used," but recommend prompt systemic administration of antimicrobial agents and collection of culture specimens when sepsis is suspected.[17]

Recommendation decision process

The guideline met the specified criteria for adoption at the fourth ballot.

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CQ7 NUTRITION

ONE OF THE goals of the Japanese Burn Care Guidelines is to provide a basis for standardizing the initial care of patients with severe burns. Nutrition was not included in the first edition, but was added in the second edition published in March 2015. Burns, especially severe burns, are subjected to extremely intense heat-induced bioinjury, resulting in a sustained state of hypermetabolism that is 1.5 to 2.0 times higher than normal, with increased protein catabolism, lipolysis, and hyperglycemia. In particular, the disintegration of muscle proteins is severe, and the key to sustaining life is how to suppress this disintegration and maintain the nutritional state. For this reason, many basic and clinical studies have been conducted over the years, and some of them are already recognized as gold standards. In the section on nutrition, we have prepared seven CQs, five of which are BQs and two as FQs.

CQ7–1

CQ and answer

CQ: Is indirect calorimetry useful in the nutritional management of burn patients?

Answer: It is most desirable to determine the amount of calories to be administered to each patient by measuring the amount of calories consumed at rest using an indirect calorimeter.

Background and importance of CQ

According to a questionnaire survey of North American burn centers by Graves *et al*.,[1] 66% of centers use indirect calorimetry, 78% add a stress factor to the measured caloric value for nutritional dosage, 81% use the measured value, and 81% added a stress factor of 10–30% to the measured value. In the United States, the use of indirect calorimetry has become widespread, and it is considered a matter of course to use indirect calorimetry in burn patients. Many papers have been published using indirect calorimetry as the established standard without RCTs. In addition, it is considered the gold standard in Brazil and Australia.[2,3] In the UK, indirect calorimetry is a standard tool for nutritional therapy, but is not used in burn centers.[4] In Japan, the use of indirect calorimetry is not widespread, and many calorie calculation formulas are used.

Evidence and commentary

Many institutions have reported that it is desirable to measure the amount of calories administered in adult burns by measuring the amount of calories consumed by each patient at rest using indirect calorimetry[5–21]. It is widely recommended to measure resting caloric expenditure by indirect calorimetry in children with burns.[15,16] However, it has been argued that caloric expenditure alone is insufficient to maintain body weight in children during growth. Gore *et al*. and Mayes *et al*. recommended a dose of 1.3 times the measured resting energy expenditure (REE).[17,18] Berger *et al*.[19] emphasized the importance of repeated measurements during inpatient care. In the second edition of the Japanese Burn Care Guidelines, indirect calorimetry was given a Recommendation B level in the sections on adult and pediatric nutritional doses. The use of indirect calorimetry is covered by the European Society of Clinical Nutrition and

Metabolism (ESPEN) guidelines for ICUs[20] and the Society of Critical Care Medicine/American Society for Parenteral and Enteral Nutrition (SCCM/ASPEN) guidelines for critically ill adults.[21] The ESPEN guidelines rate the need (to determine energy expenditure) using indirect calorimetry as a Grade B recommendation (strong agreement, 95% agreement), while the SCCM/ASPEN guidelines rate it as a very weak recommendation.

Recommendation decision process

The guideline met the specified adoption criteria at the first round of voting.

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CQ7–2

CQ and answer

CQ: How do you calculate the amount of calories administered in the nutritional treatment of patients with severe burns?

Answer: There are several methods of calculating the amount of calories to be administered in the nutritional therapy of patients with severe burns, some of which are highly correlated with measured energy expenditure, but to date there is no definitive method of calculation.

Background and importance of CQ

The measurement of energy expenditure by indirect calorimetry is said to be the gold standard for determining

nutritional dosage, but few burn centers in Japan use this method, and many facilities use formulas. However, there are many reports showing the superiority of new formulas, and there is no perfect formula. Therefore, it is necessary to clarify which formula is the most reliable.

Explanation

According to Dickerson *et al*., the calorie dosing equations reported for adults with burns are as follows: nine based on body surface area (m^2), five based on burn surface area (% TBSA), and one based on the Harris–Benedict equation.[1] For the amount of calories administered, many reports multiply the calculated REE by 1, 1.23, 1.4, 1.5, 1.7, 1.73, 1.75, 1.85, 2, or 2.1;[2–8] REE × 1.5 is the classic formula with little bias.[1] The Toronto formula by Allard *et al*.[9] was reported to be close to the indirect calorimetric value.[10] In addition, the formula by Xie *et al*.,[11] based on data from Chinese burn patients, was reported to be free of bias.[1]

On the other hand, the classic Curreri formula was based on a linear regression analysis of caloric dose and weight change in nine burn patients.[12] Xie *et al*. reported that Chinese people in particular are prone to caloric overdose.[4] However, there are few facilities in the United States that use the Curreri formula.[13]

Rimdeika *et al*. reported a significant difference in mortality, incidence of pneumonia and sepsis, and duration of hospitalization in a prospective study of enteral nutrition with one group of patients receiving 30 kcal/kg/24 h or more (group A) and the other, less than 30 kcal/kg/24 h (group B) (5.3% in group A versus 32.6% in group B, $P < 0.01$), emphasizing the need to avoid low caloric doses.[14]

Shields *et al*. conducted a prospective observational study and compared resting energy expenditure using nine prediction equations and energy expenditure measured by indirect calorimetry (measured energy expenditure [MEE]) in 31 burn patients with a mean age of 46 ± 19 years and % TBSA of 48 ± 21%. None of the equations yielded results that were strongly correlated with MEE, but the Carlson and Milner equation result was not significantly different from MEE for all burn areas. Therefore, when indirect calorimetry is not available, the Milner and Carlson equations were the most satisfactory for predicting resting energy expenditure in adult patients with severe burns.[15]

However, new equations have been reported in China and Korea.[16,17] For children with burns, Hildreth *et al*. validated the optimal caloric dose every few years at a single institution and arrived at the final optimal caloric dose formula in a report in 1990.[18–21] Goran *et al*. reported that the Curreri junior formula was difficult to evaluate because of insufficient evidence.[22] There are some reports that do not recommend the use of the Curreri junior formula.[22,23] In the second edition of the Japanese Burn Care Guidelines, the Harris–Benedict formula, Toronto formula, Xie *et al*. formula, and Curreri formula were rated at recommendation grade B for the calculation of nutritional doses for adults, and the Mayes equation, the Revised Galeri formula, and the Mayes formula were rated at recommendation A for children. The ESPEN guidelines recommend the Toronto equation for adults and the Schoffield formula for children with severe burns.[24] However, there have been reports indicating the superiority of new formulas since then, and it must be said that there is still no definitive formula.

Recommendation decision process

The guideline met the specified adoption criteria in the second round of voting.

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FORMULAS TO CALCULATE nutrition dose for burn patients

Adults

Harris–Benedict equation[15]

Male: BEE (kcal/day) = 66.5 + 13.75 × BW (kg) + 5.00 × height (cm) − 6.78 × age

Female: BEE (kcal/day) = 655.1 + 9.56 × BW (kg) + 1.85 × height (cm) − 4.68 × age

REE = BEE × IF × AF

AF, active factor (typically 1.2−1.4); BEE, basal energy expenditure; BW, body weight; IF, injury factor (1−2.1 used for burn).

Toronto formula[9]

REE = −4,343 + (10.5 × %TBSA) + (0.23 × caloric intake [CI]) + (0.84 × basal energy expenditure [BEE]) + (114 × temperature [°C]) − (4.5 × postburn days)

Xie[11]

REE = 1,000 × m (surface area) + 25 × % TBSA 2 (Carlson 15)

REE = BMR × [0.89142 + (0.01335 × % TBSA)] × BSA × 24 × AF

AF, activity factor (typically 1.2−1.4); BMR, basal metabolic rate in healthy subjects; BSA, body surface area (m^2).

Milner[7]

REE = [BMR × (0.274 + 0.0079 × % TBSA − 0.004 × post burn days [PBD]) + BMR] × BSA × 24 × AF

AF, activity factor (typically 1.2−1.4); BMR, basal metabolic rate of healthy subjects; BSA, body surface area (m^2).

Curreri formula[12]

REE = 25 × body weight (kg) + 40 × %TBSA

Xie et al.[16]

REE = (1,094.2477 + 7.3670 × %TBSA + 22.3935 × PBD − 0.0766 × % TBSA2 − 1.3496 × PBD2 + 0.4568 × %TBSA × PBD) × BSA

Hangang equation[17]

REE = 867.542 − 5.546 × age + 13.297 × weight + 4.879 ×%TBSA − 9.844 × PBD + 500.612 × V (1 = ventilator use, 0 = non-use)

Infants

REE = measured REE × 1.3[17,23]

Mayes equation[23]

3 years old and under

Mayers 1 REE = 108 + 68W + 3.9 × %burn

Mayers 2 REE = 179 + 66W + 3.2 × % third-degree burn

5–10 years old

Mayers3 REE = 818 + 37.4W + 9.3 × % burn

Mayers4 REE = 950 + 38.5W + 5.9 × % third-degree burn

Within 10–50% TBSA, W, body weight before injury (kg)

Revised Galveston formula[21]

12 years old and under

REE = 1,800 kcal/m^2 + 1,300 kcal/m^2 burned

Curreri junior formula[22]

0–1 years old: REE = basal energy needs + (15 × % TBSA)

1–3 years old: REE = basal energy needs + (25 × % TBSA)

4–15 years old: REE = basal energy needs + (40 × % TBSA)

CQ7–3

CQ and answer

SHOULD INTRAVENOUS NUTRITION be used in the nutritional therapy of burn patients?

It may be used as a supplement to enteral nutrition in burn patients when enteral nutrition does not provide sufficient nutrition.[2]

Background and importance of CQ

Lam *et al*. conducted a prospective randomized study of early enteral nutrition and complete venous nutrition and found significantly lower rates of complications and mortality in the early enteral nutrition group.[1] Herndon *et al*. reported on the harms of total venous nutrition in adult burn patients.[2,3] Enteral nutrition alone is inadequate for providing adequate caloric intake in patients with severe burns. Dylewksi *et al*. reported that a standardized protein-sparing parenteral nutrition protocol with limited glucose can be implemented to provide calorie and protein supplementation without causing respiratory blood flow complications.[4] Based on these findings, we searched the literature for the advantages and disadvantages of combined intravenous nutrition and examined the efficacy of supplemental intravenous nutrition.

Evidence and commentary

Heidegger *et al*. conducted an RCT in an ICU to evaluate whether energy-targeted 100% enteral nutrition (EN) and complementary intravenous nutrition (SPN) between days 4 and 8 in the ICU could optimize clinical outcomes. Between days 9 and 28, 41 of 153 patients (27%) in the SPN group developed nosocomial infections, compared with 58 of 152 patients in the EN group (0.65; 95% confidence interval, 0.43 to 0.97; $P = 0.0338$). The SPN group had a lower mean number of nosocomial infections per patient (−0.42 [−0.79 to −0.05]; $P = 0.0248$). They reported that energy supplementation with individually optimized SPN may reduce nosocomial infections and should be considered as a strategy to improve clinical outcomes in ICU patients with inadequate EN.[5] Berger *et al*. followed up on the work of Heidegger *et al*. and investigated the metabolic and immune responses underlying the clinical responses of the previous study. They conducted an RCT with 23 critically ill patients who received less than 60% of their energy goals on EN alone on day 3 of admission to the ICU; they examined protein and glucose metabolism, immune responses, and infection rates. Glucose metabolism, immune response, infectious complications, and muscle mass were assessed. The results showed that the SPN group ($n = 11$) received more energy (median 24.3 versus 17.8 kcal/kg/day; $P < 0.001$) and protein (1.11 versus 0.69 g/kg/day; $P < 0.001$) than the control group and, consistent with a lower rate of infection; the immune response of the SPN group was significantly higher than that of the control group. In the immune response of the SPN group, interleukin-6 (IL-6) ($P = 0.024$), IL-1 β, and IL-10 levels, and tumor necrosis factor-α secretion by peripheral blood mononuclear cells ($P = 0.018$) had decreased on day 9, and the decrease in muscle mass from day 4 to day 15 tended to be less in the SPN group (−16% versus 23%; $P = 0.06$). They concluded that nutrition to cover the individually measured energy targets in the SPN group was associated with improved immunity, decreased systemic inflammation, and a trend toward decreased muscle mass.[6] Guo *et al*. studied the relationship between nutritional therapy and clinical outcomes in 100 patients with severe burns. Ninety percent of patients had burns of at least 70% TBSA, and the mean interval between injury and start of nutrition was 2–4 days; 67 patients were started on EN with a median of 1 day, 22 patients were started on intravenous nutrition (PN), and 32 patients developed EN intolerance and were switched to PN. The patients achieved 70% of the energy and protein they were supposed to receive, and those who received less than 30% of their energy from EN had significantly higher 28-day and inhospital mortality rates than those who received more than 30%. Multiple regression analysis showed that less than 30% EN and development of septic shock were independent risk factors for 28-day prognosis, but the majority of patients needed supplementation with PN.[7] In any case, at this time, there are no data showing adverse effects of supplemental PN, and it is considered acceptable.

The Japanese Burn Care Guidelines, Second Edition, states that PN with limited carbohydrate may be used when EN is inadequate (Recommendation grade B). The ESPEN guidelines for the ICU states the following: Recommendation 20 – In patients who cannot tolerate full-dose EN during the first week in the ICU, the safety and benefits of initiating PN should be compared on a case-by-case basis (recommended grade: GPP – strong agreement [96% agreement]); Recommendation 21 – Do not initiate PN until all strategies to maximize the tolerated dose of EN have been tried (recommended grade: GPP – strong agreement [95% agreement]). However, there is no uniform standard RCT, and the role of complementary PN needs to be defined in terms of

timing, dose, and composition.[8] In addition, the ASPEN/SCCM guidelines for critically ill patients recommend considering the use of complementary PN only after 7–10 days in patients with low or high nutritional risk, when the enteral route alone cannot exceed 60% of energy and protein.[9]

Recommendation decision process

The first ballot met the specified criteria for adoption.

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CQ7–4

CQ and answer

CQ: Should EN be initiated within 24 h in patients with severe burns?

Answer: It is strongly recommended that EN be started as early as possible within 24 h of injury in patients with severe burns (level of evidence I, recommendation grade A).

Background and importance of CQ

As for the timing of nutrition in patients with severe burns, early EN within 24 h of injury has been shown to provide many clinical benefits.

However, the timing of initiation of EN varies, including immediately after admission,[1] within 1 h after admission,[2] within 4 h after admission,[3] within 3–6 h after injury,[4] within 24 h after admission,[5,6] and within 24 h after injury.[7,8]

Suri *et al*. reported that when nasogastric tubes were inserted and placed at the time of admission, the prognosis was improved by achieving the target caloric intake within 5–7 days.[9]

Khorasani *et al*. conducted a prospective randomized study of 688 burned children and found that there was a significant difference in the mean duration of hospitalization between 322 children in the slow enteral feeding group (enteral feeding started after 48 h post-injury) and 366 children in the early enteral feeding group (enteral feeding started 3–6 h post-injury) [4]. However, Kesey *et al*. reported that early EN worsened the frequency of ileus and that careful management is essential.[10]

Therefore, we proposed a CQ to review the evidence on early EN, which is already used in many institutions.

