Review

Burns management in ICU: Quality of the evidence
A systematic review

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ABSTRACT

Background: The objective of this study was to assess the quality of readily available evidence regarding critical care aspects of the management of patients with severe burn injuries.

Method: PubMed, EMBASE, Cochrane Databases and bibliographies of included studies and burns review articles were searched from inception of databases to end of February 2015. We included systematic reviews, randomised controlled trials (RCTs) and cohort studies with concurrent controls on the topics of (a) fluid resuscitation (b) analgesia (c) haemodynamic monitoring and targets (d) ventilation (e) blood transfusion. The quality of the studies was assessed using validated tools.

Results: Fifty six studies fulfilled the inclusion criteria. Twenty three on fluid resuscitation, 22 on analgesia, nine on haemodynamic monitoring and two on ventilation. No studies were found on blood transfusion practice. There were ten systematic reviews, 38 RCTs and eight cohort studies with concurrent controls. The majority of studies were single centre trials with small numbers of patients, surrogate outcomes and high risk of bias.

Conclusions: There is very little high quality evidence to guide clinical practice in the early management of the severely burnt patient. Eleven of 56 studies found in our search of critical care topics were of good methodological quality with low risk of bias.

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1. Introduction

Burn injuries are among the most devastating of all injuries and a major global public health problem [1]. An estimated 265,000 deaths are caused by burns annually with the vast majority occurring in low to middle income countries where burns are a leading cause of disability-adjusted-life-years lost [2,3].

In developed countries the acute hospital, rehabilitation and loss of income cost is high and there is variability in outcome of burn patients between admitting facilities [4]. It is possible that variability in outcomes stems from variability in practice due to lack of quality evidence and inconsistent guidelines [5].

Reviews of burn literature reveal that the amount of published literature is large but not made up of high-level evidence such as systematic reviews or RCTs. Many of the trials are poor quality with an unacceptable level of bias [6].

Guidelines are helpful in ensuring consistent best practice but the guidelines of large burn organisations, especially in the area of acute burn care, are not based on RCTs or systematic reviews but on cohort studies, observational studies, case series or expert opinion [7,8].

To investigate this issue, the study aimed to assess the quality of readily available evidence regarding critical care aspects of the management of patients with severe burns. The focus was on five key areas: fluid resuscitation, haemodynamic monitoring, analgesia, ventilation and blood transfusion practice.

2. Methods

The study was conducted according to a pre-specified protocol. We included only studies of adult, human subjects with burn injuries that were above level III-2 (NHIMRC) or 2b (Oxford CEBM) evidence [9,10]. The studies had to cover the topics of fluid resuscitation, haemodynamic monitoring and targets, analgesia (parenteral or enteral), ventilation or blood transfusion.

A detailed search of the literature using the PUBMED, EMBASE and Cochrane Databases was performed for articles published from inception of each database to the end of February 2015. The search terms used were burn OR thermal injury with filters for systematic review, meta-analyses and controlled clinical trial. Full details of the search strategy are provided in appendix A. Bibliographies of included studies and recent review articles were searched for additional articles meeting the inclusion criteria.

The abstracts of articles found in the search were reviewed by one author (AH). If it was unclear if inclusion criteria were met, the full article was retrieved. Articles were excluded if they did not address thermal injury and one of the five specific topic areas, were not written in English, did not focus on adults, or the level of evidence was below that of cohort study with concurrent controls.

We recorded information on first author, year of study, study type, domain, population, number of subjects, single/multicentre, outcomes, intervention/comparison, results and conclusion for the articles that met the inclusion criteria. Data was collated by a single investigator (AH) (appendix B).

The quality of each manuscript was assessed by two authors separately (AH and RL). Quality was assessed using appropriate and previously validated tools depending on the study type: the Overview Quality Assessment Questionnaire (OQAQ) for systematic reviews [11], the Cochrane Collaboration Tool for Assessing Risk of Bias for RCTs [12] and the National Heart, Lung and Blood Institute Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies for cohort studies [13]. These tools were modified to include the outcomes measured (patient centred or surrogate) and an assessment whether the conclusions were consistent with the data provided (if not already included). See footnotes of the relevant results tables for detailed description of the tools.