PICO

Patient: Patients with fresh severe burns
Intervention: Enteral nutrition should be started within 24 h
Control: Intervention will not be performed
Outcome: Mortality, hospitalization days, complication rate of infection

Summary of evidence (results of SR)

References used: One RCT

Vicic VK, Radman M, Kovacic V. Early initiation of enteral nutrition improves outcomes in burn disease. Asia Pac. J. Clin. Nutr. 2013; 22: 543–7.[3]

References used: Cochrane SR

Wasiak J, Cleland H, Jeffery R. Early versus delayed enteral nutrition support for burn injuries. Cochrane Database Syst. Rev. 2006; 19: CD005489.[11]

In Vicic *et al*.'s report, 101 patients with burns greater than 20% TBSA were divided into an early EN

intervention group and a control group, and blood biochemical tests and body mass index were measured until week 6.[3] The Cochrane report on studies on the safety and efficacy of early nutrition in adult patients published up to 2007 had three RCTs. We found no evidence of benefit of early EN support on standard clinical outcomes, such as number of infections, length of hospital stay, or mortality, due to the small sample sizes of all three studies.[11]

Level of evidence

Level I: SR or meta-analysis of RCTs

Summary of benefits

The Cochrane report found no significant differences in outcomes, hospitalization days, or infection complication rates.[11]

Summary of harms

Possible harms include the difficulty in selecting the appropriate timing, dosage, and rate of nutritional administration in the acute phase of severe burns and the need for nurses to deal with the disposal of waste when vomiting and diarrhea occur frequently.

Balance between benefits and harms

Shortening the fasting period for severely burned patients with marked hypermetabolism is beneficial, but the occurrence of adverse events such as frequent vomiting and diarrhea that may be associated with early initiation of EN may undermine the benefit. Therefore, it is necessary to consider the dosing plan for each patient, including the initial dose, dosing rate, and dosing method.

Medical cost of this intervention

Early and late nutrition are covered by insurance. There are no overall medical costs.

Feasibility of the intervention

In general, patients with burns who can be managed in general wards are able to take food orally, and there is no need for this intervention. Only patients who require early EN with a nasogastric tube in a BU or ICU are eligible for this intervention.

Is this intervention evaluated differently by patients, families, medical staff, and physicians?

It is assumed that there is little variation in the evaluations of patients, families, medical staff, and doctors.

Recommendation decision process

The guideline met the criteria for adoption in the first round of voting.

Recommendations in other relevant medical guidelines

The Japanese Burn Care Guidelines, Second Edition (Nutrition) recommend early EN within 24 h (recommendation A).

The SCCM/ASPEN guidelines state: "Based on expert consensus, enteral nutrition should be started very early (within 4–6 h of injury, if possible) in burn patients."[12] The ESPEN guidelines for ICUs has the following recommendation: Recommendation 4 – "If oral intake is not possible in critically ill adult patients, early enteral nutrition should be started within 48 h" (recommendation grade B – strong consensus, 100% agreement).[13]

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CQ7–5

CQ and answer

CQ: What is the best indicator for nutritional assessment in burn patients?

Answer: Transthyretin (prealbumin) is a good blood test for nutritional assessment of burn patients. Alternatively, nitrogen balance (N balance) has long been recommended.

Background and importance of CQ

For nutritional assessment, serum proteins such as albumin, transthyretin (prealbumin), retinol-binding protein, transferrin, and C-reactive protein, nitrogen balance calculated by measuring blood urea nitrogen and urinary nitrogen, and body weight are used. However, in the acute phase of burns, plasma proteins, body water content, and body weight fluctuate greatly due to changes in capillary permeability, massive infusion of fluids for treatment, and burn wound debridement surgery, making them unreliable nutritional indicators. Therefore, it was necessary to identify the most reliable nutritional index for burn patients. However, there are no high-quality RCTs, and we present the current evidence as a BQ.

Evidence and commentary

There are many reports on the use of transthyretin in burn patients. Brose stated that transthyretin is more sensitive than albumin,[1] Manelli *et al*.[2] suggested that albumin, prealbumin, and C-reactive protein should be checked twice a week when serum protein is used as a nutritional indicator, and Yang *et al*.[3] reported that there was a significant correlation between transthyretin levels in the early stage of burns and mortality. In a further analysis of a single-center retrospective study of 204 patients, burn severity and transthyretin levels were independently associated with mortality.[4]

Nitrogen balance has been used as a nutritional indicator for burn patients by Bell *et al*.[5] However, there are several reports that claim it is not accurate.[6,7] On the other hand, Milner *et al*. re-examined the report by Konstantinides *et al*.[8] that recommended actual measurement of total urinary nitrogen (TUN) based on a comparison of TUN calculated from urinary urea nitrogen (UUN) measurement and actual measurement of TUN. They reported the usefulness of nitrogen balance by accepting the substitution of UUN because there is a strong correlation between TUN and estimated TUN, and the difference is not clinically problematic.[9]

Prelack *et al*.[10] also stated that UUN is suitable as a predictive indicator of protein metabolic balance, and it may be useful as an indicator even if it is not accurate.

Shields *et al*. conducted a prospective interventional study with 10 burn patients with 20% TBSA or higher. They collected data over a 14-month period and found that nitrogen balance was useful as a nutritional indicator, whereas visceral protein had less value as an indicator.[11]

In another related guideline, the Japanese Burn Care Guidelines, Second Edition, rated the use of nitrogen balance, which was calculated by measuring transthyretin and UUN, at recommendation grade B. Dellière *et al*.[12] reviewed the guidelines of various countries and found that some Western countries, such as France, Italy, Poland, and the UK, use a transthyretin cut-off as an indicator of nutritional disorders, while others, such as the United States, Canada, Brazil, Argentina, and Israel, do not. In a study by Berger *et al*.,[13] the ESPEN group stated that transthyretin is affected by inflammation, so it would be a good indicator if CRP is measured at the same time.

Recommendation decision process

The guideline were met the adoption criteria in the first round of voting.

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CQ7–6

CQ and answer

CQ: What is the range of blood glucose control for nutritional therapy of patients with severe burns?

Answer: It has been reported that glycemic control of 130–150 mg/dL is desirable, but no conclusion has been reached yet.

Background and importance of CQ

In 2011, Jeschke *et al*. reported the efficacy of controlling blood glucose to 80–110 mg/dL.[1,2] However, the high frequency of hypoglycemia has since become a problem, and they considered this a problem and later revised the target value to 130–150 mg/dL.[3]

Explanation

Regarding the range of blood glucose levels, Jeschke *et al*. conducted a prospective randomized study on intensive insulin therapy (IIT) for pediatric burns with 30% TBSA or higher and found that controlling blood glucose levels to 80–110 mg/dL resulted in decreased incidence of infection/sepsis and the incidence of organ failure, improved organ function, alleviated catabolic conditions, and suppressed acute inflammatory reactions. However, there was no significant difference in mortality, and hypoglycemia at levels below 60 mg/dL occurred in 43% of the IIT group and 24% of the control group.[4]

Pidcoke *et al*. reported that in a single-center, retrospective study, 49 burn patients with burns of 20% TBSA or higher were treated with insulin to control blood glucose levels to between 80 and 110 mg/dL, and the mortality and infection complication rates were significantly higher in the high glucose group.[5]

These reports raised the issue of the high risk of hypoglycemia when aiming for tight glycemic control.

Gibson *et al*. showed a clear difference in the sepsis complication rate and mortality rate, and above all, fewer hypoglycemic events, when glycemia was controlled loosely to ≤150 mg/dL.[6] Murphy *et al*. also reported a significantly higher mortality rate in patients with uncontrolled hypoglycemia below 150 mg/dL.[7]

In order to avoid hypoglycemic events, strict glycemic control is essential, and related intensive insulin therapy with continuous insulin administration has been reported in many cases.[4–6,8–10]

Lee *et al*. and Sood *et al*. reported that IIT using a computer program resulted in good control and very low rate of hypoglycemic events.[11,12]

The second edition of the Japanese Burn Care Guidelines, recommends the following glycemic ranges: (i) control of glycemia to 80–110 mg/dL is recommended, but hypoglycemic events are frequent and severe intensive care management is required (recommendation level A); and (ii) control

of glycemia to ≤150 mg/dL is recommended (recommendation level B). However, the problem of hypoglycemic events was widely discussed, and Jeschke *et al*., who advocated 80–110 mg/dL, mentioned the problem of hypoglycemia and suggested a target value of 130–150 mg/dL for glycemic control.[3,13] The SCCM/ASPEN guidelines for critically ill patients recommended a blood glucose control value of 140 or 150–180 mg/dL for adult critically ill patients.[14]

To date, many reports have suggested a control level of 130–150 mg/dL in burn patients, but this has not been confirmed, and various methods of insulin administration have been proposed to enable tighter blood glucose control.[15–19]

Recommendation decision process

The criteria for adoption were met in the first round of voting.

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CQ7–7

CQ and answer

CQ: Is glutamine administered as an immunonutrient in the nutritional therapy of patients with severe burns?

Answer: It is strongly recommended that glutamine be administered as immunonutrition in the nutritional therapy of patients with severe burns (level of evidence I, recommendation grade A).

Background and importance of CQ

There are several high-quality studies on the administration of glutamine to burn patients. Zhou *et al*. conducted a randomized, double-blind, controlled study of 40 patients with burns of 50–80% TBSA (glutamine-enriched enteral nutrition versus standard enteral formulation) and reported that

the glutamine group showed improved intestinal permeability, significant differences in endotoxin levels, and a significantly shorter hospital stay.[1]

Garrel *et al*. conducted a double-blind RCT comparing glutamine and control groups, with 45 adult patients with severe burns, and reported that the frequency of positive blood cultures was three times higher in the control group than in the glutamine group, and that the mortality rate was significantly lower in the glutamine group.[2]

Soguel *et al*. conducted a prospective study of 86 patients (40 with burns and 46 with trauma), comparing the group on 30 g/day glutamine, selenium, zinc, and vitamin E (group G) with a historical control group (target group). The primary endpoint was a reduction in SOFA score in group G for burns.[3]

Peng *et al*. conducted a prospective double-blind RCT in which 48 patients (25 in the glutamine group [group G] and 23 in the control group) were treated with 0.5 g/kg/day glutamine orally or by gavage for 14 days. Lin *et al*. reported a significant decrease in hospital days[4] and improvement in cellular immunity in the group on glutamine.[5]

Later, Lin *et al*. conducted a meta-analysis and reported that the drug reduced the incidence of bacteremia caused by Gram-negative bacteria (odds ratio 0.27) and of mortality (odds ratio 0.13).[6]

Wischmeyer *et al*. conducted a prospective, double-blind randomized trial in which 26 burn patients were divided into intravenous glutamine (group G) and control groups. They reported that serum transferrin and prealbumin levels improved at 14 days after the burn injury, and CRP level decreased at that time, although there was no difference in mortality.[7]

However, the efficacy of this drug is not observed in other severe diseases such as sepsis. Therefore, we thought it necessary to review the evidence and verify the efficacy of glutamine administration, and designed this CQ.

PICO

Patient: Patients with fresh burns
Intervention: Administration of glutamine as immunonutrition
Outcome: Mortality, infection rate, hospital stay, and wound healing
Summary of evidence (results of SR)
No RCT
No Cochrane SR
Tan HB, Danilla S, Murray A *et al*. Immunonutrition as an adjuvant therapy for burns. Cochrane Database Syst. Rev. 2014; 12: CD007174.

Glutamine is the body's primary nitrogen carrier and is a conditionally essential amino acid. It functions as a fuel for lymphocytes and intestinal cells and is a precursor of glutathione, a potent antioxidant. Glutamine is the most thoroughly studied immunotroph in burns, with 285 study participants in seven studies. Only three studies reported mortality rates, which were significantly low with drug treatment.[1,2,7] The same study showed a statistically significant reduction in hospital stay in the treatment group as compared to in the control group. The studies reported infection rates, but there was no clear evidence of a difference in wound infection rates.[1,2,7] Although glutamine at 0.3 g/kg/day is preferred in many studies, it is not known whether it has a significant effect on the outcome. There is no clear evidence of optimal dose and duration. Hence, glutamine may have some beneficial effect on mortality, but routine administration cannot be recommended or opposed. The number of participants in intervention studies may be too small to draw firm statistical conclusions.[9]

Level of evidence

Level I

Summary of benefits

Glutamine treatment is associated with a reduction in hospitalization days ($P < 0.0001$) and mortality ($P = 0.002$).[8]

Summary of harms

There are no specific side effects. The possible harms include vomiting, diarrhea, and paralytic ileus caused by the stimulation of glutamine administration, but there is no such description. Possible burdens include the time and effort required to administer glutamine, and the possibility of problems such as the need to replace a clogged feeding tube.

Balance between benefits and harms

There were no harms, and the benefits were considered to be high.

Medical cost of this intervention

If glutamine administration is considered, supplemental foods such as Impact containing high levels of glutamine will be added, but this will be covered by insurance. However, if pure glutamine is administered strictly according to the patient's weight, L-glutamine granules 99% "NP" (990 mg L-glutamine in 1 g, NHI price JPY 6.5) will be

needed, which are not covered by insurance and will be borne by the hospital as part of clinical research.

Feasibility of this intervention

The fact that the L-glutamine granules are not covered by insurance may pose a feasibility problem.

Is the intervention evaluated differently by patients, families, medical staff, and physicians?

There is a possibility that their evaluations of treatment will differ as it is not covered by insurance.

Recommendation decision process

The criteria for adoption were met in the first round of voting.

Recommendations in other relevant medical guidelines

The second edition of the Japanese Burn Care Guidelines (Nutrition) recommends oral glutamine (0.5 g/kg/day or 30–40 g/day) (recommendation A).

The ESPEN guidelines for intensive care units also make a strong recommendation: "Recommendation 26: Inpatients with burns >20% body surface area, additional enteral doses of GLN (0.3–0.5 g/kg/day) should be inpatients with burns >20% body surface area, additional enteral doses of GLN (0.3–0.5 g/kg/day) should be administered for 10–15 days as soon as EN is commenced (grade of recommendation: B strong consensus [95% agreement])",[9] and the SCCM/ASPEN guidelines for critically ill patients also recommend the administration of glutamine to burn patients.[10]

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CQ8 CHEMICAL AND ELECTRICAL BURNS

ELECTRICAL BURNS, INCLUDING lightning strike, and chemical burns are less frequent than thermal burns, so their treatment is often left to burn centers. Appropriate initial treatment is necessary to prevent aggravation but it is difficult to estimate the course of tissue damage due to the different characteristics of the energization and chemical substances. The initial treatment of thermal burns is included in the second revised edition, but not of electrical burns or chemical burns. In revising the guidelines, we focused on early management and treatment of electrical burns and chemical burns and created CQs on these issues.

There are several reports[1,2] by Ohashi *et al*. regarding lightning injuries in Japan. Regarding electrical burns, we examined the need of an electrocardiogram to monitor fatal arrhythmias[3] and of escharotomy and fasciotomy for necrotic tissue removal for injured limb salvage,[4] which is a problem during initial treatment.

As the physical removal of attached chemical substances is important for the initial treatment of chemical burns in order to prevent the progression of tissue damage,[5] we examined irrigation, which is the core of the initial treatment

of chemical burns. In addition, as a treatment method for individual substances, we examined a treatment that neutralizes chemical damage caused by hydrofluoric acid using calcium gluconate.[6] These CQs were compared with the contents of the ISBI Practice Guidelines for Burn Care[7] and ABLS,[8] and the validity of the recommendations was taken into consideration according to the Japanese society and medical system.

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CQ8–1

CQ and answer

CQ: Is electrocardiogram (ECG) monitoring useful for electrical burn patients?

Answer: The use of ECG, including 12-lead ECG for initial evaluation is strongly recommended for electrical burn patients (level of evidence Ⅳ, grade of recommendation D).

Background and importance of CQ

Lethal arrhythmias may occur in patients with electrical burn due to energization of the heart. On the other hand, there may be little need for continuous ECG monitoring when cardiac arrest or loss of consciousness is not observed at the time of injury or when cardiac dysrhythmia is not detected at the time of admission. There is no consensus on the appropriate ECG monitoring period according to the conditions at the time of injury such as voltage of shock. Therefore, in this guideline, we considered it important to verify the effectiveness of ECG monitoring, especially 12-lead electrocardiography, for patients with electrical burns.

PICO

Patient: Electrical burn patients
Intervention: Perform ECG monitoring including 12-lead ECG
Control: Do not perform ECG monitoring including 12-lead ECG
Outcome: Detection of lethal arrhythmia

Summary of evidence (results of SR)

No RCT
No Cochrane SR

Level of evidence

Level IV

Summary of benefits

It is known that electrical burn, including lightning injuries, can cause fatal arrhythmias. Initial evaluation is important, namely nonspecific ST-T changes and atrial fibrillation on 12-lead ECG monitoring.[1]

Summary of harms

Electrocardiogram monitoring and 12-lead ECG are minimally invasive and simple, with few side effects or burdens on the patient. ECG monitoring of an electric shock patient is based on the findings of the 12-lead ECG findings at initial treatment. Patients without impaired consciousness or abnormal ECG at the time of initial treatment do not develop late-onset lethal arrhythmia, indicating that continuous ECG monitoring is unnecessary.[2] However, few reports have verified the appropriate ECG monitoring period for patients with high-voltage electric shock injuries of 1,000 V or more who do not have ECG abnormalities at the time of initial treatment, so further verification is required.

Balance between benefits and harms

As 12-lead ECG is a minimally invasive test, the benefits outweigh the harms at the time of initial treatment.

Lightning strikes often cause impaired consciousness, and hospitalization and follow-up are required to check for pulmonary edema and other changes of state; hence, ECG monitoring is considered to be useful as part of systemic management.[3,4]

Medical costs of this intervention

Every medical institution has a 12-lead ECG examination device and an ECG monitor, and there is no specific cost for this test.

Feasibility of this intervention

A 12-lead ECG test at the time of initial outpatient treatment can be performed in a short time and with minimal invasiveness. Continuous ECG monitoring during hospitalization may increase the burden on the observing health-care professional at some facilities. However, in cases of electrical burn injuries, it may take time to confirm the condition, and given the need for evaluation of the energized area and its surroundings, it is highly likely that the patient will be hospitalized for scrutiny and follow-up. Hence, ECG monitoring is likely to be acceptable.

Is the intervention differently evaluated by the patients, families, medical staff, and physicians?

It is unlikely that their evaluations will differ. If a patient is hospitalized for continuous ECG monitoring, there may some resistance.

Recommendations in other relevant clinical practice guidelines.

The ABA Practice Guidelines for the Management of Electrical Injuries (2006) recommend ECG monitoring at the time of initial treatment. However, hospitalization and continuous ECG monitoring are not recommended for patients with low-voltage shocks of 1,000 V or less with no loss of consciousness or ECG abnormalities at the time of initial treatment. There are few reports on the pros and cons of continuing ECG monitoring in patients with high-voltage electrical burn injuries of 1,000 V or higher and no initial ECG abnormalities, and no recommendations have been made. The ISBI Practice Guidelines for Burn Care (2016) do not provide recommendations for ECG monitoring in electrical burn patients.

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CQ8–2

CQ and answer

CQ: Is escharotomy useful for electrical burn patients?

Answer: Surgical decompression including fasciotomy for electrical burn patients is strongly recommended if compartment pressure increases or if neuropathy or blood flow disorders are observed (level of evidence IV, recommendation grade D).

Background and importance of CQ

Electrical burns may be accompanied by damage and necrosis of energized soft tissues of the extremities. There are several reports stating that aggravation and limb amputation can be avoided by performing decompression for compartment syndrome and for removing as much necrotic tissue as possible. The degree of soft tissue damage varies depending on the voltage conditions that caused the injury, which varies from case to case. It is important to examine whether escharotomy is useful for patients with electrical burns.

PICO

Patient: Electrical burn patients
Intervention: Surgical decompression including fasciotomy
Control: No surgical decompression including fasciotomy
Outcome: Limb preservation, prevention of aggravation

Summary of evidence (results of SR)

No RCT
No Cochrane SR

Level of evidence

Level IV

Summary of benefits

If an increase in compartment pressure, neuropathy, or blood flow deficit is observed, decompression of compartment syndrome and the resulting nerve and blood flow deficits can be improved by performing surgical decompression including fasciotomy. In the case of high-voltage electrical burns, the soft tissue of the upper limb may be damaged, and limb amputation can be prevented by observing the wound and excising the necrotic tissue at the same time as the escharotomy.

Summary of the harms

In cases where there is no compartment syndrome or minor soft tissue damage, surgical decompression including fasciotomy may be unnecessary but the wound may become enlarged, in which case the treatment period will be extended.

Balance between benefits and harms

If the compartment pressure is measured and the nerves and blood flow are objectively evaluated before surgical decompression is performed, it can be beneficial as a necessary treatment. It has been reported that the rate of limb amputation is 21.6–22% when early intervention is possible.[1,2] However, it is unclear to what extent it contributes to the avoidance of limb amputation, as there was no RCT on this. Of note, lightning strikes are characterized by superficial tissue damage and minimal muscle damage and necrosis.[3,4]

Medical costs of this intervention

Only the cost of surgical instruments and consumables required for surgery will be incurred. Although it depends on the tissue to be operated on and its range, the Japan medical fee points for the first year of Reiwa for the surgical procedure correspond to skin incision, debridement, and fasciotomy, at 470 to 10,030 points. In addition, anesthesia management fees and consumables required for surgery can be considered as costs.

Feasibility of this intervention

Surgery by a doctor skilled in burn treatment or escharotomy of the extremities is desirable. It is assumed that the facility that treats electric shock wounds would be specialized in burn treatment. As the surgical procedure conforms to the standard procedure in burn medical treatment, it is considered that there is no problem in implementation if the facility specializes in burn treatment.

Is the intervention differently evaluated by the patients, families, medical staff, and physicians?

It is unlikely that the evaluations of patients, family members, and health-care professionals will differ. However, if there are minor clinical findings such as minor pain or changes in general condition, the patient may be reluctant to make an incision on the seemingly healthy body surface.

Recommendations in other relevant clinical practice guidelines

The ABA Practice Guidelines for the Management of Electrical Injuries (2006) recommend surgical decompression including fasciotomy for the upper extremities when neuropathy, blood flow disorders, increased compartment pressure, and muscle necrosis are suspected. Surgical interventions, including escharotomy within 24 h of injury, are recommended based on evaluation of compartment pressure, Doppler flowmetry findings, and nuclear medicine examination. The ISBI Practice Guidelines for Burn Care (2016) recommend emergency surgical decompression including fasciotomy and necrotic tissue resection in patients with high-voltage electrical burns for limb preservation.

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CQ8–3

CQ and answer

CQ: Is irrigation with water useful for chemical injury?

Answer: It is strongly recommended to irrigate with water as soon as possible after injury for the purpose of removing or diluting the attached chemical agent (evidence level IV, recommendation grade D).

Background and importance of CQ

Different from normal burns, chemical injury progresses until the chemical agents that act on it are removed, neutralized, or react with living tissue to be completely consumed, decomposed, or absorbed.[1] Therefore, physical removal of attached chemical agents is the most important initial treatment to prevent the progression of injury depth. Considering that it is important to examine the usefulness of irrigation with water in this guideline, we devised the CQ.

PICO

Patient: Patient with chemical injury
Intervention: Irrigation
Control: No irrigation
Outcome: Prevention of aggravation

Summary of evidence (results of SR)

No RCT
No Cochrane SR

Evidence level

Level VI

Summary of benefits

Two observational studies compared immediate irrigation after the injury and no irrigation until arrival at the hospital. A statistically significant reduction in the incidence of full-thickness injury, mean hospital days, delayed complications including failure to heal, and sepsis were noted in patients who had received immediate irrigation.[2] There were no significant differences in mean TBSA, depth of burns, or mean length of stay in hospital between the immediate versus no irrigation groups.[3] However, as irrigation is performed after hospitalization, its effectiveness could be observed. The irrigation time can be 15, 20, or 30 min to 2 h long.[4,5,6]

Summary of harms

Although there were no reports of the harmful effects of irrigation, long-term irrigation is costly and adds to the workload of staff. Long-term irrigation with cold water may cause hypothermia.[4,6] The attached chemical agent that generates heat or alkali products of chemical reactions should be directly removed before irrigation with water.[6,7]

Balance between benefits and harms

The benefits outweigh the harms if attention is paid to the harm of irrigation.

Medical costs of this intervention

The cost of tap water will be incurred.

Feasibility of this intervention

Although irrigation may increase the workload for the staff, it is considered to be acceptable for the care of patients with chemical injuries.

Is the intervention evaluated differently by patients, families, comics, and physicians?

It is unlikely that the evaluations will differ among patients, family members, and health-care professionals.

Recommendations in other relevant practice guidelines

Irrigation is recommended in both the ISBI Practice Guidelines for Burn Care, Part 2[5] and the Japanese Dermatological Association's Guidelines for Burn Care.[8]

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CQ8–4

CQ and answer

CQ: Is calcium gluconate useful for chemical injury due to hydrofluoric acid?

Answer: Local administration of calcium gluconate is strongly recommended in the initial treatment of chemical injury caused by hydrofluoric acid (HF) (evidence level Ⅳ, recommendation grade D).

Background and importance

Hydrofluoric acid is a solution of hydrogen fluoride in water and a highly corrosive agent. Exposure to HF at concentrations of greater than 50% causes immediate intense pain and with apparent tissue destruction. When exposed to HF with concentrations of 21–50%, the symptoms usually become apparent 1–8 h following exposure. Less than 20% HF may not produce pain or erythema until as late as 24 h after exposure.

Hydrofluoric acid causes coagulative protein necrosis and direct destruction of exposed tissues. HF penetrates tissue readily, after which it produces large amounts of fluoride ions that bind to calcium and magnesium ions in tissues, resulting in severe pain and progressive tissue necrosis. Furthermore, as fluoride ions are easily absorbed into the blood circulation, it can also cause systemic symptoms such as arrhythmia due to hypocalcemia. As an initial treatment for chemical injury caused by HF, any residual HF should be diluted and removed and free fluoride ions should be neutralized with copious lavage and local administration of calcium gluconate.

Therefore, we considered it is important to examine the usefulness of calcium gluconate in this guideline, and formulated the CQ.

PICO

Patient: Patients with chemical injury due to HF
Intervention: Treated with calcium gluconate
Control: Not treated with calcium gluconate
Outcome: Pain relief, prevention of aggravation

Summary of evidence (results of SR)

No RCT
No Cochrane SR

Level of evidence

Level VI

Summary of benefits

Topical use of 2.5–5% calcium gluconate gel after copious lavage has been widely reported as an initial treatment for chemical injury caused by HF.[1,2] Topical application with poultices, subcutaneous injection of 0.5 m per 1 cm^2 of 8.5–10% solution, intravenous injection of 2.5% solution, and intra-arterial injection of 2–5% solution have been reported.[1,3–5] As there is a limit to the skin permeability of calcium administered externally, subcutaneous injection, intravenous injection, and intra-arterial injection are performed when the pain persists even after external application.

Many reports have stated that topical administration of calcium gluconate reduced pain and prevented aggravation.

Summary of the harms

It should be noted that excessive calcium administration may cause cell damage, delayed wound healing, vasculitis, electrolyte abnormalities such as hypercalcemia, and arrhythmia. When subcutaneous injection is given to a finger, if the dose is higher than the above-mentioned amount, severe pain may occur or peripheral circulatory disorder may occur due to exacerbation of swelling.

Balance between benefits and harms

No evidence was obtained to evaluate the effect of calcium gluconate, but from the above evaluation of benefits and disadvantages, it is considered that the benefits outweigh the harms by treating while paying attention to the harms caused by topical administration of calcium gluconate.

Medical costs of this intervention

The drug price of 8.5% calcium gluconate injection is approximately 36–50 yen per 5 mL. The dose of calcium gluconate creates costs. For example, the drug cost for preparing 50 mL of a 2.5% calcium gluconate gel is the sum of 100–180 yen for 14.7 mL of an 8.5% calcium gluconate injection and the cost of the base.

Feasibility of this intervention

Calcium gluconate is a therapeutic drug for hypocalcemia covered by insurance, but it is a preparation of an injection solution for intravenous injection or a powder for oral administration, and there is no external medicine. Currently, inhospital preparations are used for external medicines, therefore explanations to patients and their families and inhospital procedures may be required when using them.

Although there is a burden on pharmacists due to inhospital preparations, it is considered to be acceptable as an initial treatment for patients with chemical injury caused by HF.

Is the intervention differently evaluated by the patients, family members, medical staff, and physicians?

The evaluations of patients, their family members, and healthcare professionals are unlikely to differ. There may be some resistance to the fact that it is not covered by Japanese insurance.

Recommendations in other relevant clinical practice guidelines

The Japanese Dermatological Association Guidelines (2nd Edition) recommend topical application of calcium gluconate and intra-arterial infusion of 2–5% calcium gluconate solution.[6] The ISBI Practice Guidelines for Burn Care (Part 2) recommend topical application of calcium-containing gels. For severe cases, calcium injection into tissues or intra-arterial or intravenous infusion is recommended.[7]

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CQ9 ANALGESIA AND SEDATION

AS ANALGESIA AND sedation were not included in the Japanese Burn Care Guidelines (Revised 2nd Edition), they were newly established. The ISBI Practice Guidelines for Burn Care (2016)[1] and the ABA's ABLS[2] were used as references for the new section. The ISBI Practice Guidelines for Burn Care (2016) focus on developing countries with limited medical resources, and the protocol for pain relief is left to each region, while the ABLS mentions the use of morphine or equivalent opioids for pain and anxiolytics.

As for pain management guidelines, the Guidelines for the Management of Pain, Sedation, and Delirium in Adult Intensive Care Unit Patients (PADIS guidelines)[3] are well known, and there are also other guidelines and sample pain management protocols in burn textbooks such as Total Burn Care[4] and Burn Care and Treatment.[5]

Hence, this CQ targeted analgesia and sedation management during intubation in the ICU, analgesia and sedation management in the general ward after extubation, analgesia and sedation management during invasive procedures, and pain assessment methods.

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CQ9–1

CQ and answer

CQ: How do you perform analgesia/sedation during tracheal intubation?

Intravenous opioids are considered the first choice for analgesia, and opioid analgesics are used in combination to reduce the dose of intravenous opioids. Non-benzodiazepine sedative agents are preferred over benzodiazepine sedative drugs during tracheal intubation.

Background and importance of CQ

Opioids are the mainstay of pain control for patients with systemic burns under ICU management in Japan. Patient outcomes may be exacerbated because of sedatives, delirium, respiratory depression, ileus, and immunosuppressive illness. Hence, a multifaceted analgesic approach has been used in combination with nonopioid analgesics, such as acetaminophen and ketamine, to reduce the use of perioperative opioids and optimize postoperative analgesia and rehabilitation.[1] However, the choice and timing of nonopioid analgesics varies greatly depending on the patient's condition, and the consensus among institutions varies widely, so it remains controversial. Similarly, regarding sedation, it can be said that there is a large difference between the patient's condition and the institution. Therefore, this CQ was presented as a BQ to introduce the current evidence on analgesia and sedation during tracheal intubation.

Evidence and commentary

Although not a study of burn patients, one RCT combined the use of acetaminophen and opioids and showed a decrease in postoperative pain and opioid use in ICU inpatients.[2] In one study, opioid consumption was mostly reduced and the length of intubation, sedation, and complication of nausea were significantly improved in the acetaminophen group.[3] A single-facility double-blind RCT that included ICU patients after abdominal surgery showed the additional administration of ketamine was associated with a decrease in morphine usage.[4] According to the PADIS guidelines, nonbenzodiazepine sedatives (propofol or dexmedetomidine) are conditionally recommended[5] because improved short-term outcomes such as ICU admission period, mechanical ventilation period and delirium in critically ill adult patients was shown in the nonbenzodiazepine sedative group, as compared to the benzodiazepine sedative (midazolam or lorazepam) group. Seven RCTs[6–12] on sedation of patients on ventilator management after cardiac surgery and nine studies on sedation of patients on ventilator management for medical and noncardiac surgery[13–20] reported that propofol takes significantly less time to extubate than benzodiazepine.

Six RCTs[20–25] compared the effectiveness of benzodiazepines and dexmedetomidine; their pooled analysis showed no significant difference in mechanical ventilation period or delirium risk. However, in the Safety and Efficacy of Dexmedetomidine Compared with Midazolam (SEDCOM),[21] which was the least biased study, dexmedetomidine was the most useful sedative in terms of the length of intubation and the occurrence of delirium, compared to continuous intravenous benzodiazepine sedatives. In addition, in burn patients on intravenous lidocaine, the amount of opioid use reduced by 25%;[26] however, lidocaine is an off-label drug for arrhythmia in Japan.

Recommendation decision process

The guideline met the prescribed adoption criteria at the first vote.

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CQ9–2

CQ and answer

CQ: How do you perform analgesia and sedation when patients are not intubated?

Answer: Nonopioid analgesics are used to reduce the amount of intravenous opioids in patients in the recovery stage of severe burns in general wards where monitoring and observation are reduced. It has been reported that long-term administration of opioids should include comprehensive treatment including physical/occupational therapy, psychological counseling, and other alternative therapies.

Background and importance of CQ

Although there are various reports on analgesia and sedation in the acute phase of burns, little is known about the long-term pain course and patient satisfaction after severe burns.[1] Patients with severe burns have various pains and anxieties other than intubation/general care and burn treatment, and analgesia/sedation is important, especially in the convalescent or rehabilitation period. However, the causes of pain and anxiety in burn patients are complicated, and there is no unified guideline on analgesia and sedation. Therefore, in this guideline, this CQ was presented as a BQ to introduce the current evidence. Acute treatment of severe burns mainly involves opioids, and in many cases, treatment in ICU is required. CQ9–1 discusses analgesia and sedation during

intubation. CQ9–3 discusses pain during nonintubation, pain and sedation during perioperative, and treatment. CQ9–2 cites the literature on analgesia and sedation mainly for convalescent rehabilitation and chronic pain after burn.

Evidence and commentary

The situations that require pain control during nonintubation in burn patients can be broadly divided into the acute phase, from emergency transport to ICU admission, and the chronic phase, from surgery to the start of rehabilitation and transfer to the general ward. Multilateral analgesic approaches have been used in combination with nonopioid analgesics, such as acetaminophen and ketamine, to reduce the use of perioperative opioids and optimize postoperative analgesia and rehabilitation.[2] The prevalence of chronic persistent pain after burns is estimated to be 35–52%.[3,4]

In a survey of 492 survivors of burns, Browne *et al.* reported that 18% had persistent burn-related pain, 27% had depression, and 14% had posttraumatic stress symptoms.[1] Although not common in Japan, opioids may be used continuously for a long period of time overseas to manage chronic persistent pain after burns.[5] Long-term opioid use requires comprehensive treatment, including physiotherapy/occupational therapy, psychological counseling, and other alternative therapies, and patients should be referred to a pain management specialist for chronic pain.[6]

Recommendation decision process

The guideline met the prescribed adoption criteria at the first vote.

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CQ9–3

CQ and answer

CQ: What are the analgesic methods for local treatment of burns?

Answer: It has been reported that low-dose opioids should be adjusted to determine the minimal amount of analgesic effect that can be expected. The use of intravenous ketamine hydrochloride has been reported. There are reports on the use of intravenous, oral, and transrectal nonsteroidal anti-inflammatory drugs (NSAIDs) as alternatives to opioids.

Background and importance of CQ

The pain of burn treatment varies depending on the area and depth of the burn wound, the progress of treatment, and the degree of scarring, as well as the patient's pain threshold. In any case, it is essential to consider adequate analgesia, and opioids may be the first choice for analgesia during local treatment such as dressing changes. However, it is important to consider the choice of medication when pain at rest has improved and opioids are no longer needed or when temporary intravenous or oral analgesia is sufficient. This CQ was presented as a BQ to introduce the current evidence on analgesia during treatment, as we did not find a valid RCT on this topic.

Evidence and commentary

The 2018 PADIS guidelines reported the efficacy of non-pharmacological interventions such as relaxation and the use of analgesics prior to the procedure to reduce the pain associated with local treatment.[1] As a pharmacological intervention, opioids such as fentanyl, hydromorphone, morphine, and remifentanil can be used at the lowest possible volume for analgesic effect. In a comparison of the analgesic effects of high-dose and low-dose remifentanil before and after invasive procedures such as repositioning and removal of chest drains, pain was reduced in both groups, but the effect was significant in the high-dose group.[2] In one study, the behavioral pain scale score was significantly lower in the intravenous fentanyl group than in the placebo group before repositioning.[3] However, several patients in the high-dose opioid group developed complications such as apnea and respiratory depression requiring back-mask ventilation. Hence, the use of opioids at the lowest effective dose was

desirable for pain associated with the procedure because of the adverse effects of high-dose opioids in critically ill patients and the fact that certain effects can be achieved even at low doses. Other reports indicated that intravenous ketamine (0.5 to 1.0 mg/kg) was effective for analgesia during procedures such as dressing changes,[4] but problems such as hallucinations and a rather long duration of action were pointed out. Some studies reported that extreme deep sedation could be avoided by using intravenous midazolam if necessary.[5] One study reported the use of intravenous, oral, and transrectal NSAIDs as an alternative to opioids.[6] This study did not focus on the treatment of burns, but on the pain of thoracic drain removal; it reported that there was no significant difference between a single dose of 4 mg intravenous morphine and a single dose of 30 mg ketorolac (non-COX-1 selective NSAIDs). This suggests that NSAIDs may be an alternative to opioid-based analgesia.

Recommendation decision process

The guideline met the specified criteria for adoption at the first ballot.

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CQ9–4

CQ and answer

HOW DO YOU assess pain in burn patients?

There are reports on pain assessment to ensure appropriate analgesia. Pain assessment should be performed multiple times per day, depending on the timing of treatment, and should be protocolized for pain. There are reports that the Burn Specific Pain Anxiety Scale (BSPAS) is used as a tool to assess pain in the acute phase of burn injury.

If the patient is able to self-report pain, the Numeric Rating Scale (NRS), Visual Analogue Scale (VAS), Behavioral Pain Scale (BPS), and Critical-Care Pain Observation Tool (CPOT) have been reported to be used.

Background and importance of CQ

Burn patients often experience not only physical pain but also psychological distress such as fear of death and anxiety due to wound scarring in severe cases. Pain assessment is necessary for appropriate analgesia, but the "pain" complained of by burn patients is complex, and its mechanism is still controversial. Therefore, this guideline was presented as a BQ to introduce current evidence on pain assessment.

Evidence and commentary

Burn injuries are said to be one of the most painful conditions that a person can endure.[1] In addition, burn pain varies according to the time of injury, type of treatment such as debridement, skin grafting, and burn treatment, and rehabilitation.[2]

Therefore, it is necessary to conduct multiple evaluations and develop protocols for burn treatment.

There are very few pain assessment criteria specific to burns, and although there are reports of BSPAS for pain assessment in the acute phase of burns, it is usually assessed in accordance with general trauma criteria.[3,4] Hence, we will refer to the 2018 PADIS guidelines.[5]

Self-reporting scales and behavioral assessment tools have been used as methods for assessing pain in critically ill adult patients who can self-report their pain. The following assessment methods are used: (i) 0–10 cm VAS-Horizontal, (ii) 0–10 cm VAS-Vertical, (iii) Verbal Descriptor Scale, (iv) 0–10 NRS-Oral, and (v) 0–10 NRS-Visual (NRS-V).

The NRS-V has the highest sensitivity, negative predictive value, and accuracy;[6–8] it is the most appropriate test method due to its simplicity. For patients who cannot express the degree of pain, the BPS and CPOT, as behavioral assessment tools, showed the best validity and reliability for pain monitoring.[9–12]

Recommendation decision process

The criteria for adoption were met in the first round of voting.

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CQ10 TRANSFUSION

BLOOD TRANSFUSION IS an important treatment for burn patients, especially for severe burns that require intensive care.[1] Insurance in Japan is required to comply with the Practical Guidelines for Blood Products by the Ministry of Health, Labor and Welfare, Japan.[2] There are few descriptions and guidelines regarding blood transfusion therapy for burn patients.[2,3] In the third revised edition of these Guidelines, a new section on blood transfusion therapy has been added, and three CQs that are often encountered in clinical practice regarding red blood cells, plasma, and platelets, which are blood products mainly used in burn treatment, are discussed in this section. Red blood cell transfusion is often required during the perioperative period for bleeding and anemia associated with burn surgery, rather than for initial treatment or resuscitation of burn patients.[3] In recent years, restricted blood transfusion strategies for critically ill patients have been attracting attention in various fields.[4] CQ10–1 explains the strategies for red blood cell transfusion for burn patients. Fresh frozen plasma may be used for initial treatment and resuscitation in patients with severe burns with coagulopathy (see the section on initial fluid replacement). In this section, CQ10–2 describes the indications for administering FFP during the perioperative period. Furthermore, in burn patients who frequently undergo surgery or treatment with bleeding, a decrease in platelet count and bleeding tendency may be observed, and it is often difficult to manage. CQ10–3 explains the threshold for administering platelet transfusions to burn patients.

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CQ10–1

CQ and answer

CQ: What is the target hemoglobin level for red blood cell transfusion in patients with acute burns?

Answer: It is weakly recommended for a target of 7–8 g/dL (level of evidence Ⅱ, grade of recommendation B).

Background and importance of CQ

In the ICU, approximately 25% of the patients receive red blood cell transfusion. Red blood cell transfusion plays an

important role in the acute treatment of critically ill patients.[1] A study of patients in the ICU compared a restrictive strategy for red blood cell transfusion with a hemoglobin level target of 7–8 g/dL and a liberal transfusion strategy with a target of 10–11 g/dL, and there was no significant difference in mortality among them.[2] In recent years, the effectiveness of restrictive blood transfusion strategies has been reported in various diseases.[3]

Patients with burns may develop anemia due to bleeding during surgery, decreased red blood cell production, destruction of red blood cells, and iatrogenic factors from frequent blood tests and may require red blood cell transfusion.[4] It has been reported that 34–74.7% of burn patients required red blood cell transfusion during hospitalization.[5,6] This CQ was designed as a highly important CQ about red blood cell transfusion, which is a frequently used treatment strategy for burn patients.

PICO

Patient: Patients with acute burns requiring red blood cell transfusion
Intervention: Red blood cell transfusion at a target of 7–8 g/dL.
Control: Red blood cell transfusion at a target of 10–11 g/dL.
Outcome: Mortality, blood transfusion volume, complications

Summary of evidence (results of SR)

References used: One RCT

Palmieri TL, Holmes JH, Arnoldo B *et al*. Transfusion requirement in burn care evaluation (TRIBE). Ann. Surg. 2017; 266: 595–602.[7]

This prospective, multicenter RCT compared a restrictive transfusion strategy (target hemoglobin level of 7–8 g/dL) with a liberal transfusion strategy (target hemoglobin level of 10–11 g/dL) for burn patients with a burn area of 20% or more during their hospital stay. There was no significant difference in the 30-day mortality between the two groups. In addition, the transfusion volume of the restrictive blood transfusion strategy group was smaller than that of the liberal transfusion strategy group, and there were no significant differences in the incidence of wound infection or organ failure, the number of days of mechanical ventilation, or the time to wound healing.[7]

No Cochrane SR

Level of evidence

Level II: One or more RCTs

Summary of benefits

The benefits of restrictive transfusion strategies that limit hemoglobin levels to 7–8 g/dL have not been confirmed, but reducing transfusion volume may reduce the risk of infections and allergies as well as medical costs.

Summary of harms

Restrictive transfusion strategies did not significantly affect the incidence of wound infection or organ failure, ventilator free days, 30-day mortality, or time to wound healing. It is considered that there is no harm associated with restrictive transfusion strategy. However, ischemic complications due to restricted blood transfusions may occur in burn patients with heart disease.

Balance between benefits and harms

The benefits outweigh the harms. Restrictive transfusion strategies can reduce the amount of transfusions without increasing mortality. The balance between benefits and harms is unclear as this aspect has not been examined for burn patients with heart disease. In addition, special caution is required in cases of massive bleeding during surgery and procedures.

Medical cost of this intervention

Irradiated Red Blood Cells, Leukocytes Reduced (Nisseki; 280 mL), which is commonly used for red blood cell transfusion in Japan, costs JPY 18,132.

Feasibility of this intervention

Red blood cell transfusions can be carried out in most hospitals in Japan. In some hospitals, it is difficult to obtain red blood cells at night and on holidays. The same is true when massive transfusions are required to treat massive hemorrhage. It is necessary to consider that blood products are a limited medical resource derived from blood donations.

Are the interventions evaluated differently by patients, families, medical staff, and physicians?

There are individual differences in their evaluations. Some patients and their families may refuse blood transfusions for religious reasons. However, there is no significant difference in the evaluations for restricted blood transfusions.

Recommendation of the final project

The guideline met the specified criteria for adoption at the first ballot.

Recommendation in other relevant practice guidelines

This recommendation is not listed in the JSBI Clinical Practice Guidelines for Management of Burn Care (2nd Edition), Guidelines for the Management of Burns of the Japanese Dermatological Association (2016), ISBI Practice Guidelines for Burn Care Part 2 (2018), European Practice Guidelines for Burn Care (2017), or ABLS.

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CQ10–2

CQ and answer

CQ: What are the indicators for the administration of FFP to patients with acute burns?

Answer: It is weakly recommended based on the results of viscoelastic testing during the perioperative period of burn patients (level of evidence II, grade of recommendation B) (*).

There are no indicators for administration of FFP specific to burn patients, except in the perioperative period, and it should be used according to the results of conventional blood coagulation testing (level of evidence VI, grade of recommendation C).

Background and importance of CQ

In recent years, coagulopathy in trauma patients has attracted attention. It is recommended to administer FFP early for massive traumatic hemorrhage.[1] Coagulopathy is also common in burn patients. Hypercoagulation is common in burn patients in the acute phase,[2,3] and hyperfibrinolysis in burn patients is associated with increased mortality.[4,5] Burn surgery often results in a large amount of bleeding,[6] and coagulopathy may be observed with bleeding. Therefore, in addition to red blood cell transfusion, FFP is administered intraoperatively.[7–9]

According to the practical guidelines for blood products by the Ministry of Health, Labor and Welfare, Japan,[10] prolongation of PT and APTT (PT of international normalized ratio 2.0 or more or activity of 30% or less, APTT of more than twice the upper limit of the standard in each medical institution or 25% or less of activity value), and the fibrinogen level of less than 150 mg/dL is the threshold for administering FFP. However, these are not specific indicators for burn patients and are controversial.

In this CQ, we examined the indications for administration of FFP to burn patients.

PICO

Patient: Acute burn patients requiring FFP
Intervention: Administer FFP based on some indicator (red blood cell transfusion ratio, conventional coagulation testing, viscoelastic testing, etc.)
Control: Administer FFP without considering indicators
Outcome: Mortality, blood transfusion volume, complications

Summary of evidence (results of SR)

References used: One RCT

Schaden E, Kimberger O, Kraincuk P *et al*. Perioperative treatment algorithm for bleeding burn patients reduces allogeneic blood product requirements. Br. J. Anaesth. 2012; 109: 376–81.[11]

This was a single-center RCT that compared a group of burn patients treated for coagulopathy based on the clinician's decision in the perioperative period and a group treated for coagulopathy based on the algorithm of Australian

guidelines using viscoelastic testing. Mortality was not investigated, but the dose of FFP was reduced in the group using viscoelastic testing.

No Cochrane SR

Level of evidence

Level II: One or more RCTs

Summary of benefits

In the perioperative period of burn surgery, it is expected that the amount of blood products transfused will be reduced by administering FFP based on the results of viscoelastic testing. However, the reduction of mortality and morbidity in burn patients has not been reported.

There was no evidence of indications for the administration of FFP to burn patients, except in the perioperative period.

Summary of harms

When performing the viscoelastic test, there is a small physical burden on the patient, as approximately 2 mL blood is collected for the test. In the case of other diseases, the administration of FFP based on the viscoelastic testing may increase the risk of acute kidney injury and dialysis. However, such adverse events have not been reported in burn patients.

Balance between benefits and harms

In the perioperative period, the benefits of administering FFP to burn patients using viscoelastic testing as an indicator are likely to outweigh the harms. In the guidelines of the Ministry of Health, Labor and Welfare, Japan, there was no specific mention about burn patients.

Medical costs of this intervention

The drug price of FFP, leukocytes reduced (Nisseki; 240 mL), which is commonly used in Japan, is 18,322 yen. The cost of the viscoelastic testing devices, ROTEM sigma and TEG6s, is high. The cost of one examination is approximately 10,000 yen; 28 medical remuneration points can be calculated as the cost of thromboelastography.

Feasibility of this intervention

Viscoelastic tests for burn patients are not covered by national health insurance in Japan, so the cost is a problem. The expensive testing device is only available in a few hospitals in Japan. If the testing device is installed in the hospital, the testing itself is simple and can generally be performed at the bedside.

Are the interventions evaluated differently by patients, families, medical staff, and physicians?

It is presumed that there is little variation in their evaluations of viscoelastic tests. As the test is not covered by insurance, the cost may be evaluated differently. In addition, the effect of using viscoelastic testing on mortality is not certain and may be evaluated differently.

Recommendation decision process

The guideline met the prescribed adoption criteria at the second vote. After that, discussions were held by the committee. After dividing the recommendation text into two parts, a third vote was held to confirm the adoption.

Recommendation in other relevant practice guidelines

This intervention is not listed in the JSBI Clinical Practice Guidelines for Management of Burn Care (2nd Edition), Guidelines for the Management of Burns of the Japanese Dermatological Association (2016), ISBI Practice Guidelines for Burn Care Part 2 (2018), European Practice Guidelines for Burn Care (2017), or ABLS.

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CQ10–3

CQ and answer

CQ: Is platelet transfusion necessary for patients with acute burns?

Answer: If the patient does not have bleeding tendency and does not require surgical procedures, it is strongly recommended not to transfuse platelets to patients with acute burns (level of evidence VI, grade of recommendation D).

If the patient has bleeding tendency or requires surgical procedures, it is recommended to administer platelet transfusion so that the platelet count is maintained at 50,000/μL or more, according to the Guidelines for Blood Products of the Ministry of Health, Labor and Welfare, Japan (level of evidence VI, grade of recommendation C).

Background and importance of CQ

In Japan, platelets transfusion are often administered in accordance with the guideline for blood products of Ministry of Health, Labor and Welfare, Japan.[1] In general, when the platelet count is 50,000/μL or higher, serious bleeding due to thrombocytopenia is rare and platelet transfusion is rarely required. When the platelet count is 20,000–50,000/μL, bleeding tendency is sometimes observed, and platelet transfusion is required when hemostasis is difficult. During the perioperative period, it is recommended to perform platelet transfusion to maintain a platelet count of 50,000/μL or higher.

In the treatment of burn patients, there is a high risk of bleeding due to multiple surgeries and surgical procedures.[2] Patients with severe burns often have low platelet counts and are given platelet transfusions.[3,4] Therefore, platelet transfusion in burn patients is an important clinical issue and taken up as CQ.

PICO

Patient: Patient with fresh burns
Intervention: Administer platelet transfusion, when there is no bleeding tendency and no surgical procedure is required
Control: Do not administer platelet transfusion if there is no bleeding tendency and no surgical procedure is required
Outcome: Mortality, transfusion volume, complications

Summary of evidence (results of SR)

No RCT
No Cochrane SR

Level of evidence

Level VI: Reports and opinions of expert committees or clinical experience of experts

Summary of benefits

There was no literature adopted for benefits. The benefits of transfusing platelets to burn patients who have no bleeding tendency and do not require surgical procedures have not been demonstrated. There is no evidence of the number of platelets that should be used as the threshold for administering platelet transfusion during the perioperative period of patients with burns. The benefit of administering platelets transfusion with a specific platelet count such as 50,000/μL or more as the threshold has not been proven. As patients with burns often bleed due to frequent dressing changes and surgical procedures, keeping the platelet count high may reduce the amount of bleeding. But its effectiveness has not been proven.

Summary of harms

Platelet transfusions if provided more than necessary may increase the risk of allergies and infections and medical costs.

Balance between benefits and harms

The benefits of platelet transfusions for burn patients have not been demonstrated when patients do not have a bleeding tendency and do not require surgical intervention.

Considering that transfusions more than necessary may increase the risk of allergies and infectious diseases, the harm caused by the intervention is considered to outweigh the benefits. Because burn patients require frequent dressing changes and surgical procedures, signs of bleeding tendency should be carefully observed. According to the Guidelines for Blood Products of the Ministry of Health, Labor and Welfare, Japan,[1] when the platelet count is 10,000–20,000/μL, severe bleeding may occur and platelet transfusion may be required. Platelet transfusion is required when the platelet count is less than 10,000/μL, as severe bleeding often occurs. If thrombocytopenia is significant, it is advisable to follow this guideline.

Medical costs of this intervention

The platelet transfusion product commonly used in Japan, Irradiated Platelet Concentrate, Leukocytes Reduced, (Nisseki) costs JPY 80,872/10 units.

Feasibility of this intervention

Transfusion of platelets to patients with decreased platelet count is a common clinical practice in Japan, as described in the Guidelines for Blood Products of the Ministry of Health, Labor and Welfare, Japan. Platelet transfusions are possible in most hospitals in Japan. However, in some hospitals and regions, it may be difficult to obtain platelet products and emergency transfusions at night and on holidays.

Are the interventions evaluated differently by patients, families, co-medical, and physicians?

Individuals have different ideas about blood transfusions. Some patients and their families refuse blood transfusions for religious reasons. The assessment of not performing platelet transfusions more than necessary does not differ significantly.

Recommendation of the final project

The first vote met the prescribed adoption criteria. After that, the committee discussed and divided the recommended text into two parts. The third vote met the adoption criteria.

Recommendation in other relevant practice guidelines

Not listed in the JSBI Clinical Practice Guidelines for Management of Burn Care (2nd Edition), Guidelines for the Management of Burns of the Japanese Dermatological Association (2016), the ISBI Practice Guidelines for Burn Care Part 2 (2018), European Practice Guidelines for Burn Care (2017), or ABLS.

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CQ11 DEEP VEIN THROMBOSIS

VENOUS THROMBOEMBOLISM, INCLUDING deep vein thrombosis (DVT) and pulmonary embolism, are fatal complications of hospitalized patients. The number of patients is increasing in Japan due to the improvement of diagnosis.[1] The importance of prophylaxis against DVT is widely recognized in postoperative patients and critically ill patients in hospital, and several guidelines have been published in Japan.[2,3] However, there are few descriptions in the guidelines about prophylaxis against DVT of hospitalized burn patients.

Burn patients may be at high risk of DVT due to acute coagulopathy, multiple surgeries, wound rest, bed rest, and long-term stay in ICU and hospital.[4,5] On the other hand, surgical bleeding and bleeding tendency associated with frequent wound treatment are important issues when introducing anticoagulant as the prophylaxis against DVT. Risk assessment and prevention of DVT based on the specificity of pathophysiology and the treatment of burns are necessary.

In this revised guideline, a new section on prophylaxis against DVT for burn patients has been added.

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CQ11–1

CQ and answer

CQ: How are risk assessment and indications for prophylaxis against DVT determined for burn patients?

Answer: There is no specific method of risk assessment of DVT in burn patients. Indications for prophylaxis against DVT in burn patients are determined according to the risk assessment of DVT in general inpatients and ICU patients. Specific risks of DVT for burn patients include burn area, multiple surgeries, and inhalation injury.

Background and importance of CQ

Venous thromboembolism in inpatients, postoperative patients, and critically ill patients in the ICU is a widely recognized complication requiring prophylaxis. This also applies to burn patients. The frequency of DVT in burn patients is reported to be 0.25–5.92%.[1–9]

Although prophylaxis against DVT would be based on individual risk assessments, the specific methods of risk assessment of DVT for burn patients are not yet established. This CQ is presented as a BQ that introduces current evidence on the assessment of DVT risk in burn patients.

Evidence and commentary

Practical guidelines for the prevention of DVT in burn patients have been published, but no explanation has been given for risk assessment methods specific to burn patients.[10,11] A study showed that the Caprini score,[12] one of the famous risk assessment scores for DVT, is also useful for burn patients.[13] Other risk factors for DVT in burn patients include Black race,[2] age,[5,7,14] male sex,[7] Abbreviated Burn Severity Index,[13] burn area,[1,2,5–7,14,15] central venous catheter,[6,7,16] obesity,[7,14] ventilator management,[2,5] ICU stay,[5,15] length of hospital stay,[5,6,15] multiple surgeries,[3,5,7] burn wound infection,[3] blood transfusion,[2,7,16] inhalation injury,[5,15] and lower limb burn.[3] On the other hand, there is a report that age and burn area were not related to the frequency of DVT in burn patients.[3]

Recommendation decision process

The guideline met the prescribed adoption criteria at the first vote.

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CQ11–2

CQ and answer

CQ: Is mechanical prophylaxis used to prevent DVT in burn patients?

Answer: Mechanical prophylaxis is recommended to prevent DVT in burn patients. However, in patients with lower limb burns, the indication should be carefully decided (level of evidence VI, grade of recommendation C).

Background and importance of CQ

Venous thromboembolism in inpatients and postoperative patients is widely recognized as a complication requiring prevention. Assessment of the risk of developing DVT and prevention are recommended. Mechanical prophylaxis includes compression stockings and intermittent pneumatic compression. These are mainly used at moderate risk and are recommended in combination with anticoagulant therapy at high risk. It is also an option when the risk of bleeding is high and anticoagulants cannot be introduced.[1,2] This CQ was designed to address mechanical prophylaxis against DVT in burn patients.

PICO

Patient: Patient with fresh burns
Intervention: Mechanical prophylaxis
Control: No mechanical prophylaxis
Outcome: 28-day mortality, incidence of DVT and pulmonary embolism

Summary of evidence (results of SR)

No RCT
No Cochrane SR

Level of evidence

Level VI: Reports and opinions of expert committees or clinical experience of experts

Summary of benefits

Although there was no evidence limited to burn patients, mechanical prophylaxis is expected to prevent the development of DVT and pulmonary embolism in burn patients.

Summary of harms

There is no evidence evaluated exclusively for burn patients, and the frequency and severity of side effects of mechanical prophylaxis to burn patients are unknown. Regarding mechanical prophylaxis, there is concern about the risk of delaying wound healing due to compression in patients with lower extremity burns.

Balance between benefits and harms

In the absence of lower limb burns, the benefits are considered to outweigh the harms. There is no evidence to evaluate the choice of compression stockings or intermittent pneumatic compression in burn patients.

Medical cost of this intervention

A set of compression stockings costs approximately 3,000 yen, which is not expensive. The intermittent pneumatic compression device costs approximately 300,000 yen per unit, and it may be difficult to install for all target patients depending on the facility. When using compression stockings or intermittent pneumatic compression devices, 305 medical remuneration points are calculated only once during a hospitalization as a pulmonary thromboembolism prophylaxis management cost.

Feasibility of this intervention

Compression stockings are marketed for medical use and are commonly adopted in perioperative patients and

inpatients who require bed rest. The numbers of intermittent pneumatic compression devices are limited at some hospitals, and it can be difficult to use them for all target patients.

Are the interventions evaluated differently by patients, families, medical staff, and physicians?

The evaluations might not differ much. However, if there are burns in the lower limbs, physicians, nurses, and patients may have different assessments of the need for the mechanical prophylaxis.

Recommendation decision process

The guideline met the prescribed adoption criteria at the first vote.

Recommendation in other relevant practice guidelines

It is not mentioned in the JSBI Clinical Practice Guidelines for Management of Burn Care (Revised 2nd Edition) or Guidelines for the Management of Burns of the Japanese Dermatological Association (2016). The ISBI Practice Guidelines for Burn Care Part 2 (2018) recommends that mechanical prophylaxis would be used in combination with anticoagulant depending on the risk of DVT in burn patients.[3] The Guidelines for Diagnosis, Treatment, and Prevention of Pulmonary Thromboembolism and Deep Vein Thrombosis (JCS 2017) recommends the use of compression stockings or intermittent pneumatic compression for moderate-risk patients, and intermittent pneumatic compression or anticoagulant for high-risk patients. For extremely high-risk patients, it is recommended to combine pharmacological prophylaxis with intermittent pneumatic compression or pharmacological prophylaxis with compression stockings. Intermittent pneumatic compression is recommended for patients at high risk of bleeding, but there is no specific mention about burn patients.[1] The Japanese Guideline for Prevention of Venous Thromboembolism describes the prophylaxis against DVT for a patient with burns: "Although there is little evidence for the prophylaxis against venous thrombosis in burn patients, prophylaxis should be considered if risk factors such as leg injuries, older age, major burns, obesity, long-term bed rest, and central venous catheter placement are present."[2]

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CQ11–3

CQ and answer

CQ: Can anticoagulants be used as pharmacologic prophylaxis against DVT in burn patients?

Answer: We weakly recommend the use of low-molecular-weight heparin against DVT in burn patients (level of evidence II, grade of recommendation B) (*).

Background and importance of CQ

Venous thromboembolism in inpatients and postoperative patients is widely recognized as a complication requiring prophylaxis. Risk assessment and prevention of developing DVT are recommended. Anticoagulants such as unfractionated heparin and low-molecular-weight heparin are recommended.[1] In recent years, direct oral anticoagulant has been used after orthopedic surgery.[2] These anticoagulants are mainly used for patients at moderate or high risk, and it is recommended to use them in combination with mechanical prophylaxis.[1] If the risk of bleeding is high, their indication should be decided carefully. The prophylaxis against DVT by anticoagulants is important for burn patients; hence, this CQ is important.

PICO

Patient: Patient with fresh burns
Intervention: Anticoagulants (unfractionated heparin, low-molecular-weight heparin, warfarin, direct oral anticoagulant)
Control: No anticoagulants were used
Outcome: 28-day mortality, incidence of DVT and pulmonary embolus

Summary of evidence (results of SR)

References used: One RCT

Ahuja RB, Bansal P, Pradhan GS *et al*. An analysis of deep vein thrombosis in burn patients (part Ⅱ) : A randomized and controlled study of thrombo-prophylaxis with low molecular weight heparin. Burns 2016; 42: 1693–8.[3]

This study compared two groups of severe burn patients with a burn area of 30–60% TBSA: the treatment group received prophylaxis with enoxaparin, which is a low-molecular-weight heparin, and the control group did not receive prophylaxis. In the prophylaxis group, 0.5 mg/kg (maximum 30 mg/day) enoxaparin was subcutaneously injected twice daily from the day of admission. Eight percent of patients in the control group had DVT, whereas none in the prophylaxis group had DVT.

No Cochrane SR

Level of evidence

Level II: One or more RCTs

Summary of benefits

Pharmacological prophylaxis with anticoagulant in burn patients is expected to reduce the incidence of DVT. The literature adopted as evidence did not examine the incidence of pulmonary embolism or mortality.

Summary of harms

There is no description of the harm caused by anticoagulant in the literature adopted. Possible complications with heparin administration are hemorrhagic complications and heparin-induced thrombocytopenia associated, which requires careful management.

Balance between benefits and harms

The benefits outweigh the harms.

Medical cost of this intervention

The price of pharmacological prophylaxis with unfractionated heparin is approximately 1,000 yen/day and that of prophylaxis with enoxaparin is approximately 2,000 yen/day. The cost of anticoagulants is considered to be acceptable.

Feasibility of this intervention

Unfractionated heparin and low-molecular-weight heparin are common drugs adopted and used in many hospitals, and there is no problem with their feasibility. However, prophylactic administration of low-molecular-weight heparin to burn patients is not covered by national health insurance in Japan.

Are the interventions evaluated differently by patients, families, medical staff, and physicians?

The evaluations do not differ among them. However, if the risk of bleeding is high due to burn surgery or wound management, physicians, nurses, and patients may have different assessments of the indication for the intervention.

Recommendation of the final project

The guideline met the prescribed adoption criteria at the first vote.

Recommendation in other relevant practice guidelines

It is not mentioned in The Japanese Society for Burn Injuries (JSBI) Clinical Practice Guidelines for Management of Burn Care (Revised 2nd Edition) or Guidelines for the Management of Burns of the Japanese Dermatological Association (2016). The ISBI Practice Guidelines for Burn Care Part 2 (2018) recommends anticoagulant therapy for patients at moderate-to-high risk of DVT in burn patients.[4] The Guidelines for Diagnosis, Treatment, and Prevention of Pulmonary Thromboembolism and Deep Vein Thrombosis (JCS 2017) recommend intermittent pneumatic compression or anticoagulants for patients at high risk. For extremely high-risk patients, it is recommended to combine pharmacologic prophylaxis with intermittent pneumatic compression or pharmacologic prophylaxis with compression stockings, but there is no specific mention about burn patients.[1] The Japanese Guideline for Prevention of Venous Thromboembolism describes the prophylaxis against DVT for burn patients: "Although there is little evidence for the prophylaxis against venous thrombosis in burn patients, prophylaxis should be considered if risk factors such as leg injuries, older age, major burns, obesity, long-term bed rest, and central venous catheter placement are present."[5]

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CQ12 REHABILITATION

SEVERE BURNS ARE considered to be the most aggressive form of injury with a high risk of progressive physical dysfunction at all stages of the disease. Therefore, appropriate rehabilitation should be continued from the acute phase through the recovery and maintenance phases to minimize the risk of disability.[1] Rehabilitation is very important for burn patients, as it could help them return to the functions and activities of daily life.[1–3] However, there are many cases of delayed recovery and functional impairment due to inappropriate timing and content of interventions.

Rehabilitation was once considered to be an after-treatment, but now it has been proven to be effective and beneficial for a variety of diseases and disorders and is recognized as an essential aspect of good functional prognosis of intensive care patients. On the other hand, the number of severe burns in Japan has been decreasing due to changes in the living environment. In addition, patients with severe diseases are concentrated in specific facilities, and there are differences in the experience of rehabilitation among facilities. The problem is that the content and quality of rehabilitation services provided by different facilities have not been standardized. In order to solve this problem, there is an urgent need to publish a medical guideline that addresses relevant CQs.

Of the seven domestic and international guidelines for burn care, only one included sufficient information on rehabilitation, and the Society's Guidelines for Burn Care (1st and 2nd editions) did not include information on rehabilitation.[4] Fortunately, in this revision, rehabilitation was included for the first time. Furthermore, it is important to note that the working group in charge of this section included many front-line physiotherapists and occupational therapists, and this section was created from a multidisciplinary perspective.

The end users of these Guidelines are not only facilities where patients with severe burns are hospitalized on a regular basis, but also medical personnel in hospitals that treat very few burn patients but at a level of inpatient management. Therefore, we selected CQs that directly relate to questions such as "when can I start moving this patient?" and "how should I perform rehabilitation?" It is hoped that this section will lead to the early return of burn patients to society and improvement of their quality of life (QOL), and will serve as a catalyst for future progress in burn rehabilitation.

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CQ12–1

CQ and answer

CQ: How is postural management performed in general care during the acute phase of burns?

Answer: In clinical practice, the usefulness of postural management in systemic management during the acute phase of burns is well recognized, but the evidence is poor. Several reports recommend the active use of lateral and prone positions as supportive care for respiratory management.

Background and importance of CQ

In general care during the acute phase of burns, postural management is actively practiced not only for the purpose of

protecting skin grafts and wounds,[1] but also as a means for improving the ventilation–perfusion ratio and maintaining and improving oxygenation. However, there are few RCTs that fully demonstrate its importance, and the evidence is scarce. In this guideline, the CQ is answered as a BQ to introduce the current evidence.

Evidence and commentary

There is an SR on body positioning in adult critically ill patients. Twenty-two RCTs involving critically ill adults examined the effects of lateral positioning and respiratory and circulatory complications. Eight studies reported that lateral positioning contributed to improvement in PaO2 levels, but the positionings and repositioning schedules differed between studies, and no clear benefit or risk could be identified; they conclude that further studies are needed.[2]

There is no mention of postural management in the ISBI Practice Guidelines for Burn Care, the Japanese Burn Association's Burn Care Guidelines (1st and revised 2nd editions), or the Japanese Dermatological Association's Burn Care Guidelines (2017 edition). On the other hand, the Guidelines for the Treatment of ARDS (2016) by the Japanese Society of Intensive Care Medicine, the Japanese Respiratory Society, and the Japanese Society of Respiratory Therapy clearly state that the importance of not managing ventilated patients in the supine position is widely accepted.[3]

The management of patients with severe burns in the acute phase in the supine position frequently causes respiratory and motor dysfunction due to immobility, and there is concern about the impact on the prognosis of life and physical function. In patients with severe burns in the acute phase, positional management is presumed to contribute to the prevention of respiratory complications, prevention of bedsores, reduction of edema, maintenance of joint mobility, prevention of scar contracture, and improvement of functional prognosis as supportive care for systemic management.

For postural management, nothing significant is required other than the cost for ward management and training of the staff.

Rehabilitation intervention costs can be calculated in accordance with Japan's public medical insurance system (see 6. Rehabilitation fee).

Recommendation decision process

The guideline met the specified criteria for adoption at the first ballot.

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Rehabilitation fees

MUSCULOSKELETAL REHABILITATION FEE in the disease-specific rehabilitation fee is covered by insurance for burn patients (2020.4.2).

Depending on the medical institution's facility criteria I–III (defined by the number of physicians, full-time physical therapists, and occupational therapists dedicated to musculoskeletal rehabilitation), the volume of rehabilitation interventions can be calculated on a volume-based basis (added to the inpatient management fee). In addition, a comprehensive rehabilitation plan evaluation fee and additional fee for initial and early rehabilitation can be calculated.

1. Rehabilitation fees defined of the disease

Motor rehabilitation fee (I): 185 points per unit (20 min)

Motor unit rehabilitation fee (II): 170 points per unit

Motor unit rehabilitation fee (III): 85 points per unit

Comprehensive rehabilitation plan evaluation (once a month)

2. Comprehensive rehabilitation plan evaluation fee (once a month). Musculoskeletal rehabilitation fee (I, II): 300 points

3. Additional fee for initial and early rehabilitation

Up to 14 days: additional initial cost per unit of 45 points

Thirty points per unit of additional early rehabilitation up to 30 days

Seventy five points per unit up to 14 days

If a patient is admitted to a specific ICU and comprehensive efforts to wean the patient are made by the "early weaning and rehabilitation team," 500 points per day of additional fee for early weaning and rehabilitation will be calculated.

CQ12–2

CQ and answer

CQ: Is physical therapy useful for preventing contracture in the acute phase of burns?

Answer: Physical therapy is recommended in the acute phase of burn injury to prevent contractures (evidence level VI, recommendation grade C).

Background and importance of the CQ

Burn patients (especially extensive) tend to require bed rest to keep the wound rested or to avoid accidental removal of the intubation tube or catheter. Furthermore, in the early stage of injury, thick dressing is applied to absorb a large amount of exudate, so that the movement of moving parts is suppressed. Significant edema persists in poor limb position and joint contracture occurs in areas not directly affected by thermal injury. Immediately after skin grafting, rest is often required. The range of motion is further reduced by scar contracture. Contractures directly lead to a decrease in activities of daily life (ADLs), and even after wound closure is achieved, patients are forced to undergo long-term rehabilitation and surgery to release the contractures, leading to a delay in their return to daily life.

Rehabilitation for the purpose of preventing contracture includes exercise therapy and physical therapy. In exercise therapy, range of motion training, muscle strengthening, and basic movement training are mainly performed, and in physical therapy, hot packs and compression therapy (hand incubator) are used. Many of these interventions can be introduced from the early stages of injury. In addition to exercise therapy and physical therapy, joint contracture may be prevented by orthosis therapy and positioning.

As there are still some cases in which the start of physical therapy is delayed considering the importance of rest, and the recovery of function is significantly prolonged, we designed this CQ to clarify the usefulness of actively introducing physical therapy from the acute stage.

PICO

Patient: Acute burn patients
Intervention: Actively perform physical therapy from the acute stage
Control: No physical therapy or only passive physiotherapy in the acute phase

Outcome: Prevention of joint contracture (maintenance of range of motion), prevention of deep vein thrombosis, reduction of surgery (for release of contracture), improvement of ADL, shortening of hospitalization period, early reintegration into daily life, graft failure, increased number of surgeries (due to reoperations), pain

Summary of evidence (results of SR)

No RCT
No Cochrane SR

Level of evidence

Level VI: Reports and opinions of expert committees or clinical experience of experts

Summary of benefits

One RCT showed a significant decrease in contractures at discharge in the group that had a fuller treatment time and frequency, exercise menu, and active orthotic therapy. However, the timing of the start of physical therapy between the two groups was different (on the day of admission and 2 weeks later), and there was no difference in the length of hospital stay or incidence of deep vein thrombosis.[1] A cohort study found that active exercise therapy reduced the length of hospitalization and burn ICU length of stay and improved range of motion more than passive range of motion training.[2]

Summary of harms

Regarding the effect on the wound, a prospective study found that resuming physical therapy early after skin grafting did not increase the number of surgeries or make a difference in the outcome of the skin graft.[3] There was no mention of pain enhancement during the intervention.

Balance between benefits and harms

If contractures are reduced, surgery for contracture release can be avoided and the time to return to daily life can be shortened, which is a great benefit. By checking the skin graft site, unstable scars, and areas with deep burns and sensory disturbances before intervention, the damage to the skin grafts and pain can be reduced.

Medical costs of this intervention

Human resources are required to provide physical therapy with ventilatory management. Additional analgesia and sedation with medication may be required.

Feasibility of this intervention

A certain amount of staff experience and manpower to ensure safety are required. It may be difficult to provide the

best interventions at all facilities, but there may be interventions that can be introduced depending on the conditions of the facility.

Is the intervention evaluated differently by patients, families, doctors, and other medical staff?

There is little variation in the evaluations of patients, families, doctors, and other medical staff. However, there may be disagreements between doctors and medical staff regarding specific intervention initiation times and rehabilitation programs (intensity, frequency, duration). Depending on the facility, the policies may differ regarding the necessity and resumption time of rehabilitation after skin grafting.

Recommendation decision process

The guideline met the specified criteria for adoption at the first ballot.

Recommendations in other relevant practice guidelines

The Japanese Burn Association's Guidelines for Burn Care (1st edition, revised 2nd edition) and the Japanese Dermatological Association's Guidelines for Burn Care (2017 edition) do not recommend physical therapy. The ISBI Practice Guidelines for Burn Care (2016, 2018)[4,5] recommend early release from the bed and continuation of exercise therapy for a period of time, but no other recommendations. The ABA published the Burn Rehabilitation Therapist Competency Tool (BRTCT), which is a set of skills that occupational and physical therapists involved in acute burn care should learn,[6] and recommended appropriate positioning and the use of static splints to prevent contractures.

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Rehabilitation fees

SEE CQ12 –1 for rehabilitation fees.

CQ12–3

CQ and answer

CQ: Are early rehabilitation interventions and early ambulation more useful than usual interventions in burn patients?

Answer: Early rehabilitation is recommended for burn patients (evidence level II, recommendation grade B).

Background and importance

Rehabilitation of burn patients has traditionally focused on physical therapy interventions and orthotic therapy to prevent contractures. In recent years, there has been an increasing number of reports on the usefulness of early rehabilitation for critically ill patients who require admission to the ICU.[1–3] However, in actual clinical practice, there are some cases in which the start of rehabilitation intervention is delayed because of concerns about unstable breathing and circulation or grafted skin. In this CQ, we addressed the usefulness of early rehabilitation intervention for burn patients. We believe that this CQ is important for clarifying the appropriate time to start rehabilitation.

PICO

Patient: Acute burn patients
Intervention: Start some form of rehabilitation as soon as possible after the burn injury
Control: No rehabilitation provided at an early stage (provided only after general condition has improved and the skin graft has stabilized)
Outcome: Hospital stay, motor function, ADL, incidence of DVT, incidence of accidental removal of tubes, incidence of graft failure (reoperation rate)

Summary of evidence (results of SR)

References used: Three RCTs

(1) Lorello DJ, Peck M, Albrecht M *et al*. Results of a prospective randomized controlled trial of early ambulation for patients with lower extremity autografts. J. Burn Care Res. 2014; 35: 431–6.[4]

The maximum walking time, graft failure rate, and pain on postoperative day 5 were evaluated in patients with lower extremity burns who began walking practice on postoperative day 1 and those who rested until postoperative day 5. The group that started walking on postoperative day 1 had significantly longer continuous walking time and less pain at the wound site. There was no difference in the graft failure rate between the two groups, and the area of graft failure was significantly smaller in the group that started walking on the first postoperative day.

(2) Guillot A, Lebon F, Vernay M *et al*. Effect of motor imagery in the rehabilitation of burn patients. J. Burn Care Res. 2009; 30: 686–93 [5].

In patients with hand burns, early rehabilitation and motor imagery exercises for functional recovery (within 2 days after injury) significantly improved confrontation, hand flexion, and tenodesis movements.

(3) Okhovatian F, Zoubine N. A comparison between two burn rehabilitation protocols. Burns 2007; 33: 429–34.[6]

The group that received physical therapy from the day of admission (from the third day after skin implantation) had significantly fewer contractures than the group that received physical therapy from approximately 2 weeks after admission (from the 10th to 15th day after skin implantation). There was no difference in the grafting rate, the incidence of deep vein thrombosis, or the length of hospital stay.

No Cochrane SR

Level of evidence

Level II: RCT

Summary of benefits The results showed a significant decrease in contractures. In cases of hand burns, it improved hand function, and in lower limbs, it prolonged continuous walking time and reduced pain at the wound site.

Summary of harms

There were cases of graft failure, but there was no difference in the timing of resumption of rehabilitation. In an SR of early rehabilitation under ICU management not limited to burns, four studies reported adverse events, including decreased oxygenation with SpO2 of 80% or less (1/49), catheter removal (1/49), asymptomatic bradycardia (1/150), discontinuation due to deterioration of general condition (19/498 cases), and postoperative respiratory complications (5/101, the same number as in the control group).[1]

Balance of benefits and harms

The early start of rehabilitation in burn patients was superior in terms of improving pain, prolonging walking time, and preventing contractures. The benefits outweigh the harms because there is no significant graft failure even when it is started immediately after skin grafting.

Medical cost of this intervention

See CQ12–1 for rehabilitation fees.

Feasibility of this intervention

In order to perform rehabilitation safely and early on in cases of severe burns, it is necessary to respond quickly to changes in the patient's condition and prevent accidental removal of lines, so manpower and multidisciplinary cooperation are essential. The contents that can be implemented vary depending on the situation of the facility, but we believe that some of these interventions can be implemented.

Is the intervention evaluated differently by patients, families, doctors, and other medical staff?

There is little variation in the evaluations of patients, families, doctors and other medical staff. In the case of early rehabilitation after skin grafting, the surgeon and rehabilitation staff may have different opinions about when to start the intervention.

Recommendation decision process

The guideline met the specified criteria for adoption at the first ballot.

Recommendations in other relevant practice guidelines

The ISBI Practice Guidelines for Burn Care (2016, 2018)[2,3] recommend early ambulation as much as possible, but do not state the degree of recommendation. Some guidelines specific to the lower extremities after skin grafting recommend starting the walking practice as early as possible (but in cases of joint areas covered by skin grafts, fixation is confirmed at the first dressing change),[7] and others recommend starting joint exercises and ambulation 5–7 days after skin grafting.[8] Although not exclusively for burn patients, the

Early Rehabilitation Expert Consensus[9] of the Japanese Society of Intensive Care Medicine has shown that early release from bed is associated with improved ADL capacity at discharge, reduced length of stay in ICU and length of hospital stay. In addition, The J-PAD Guideline[10] of the Japanese Society of Intensive Care Medicine recommends early rehabilitation intervention to reduce the onset and duration of delirium (+1B).

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Rehabilitation fees

SEE CQ12 –1 for rehabilitation fees.

CQ12–4

CQ and answer

CQ: Is exercise therapy (resistance training and aerobic exercise) useful for burn patients?

Answer: Exercise therapy (resistance training, aerobic exercise) is weakly recommended for burn patients with stable vital signs (evidence level II, recommendation level B).

Background and importance of CQ

The prognosis of burn patients has improved with recent advances in treatment technology, and rehabilitation after acute treatment is required to improve not only motor function but also ADL, QOL, and the rate of return to daily life. In addition to the direct tissue damage caused by burns, patients with burns may present with low-volume shock, renal failure, pulmonary edema, cardiac failure, and severe sepsis in the acute phase. The acute inflammatory response and the associated increase in cytokines and other chemical messengers increase vascular permeability, impair vascular endothelium, and cause impaired oxygenation and edema due to impaired peripheral circulation, resulting in inadequate oxygen and energy supply to the locomotor system and significant motor dysfunction. On the other hand, the effects of exercise therapy on burn patients have not been clearly defined. Thus, we developed this CQ on the importance of examining the effects of exercise therapy on burn patients.

PICO

Patient: Burn patients with stable vital signs and able to perform indicated actions
Intervention: Exercise therapy (resistance training, aerobic exercise) is performed
Control: Exercise therapy (resistance training, aerobic exercise) should not be performed
Outcome: Improved motor function, exercise tolerance, ADL, QOL, and rate of reintegration into society

Summary of evidence (results of SR)

References used: Three RCTs

(1) de Lateur BJ, Magyar-Russell G, Bresnick MG *et al*. Augmented exercise in the treatment of deconditioning from major burn injury. Arch. Phys. Med. Rehabil. 2007; 88: S18–23.[1]

In adult patients with burns (%TBSA 16–21), maximum oxygen uptake was significantly increased in the 12-week aerobic exercise group.

(2) Al-Mousawi AM, Williams FN, Mlcak RP *et al*. Effects of exercise training on resting energy expenditure and lean mass during pediatric burn rehabilitation. J. Burn Care Res. 2010; 31: 400–8.[2]

Among pediatric burn patients (7–17 years of age, ≥40% TBSA), there was a significant improvement in lean body mass and knee extensor strength in those who participated in a 12-week exercise program at the hospital, compared to those who participated in the standard treatment program at home. There was no extreme increase in resting energy expenditure in either group.

(3) Ebid AA, El-Shamy SM, Draz AH. Effect of isokinetic training on muscle strength, size and gait after healed pediatric burn: A randomized controlled study. Burns 2014; 40: 97–105.[3]

In pediatric burn patients (10–15 years of age, 36–45% TBSA), quadriceps strength and muscle mass as well as stride length, gait speed, and gait rate improved in the group that received conventional physical therapy plus 3 times a week of isokinetic strength training program. None of the referenced studies focused on the effect of exercise therapy (resistance training and aerobic exercise) on ADL, QOL, or social reintegration rate.

No Cochrane SR

Level of evidence

Level II: RCT

Summary of benefits

One RCT of adult burn patients reported that aerobic exercise improved exercise tolerance. No study examined the effects of aerobic exercise on motor function, ADL, QOL, or social rehabilitation. In addition, there are no reports on the outcomes of resistance training or resistance training combined with aerobic exercise. Two RCTs of pediatric burn patients reported that 12 weeks of exercise therapy improved lean body mass and motor function. However, as with adults, none of the examined papers focused on the improvement in ADL or QOL with exercise therapy.

Summary of harms

Skin damage can occur from falls, falling off the ergometer, or contact while walking or using a treadmill, but there were no reports of harm.

Balance of benefits and harms

Although the area and depth of burns are not consistent in the studies, we believe that the benefits outweigh the disadvantages of exercise therapy for burn patients with stable conditions.

Medical costs of this intervention

See CQ12–1 for rehabilitation fees.

Feasibility of this intervention

The feasibility of this intervention is high if there are sufficient doctors, nurses, and medical staff to provide instructions and guide appropriate exercise therapy.

Is the intervention evaluated differently by patients, families, doctors, and other medical staff?

Recommendation decision process

The guideline met the specified criteria for adoption at the first ballot.

Recommendations in other relevant practice guidelines

Exercise therapy has not been mentioned in the previous guidelines of the Japanese Burn Association, the Japanese Dermatological Association, the Japanese Society of Physical Therapists, or the Japanese Society of Rehabilitation Medicine. Practice Guidelines for Cardiovascular Fitness and Strengthening Exercise Prescription After Burn Injury edited by ABA[4] recommend resistance training and aerobic exercise.

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Rehabilitation fees

SEE CQ12 –1 for rehabilitation fees.

CQ13 LIAISON

AS THE TREATMENT >of burns becomes prolonged, the physical, emotional, and financial burden on patients and their families increases, as does the psychological burden on medical staff who must continue to perform invasive procedures on patients whose prognosis is uncertain. Previous burn treatment guidelines (2nd edition) have focused on "how to treat burn patients" and not on "how to care for burn patients" or "how to care for burn patients and their families." Given the background of burn patients, it is necessary to use a variety of approaches in the acute and chronic medical and rehabilitation processes.[1,2] At the same time, proper support for the families of burn patients is also important.[3]

Currently, in the fields of emergency and intensive care, the guidelines of the Ministry of Health, Labor and Welfare, Japan for terminal care are being followed, and recommendations are being made by various academic societies, and efforts are being made regarding best supportive care (BSC) and the process of surrogate decision-making in terminal care.[4,5] At present, these processes are not mentioned in national and international guidelines on severe burns; therefore, "end-of-life for lethal burn" should be considered a very important issue in future clinical practice. Hence, the "Liaison" section of this guideline contains CQs about the clinical aspects of BSC for burn patients, surrogate decisions for burn care, the relationship between interdisciplinary care and prognosis for burn patients, psychiatric liaison for burn patients, and family support resources.

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CQ13–1

CQ and answer

CQ: What are the indications for BSC in burn patients?

Answer: BSC should be considered only when it is judged to be the best choice for the patient and family after a comprehensive review of medical and ethical aspects by a burn team consisting of multiple professionals and departments.

Background and importance of CQ

In an analysis of 1,204 deaths, excluding cardiopulmonary arrest, registered between 2010 and 2019 in the Japanese Burn Association's Burn Inpatient Registry, 46% of the deaths were due to early shock and organ failure, and 28% were due to infectious diseases.[1] Deaths due to shock and organ failure occurred within 1 week of injury in 86% of the cases, while deaths due to infectious diseases occurred after 1 month of injury in 91% of the cases.[1] Approximately 86% of the deaths due to shock and organ failure occurred within 1 week of injury, while 91% of the deaths due to infection occurred after 1 month of injury. The longer the time taken to treat burns, the more excruciating the pain, disfigurement, functional and psychological distress, the greater the handicap to return to normal life, and the greater the medical and economic burden. Therefore, the physical, mental, and economic burden of prolonged burn treatment on patients and their families is extremely high. In addition, the psychological burden on medical staff who continue to perform painful invasive procedures on patients with an uncertain prognosis is high.

These findings suggest that the conditions under which BSC should be considered in burn patients are currently not mentioned in national or international guidelines on burns, and it is very important to provide guidelines for BSC from a standard clinical care point of view. However, it is extremely difficult to conduct a controlled study for this CQ, so we decided to answer this using a BQ to introduce the concept of the end-of-life in the emergency and intensive care fields in Japan.

Evidence and commentary

In 2014, the Japanese Society of Intensive Care Medicine, the Japanese Association for Acute Medicine, and the Japanese Circulation Society proposed the Guidelines for End-of-Life Care in Emergency and Intensive Care to define, determine, and respond to the end-of-life stage in the emergency and intensive care fields, and clearly stated the importance of the role of the medical team involved in emergency and intensive care.[2] Accordingly, the "terminal stage in emergency and intensive care" is defined as the period in which it is judged that there is no hope of saving the life of a patient with an acute serious condition who is being treated in an ICU, etc., even if appropriate treatment is given.

As mentioned above, the main causes of death in severe burn patients are shock and organ failure in the acute phase and infectious complications in the subacute and chronic phases, so the timing of death may fall in the acute, subacute, or chronic phase. As shown in CQ1–1 of this guideline, burn area (% TBSA), age, presence of airway burns, degree of DB, burn index, suicidal attempt, revised trauma score, and PBI are useful in assessing burn prognosis and may be helpful in making end-of-life decisions. In addition, various reports have shown the prognosis of sepsis and septic shock, which may be helpful in determining the terminal stage in the subacute and chronic phases.[3,4]

The treatment of severe burns is associated with excruciating pain, cosmetic, functional, and psychological distress, as described above.[5] For this reason, it is considered necessary to provide patients and their families with sufficient information about the objective results of treatment, the content of treatment, the possibility of recovery, the time required for recovery, and the quality of life after recovery.[5] In addition, when complications such as shock, organ failure, and infectious complications occur, it is necessary to provide accurate information about the patient's condition at each time. Throughout the course of medical treatment, the multidisciplinary medical team treating the burn patients should be aware that the prognosis of the patient's condition is absolutely poor, and that the patient's condition is likely to worsen in the future. It has been reported that when it has been determined that there is no hope of saving the patient's life even if burn treatment is continued and that further invasive procedures or treatment may not be in the best interest of the patient and may even compromise the patient's dignity, the patient and family should be given many opportunities to fully understand this fact and make a decision.[2]

Hence, BSC may be considered when the patient and family members clearly express a desire for treatment that alleviates physical and psychological distress, rather than enduring the pain and disfigurement, functional, and psychological distress associated with continued treatment of burns and complications, with full understanding of the prospects for recovery.[2,5]

According to the Guidelines for End-of-Life Care in Emergency and Intensive Care, the medical team should carefully assess the patient's ability to make decisions and then decide on the best course of action.

1. When the patient's intention is clear.
2. When the prior declaration of intent is confirmed in writing.
3. In cases where the patient's will is difficult to confirm, but the patient's presumed will can be confirmed by family members.

Best supportive care may be considered if the medical team can confirm the above conditions.[2] In the absence of a family member to confirm the presumed intention, the proxy is discussed in CQ13–2.

In the process of deciding the BSC for burn patients, the decision should not be made by an individual physician, but by a medical team consisting of multiple professionals and departments.[2,6,7]

1. Appropriately determine that a burn patient is at the end-of-life based on individual expertise and medical ethical considerations.
2. Appropriate assessment of the patient's decision-making capacity.
3. Consider treatment and support for patients and their families to achieve the most desirable end-of-life.
4. Establish a system to accept the grief reactions of family members and provide appropriate supports.

Recommendation decision process

The guideline met the specified criteria for adoption at the first vote.

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CQ13–2

CQ and answer

CQ: When should a proxy make decisions in burn care?

Answer: Proxy decision-making is the practice of making decisions on behalf of the patient during burn care when the medical decision to treat involves urgent and serious policy issues. When a surrogate decision is necessary, the patient should be consulted. Proxy decision-making is necessary when the patient does not have the capacity to make decisions about treatment, or when the patient's advance directive or presumed intent cannot be confirmed.

Background and importance of CQ

In the case of burns, proxy decision-making is required for pediatric patients (minors), patients with decision-making problems including sedation, critically ill patients with life-threatening conditions, and patients who lack the ability to make normal decisions prior to injury. In such cases, it is difficult to explain the condition of burns and the future treatment plan, the predicted outcome, and their intentions regarding the treatment plan. In the case of children, this is left to the parents or custodians, and in the case of adults, to the patient's closest relatives. It is also necessary to deal with the situation where the patient has no relatives. Currently, Japan is a super-aged society, and the number of elderly people living alone is increasing. Therefore, this guideline introduces evidence and guidelines based on the current situation in BQ.

Evidence and commentary

There are little data on proxy decision-making in burn care. In the management of severe burns, while treatment formulas and algorithms support burn care, there are few clear principles or alternative judgments that support decision-making in terms of ethics, so it is necessary to develop certain standards.[1,2] From the perspective of nursing, support for family members who make decisions by proxy for patients with severe burns has been reported in a few case studies.[3,4]

The issue of starting/not starting or stopping medical treatment in the final stages of life has been an important issue in the medical field for some time. In 1987, the Ministry of Health and Welfare started a study group, which has been held four times. In 2007, the Ministry of Health, Labor and Welfare published the Guidelines for Decision-making Process for Terminal Care and Commentary on Guidelines for Decision-making Process for Terminal Care, which indicated that, as a procedure for deciding the policy for terminal care and medical treatment, careful judgment should be made by the medical and care team when the patient's will has not been confirmed.[5,6] Later, in 2018, the term "terminal care" was revised to "medical care in the final stage of life" in response to the changing times. These revised guidelines were presented as Guidelines for the Decision-making Process for Medical Treatment and Care in the Final Stage of Life and Guidelines for the Decision-making Process for Medical Treatment and Care in the Final Stage of Life, Explanatory Volume.[7,8]

The revised guidelines provide recommendations for the decision-making process in all aspects of Medical Care at the End of Life, which is not necessarily limited to burns. It is important to note that this is a relatively clear decision for a national guideline. In particular, when the patient's intentions cannot be confirmed, the following steps should be taken by the medical and care team to make a careful decision.

1. Family members should respect the presumed will of the patient and follow the best policy for the patient.
2. The decision-making process is repeated as time passes, physical and mental conditions change, and medical evaluations change.
3. In the absence of family members, the best policy for the patient should be adopted.

However, "family" in this context refers to those whom the individual trusts to support him or her in the final stages of life. It is considered to be broader in scope, including not only legal kinship but also close friends. In addition, it is necessary for the family and the medical/care team to fully discuss and reach a consensus on what is in the best interest of the patient based on the patient's desires. In cases where consensus cannot be reached through these processes, it is necessary to establish a separate committee consisting of multiple experts to discuss treatment policies. In addition, in 2019, the Ministry of Health, Labor and Welfare, Japan formulated the Guidelines for Hospitalization of People without Relatives and Support for People with Difficulties in Decision-making Related to Medical Care to enable medical institutions and medical professionals to provide necessary medical care to patients in the absence of their relatives.[9] In addition to the above, the medical/care team and the ethics committee must make decisions based on the concept of the Guidelines for the Decision-Making Process for Medical Care in the Final Stage of Life.

In the field of emergency and intensive care, the Japanese Society of Intensive Care Medicine, the Japanese Society of Emergency Medicine, and the Japanese Circulation Society proposed the Guidelines for End-of-Life Care in Emergency and Intensive Care in 2014. It provides definitions, judgments, and responses to end-of-life situations, including a detailed description of life-prolonging measures.[10] In addition, the Japan Nurses Association states on its website that from the perspective of nursing ethics, it is necessary to seek the best interests of patients or users in cases where the patient's will cannot be estimated for making decisions.[11] In particular, when providing support to family members who have made decisions by proxy, it should be noted that even when a decision has been made, the family's feelings are constantly changing.

Recommendation decision process

The guideline met the specified criteria for adoption after the first ballot.

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CQ13–3

CQ and answer

CQ: Does multidisciplinary care for burn patients affect prognosis?

Answer: Burn care by a multidisciplinary burn team may improve prognosis during the entire process from the acute phase to the chronic phase.

Background and importance of CQ

The treatment of severe burns in acute phase requires comprehensive diagnosis and care in a variety of areas, including airway, respiratory, circulatory, and fluid management, sedation and analgesia, nutritional management, infection control, wound management, rehabilitation, and mental and psychological support.[1] Therefore, in the treatment of severe burns, it is desirable to promote "team medicine," in which a variety of staff members, based on their level of expertise, share objectives and information, share tasks, and collaborate and complement each other to provide medical care that accurately responds to the patient's situation.[2] In general, the promotion of multidisciplinary team medicine is expected to improve the efficiency and quality of treatment as well as to be effective in terms of medical economy and safety.[2] In recent years, it is also expected to contribute to the reform of work styles.[3]

Infection control (CQ6), nutritional management (CQ7), analgesia and sedation (CQ9), rehabilitation (CQ12), and psychiatric liaison (CQ13–4) discussed in these Guidelines require close cooperation among the various specialties, and multidisciplinary care is considered to function effectively. In addition, depending on the stage of burn care, cooperation with clinical engineers, pharmacists, material departments, blood transfusion departments, and surgical and anesthesiology departments is extremely important. In addition, cooperation with social workers is required for discharge, and cooperation with public institutions is also important in cases of abuse. This CQ was presented as a BQ to introduce the effects of multidisciplinary care and team medicine on burn care.

Evidence and commentary

A few RCTs evaluated the impact of multidisciplinary care on the outcome of burn injuries. On the other hand, in the field of intensive care, which is not limited to burns but also treats cases of severe burns, RCTs on multidisciplinary care such as analgesia, sedation, and rehabilitation have shown the benefits of such care. In a propensity analysis database analysis of 1,759 adult burn patients in 13 ICUs in the UK, a significant improvement in mortality was observed in facilities staffed by multidisciplinary burn teams. Compared to the resident facilities of the multidisciplinary burn specialist team, the odds ratio to the mortality rate was 1.81 for the ICU where a specialized team was dispatched and 2.24 for the ICU where a specialized team was not involved.[4]

In addition, a prospective study in two ICUs in Iran compared protocol-based medication with multidisciplinary team using defined scores to evaluate analgesia, insensitivity, and delirium and conventional physician-led medication reconciliation management. The results showed not only a significant decrease in the use of analgesics and sedatives, but also a significant improvement in the duration of ventilation, ICU stay, and mortality, indicating the effectiveness of multidisciplinary evaluation of analgesia, sedation, and drug adjustment.[5] However, this study was not limited to burn patients.

In Japan, there are more facilities that effectively utilize existing Infection Control Teams and Nutritional Support Teams to provide burn care than those that provide specialized team medicine and multidisciplinary care. It is hoped that the evidence and information presented in this guideline will be used effectively by each team to promote team-based medical care for burns.

Recommendation decision process

The guideline met the specified criteria for adoption at the first vote.

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CQ13–4

CQ and answer

CQ: Should psychiatric liaison be provided for burn patients?

Answer: Psychiatric liaison (psychiatric consultation) can be useful for improving outcomes of burn patients from the

acute to the chronic phase and help them resume activities of daily life.

Background and importance of CQ

Before 1980, psychiatrists were rarely involved in the treatment of burns; in Europe and the United States, psychotherapists provided counseling. However, severe burns are physically invasive and require pharmacotherapy. In the process of treatment, there are many psychosocial problems. This CQ was answered as a BQ to introduce the evidence for psychiatric liaison in burn care.

Evidence and commentary

The treatment of severe burns begins with the patient's confused psychological state immediately after injury. It has been reported that psychiatrists should be involved in mental health care in the acute phase of burn treatment because patients experience "acute stress reaction."[1]

Mental health care for burns has historically been provided primarily by psychiatrists at Shriner's Hospital for Children and the University of Texas in the United States. Their studies focused on children and adolescents, but did not follow children into adulthood.[2–4] After the terrorist attacks on the United States on September 11, 2001, many of these psychiatrists turned to disaster psychiatry. Currently, the "Burn Patients" section of the Handbook of General Hospital Psychiatry (7th edn., no Japanese translation available) describes diagnosis and treatment methods for mental care of burns.[5]

Mental care for burn patients should include physiological, recovery, and social aspects. As the physical treatment shifts from acute life-saving treatment to cosmetic and functional plastic treatment, psychiatrists are expected to cooperate in the mental care of patients. Often, burns cause a loss of function or other limitations. In addition, fire and accidents can cause loss of relationships and social status due to bereavement of family and friends and loss of property.[6] As a result, patients may develop posttraumatic stress disorder or depression. Psychiatrists would need to treat depression, alcohol-related disorders, and suicide ideation.[7] In the case of suicide attempts or injuries due to accidents, it is important to provide care not only to the patient but also to the family[8] because the treatment of severe burns takes a long time and results in high medical costs.[9] It is also necessary to understand insurance policies and local social resources when providing mental health care.

In the case of severe burns, it is not uncommon for the patient to be transferred to a specialized burn facility after initial treatment by a local physician or to be transferred to a hospital for rehabilitation and social reintegration after acute treatment is completed. It is believed that multidisciplinary treatment in the community can provide an environment in which patients can easily return to their homes and society.

In addition, burn care is a heavy burden on the medical team and may cause "burn-out." There is an opinion that psychiatrists should provide mental support to medical staff.[10]

Recommendation of the final project

The guideline met the specified criteria for adoption at the first vote.

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CQ13–5

CQ and answer

CQ: Is it useful to provide family support in the care of burn patients?

Answer: It is recommended that family support be provided in the care of pediatric patients with burns (evidence level VI; grade of recommendation C).

Background and importance of CQ

The importance of support for the families of burn patients has been reported. Most studies discuss the psychological problems of burn patients and their parents during childhood and adolescence.[1–5]

In the case of burn patients, it is important to consider their families, especially parents of children, experience a wide range of psychological reactions and symptoms. Therefore, the risk of posttraumatic stress disorder is high. There are various reports on the relationship of the extent and severity of burns with posttraumatic stress in the parents of pediatric burn patients, and this tends to occur regardless of the severity of the burn.[3–5] It has been suggested that this is in part due to the subjectivity of the family, so support should be provided to all parents of pediatric burn patients.

Good communication and reassurance between the burn team and the family can lead to psychological recovery for the burn patient, not just for the family. In addition, households with burn patients suffer tremendous economic damage, so financial support, including medical expenses, is also necessary.[1,6,7]

This guideline is intended to help families with burn patients understand the importance of providing support to their children. Therefore, it is important to consider family support for burn patients in this guideline, and we designed the CQ.

PICO

Patient: A family member of a patient with fresh burns
Intervention: A multidisciplinary medical team provides psychological and psychiatric support
Control: No psychological or psychiatric support by the multidisciplinary medical team
Outcome: Psycho-psychological response of the patient's family

Summary of evidence (results of SR)

No RCT

No Cochrane SR

Level of evidence

Level VI: Reports and opinions of expert committees or clinical experience of experts

Summary of benefits

Unexpected burns can cause psychiatric and psychological disturbances in the family members, especially mothers of pediatric burn patients, due to anxiety about the life prognosis and sequelae as well as guilt for being responsible for the burn. Providing multidisciplinary medical support to the family, including psychological care, from the early stage of treatment is effective in treating so-called fear-avoidance thinking and posttraumatic stress, which could form a vicious cycle of anxiety and avoidance.[3] Although there is no evidence to support this, support for families of pediatric burn patients may help stabilize their emotional state and lead to a sense of trust in medical professionals, as well as a positive attitude toward treatment and rehabilitation among the patients themselves.

Summary of harms

No concrete evidence of apparent harm was obtained. However, the intervention may induce anxiety and fear, which may lead to posttraumatic stress syndrome, so careful handling is necessary.

Balance of benefits and harms

Although there was no objective evidence that the psychological and emotional support provided by the multidisciplinary medical team was effective, the above assessment of benefits and harms suggests that the benefits of family support outweigh the harms, especially for pediatric burn patients.

Medical costs required for this intervention

An additional cost of 300 points for the psychiatric liaison team can be calculated once a week.

Feasibility of this intervention

While this intervention is suitable for burn patients, the mindset of the family should also be considered. The composition of the multidisciplinary medical team must be

decided in advance, and its role must be clarified. There are some medical institutions that have difficulty in implementing this intervention.

Are the interventions evaluated differently by patients, families, medical staff, and physicians?

In a multidisciplinary team, the evaluations of the assessment and support may differ due to the different roles of those involved.

Recommendation of the final guideline

The guideline met the specified criteria for adoption at the first vote.

Recommendations in other relevant practice guidelines

Not found.

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