A global assessment of overall manuscript quality and its clinical applicability was determined by two authors (AH and RL) based on the results of the modified tools. For a manuscript to be judged as ‘acceptable’ quality, the results were considered...
valid and conclusions clinically applicable. If the methodological flaws and risk of bias identified were significant enough to affect the validity of the results, the overall quality was deemed ‘unacceptable’. If there was disagreement between the two assessors on any aspects of the assessments, the third author (AD) adjudicated.

3. Results

Six thousand three hundred and thirty nine references were identified using the search strategy with 56 articles fitting the inclusion criteria. See Fig. 1, PRISMA 2009 flow diagram [14]. Of the included studies, 23 covered fluid resuscitation [15–37], 22 covered parenteral and enteral analgesia [38–59], nine addressed haemodynamic monitoring and targets [60–68] and two were on the topic of ventilation [69,70]. No studies on the topic of blood transfusion practice that met the inclusion criteria were found. Please refer to Tables 1-3 for detailed results of assessment tools.

3.1. Fluid resuscitation

3.1.1. Systematic reviews: Table 1

Four systematic reviews covered burn fluid resuscitation. They compared different fluid types and aspects of the topic, including albumin vs crystalloids [18], hypertonic vs isotonic crystalloids [16], association between fluid resuscitation volume and development of abdominal compartment syndrome [15] and fluid resuscitation volumes compared to formula calculated amounts [17]. Two systematic reviews were of acceptable methodological quality [16,18]. Common weaknesses in the other two included insufficient detail of inclusion criteria, lack of explicit validity assessment of the included studies, surrogate outcomes and conclusions not supported by reported data [15,17].

3.1.2. Randomised controlled trials (RCTs): Table 2

Sixteen RCTs covered burn fluid resuscitation. Nine compared crystalloid with colloid supplemented crystalloid resuscitation. The colloid studied was 6% hydroxyethyl starch (HES) in three trials [19,31,33], albumin in two trials [22,23], Dextrans 70 in three trials [25–27] and fresh frozen plasma (FFP) in one trial [30]. Four trials compared hypertonic to isotonic fluid resuscitation [20,21,24,29]. Two trials compared different colloids, plasma with Gelofusin [28] and 10% Pentastarch with 5% albumin [34]. Only one of the 16 RCTs was of acceptable overall quality [20]. The remaining RCTs had significant risk of selection bias, performance bias and inadequate power (mostly <100 participants). All RCTs measured surrogate outcomes.

3.1.3. Cohort studies with concurrent controls: Table 3

The three cohort studies with concurrent controls observed different study fluid types [35–37]. One compared crystalloid with crystalloid + colloid (10%HES) resuscitation [35] another compared crystalloid (lactated Ringer’s solution) with crystalloid + hypertonic solution [37]. The third study compared crystalloid to colloid (plasma) solution [36]. One cohort study was of acceptable overall quality [35]. The methodological flaws of the other studies included no sample size justification, no binding of assessors and no attempt to measure and account for confounding factors [36,37].

3.2. Analgesia

3.2.1. Systematic reviews: Table 1

Four systematic reviews covered parenteral or enteral analgesia. A variety of medication options were studied including dexmedetomidine [38], ketamine [39] and intravenous lignocaine [40,41]. Only one systematic review was of acceptable overall quality [41]. Two others did not clearly assess the validity of the included studies with explicit criteria [38,39]. The fourth did not include any trials [40].

3.2.2. Randomised trials (RCTs): Table 2

The 16 RCTs investigated a variety of aspects of acute burn analgesia ranging from type of analgesic agent [44,47–52,54–57], optimal dose [42,45,53] and method of administration. Four of these trials were of acceptable quality [46,47,55,56]. The other RCTs had high risk of selection bias, performance bias and of being underpowered.

3.2.3. Cohort studies with concurrent controls: Table 3

The two cohort studies with concurrent controls studied the type of analgesic agent (morphine) [58] and method of delivery (patient controlled vs anaesthetist administered) [59]. Both studies were of unacceptable overall quality. The methodological weaknesses included small numbers with no sample size justification, no binding of assessors, surrogate outcomes and no attempt to account for confounding factors [58,59].

3.3. Haemodynamic monitoring and targets

3.3.1. Systematic reviews: Table 1

Two systematic reviews (SRs) were found. One compared the traditional resuscitation target of urine output to
Table 1 – Systematic review assessment—based on Overview Quality Assessment Questionnaire (OQAQ) [11].

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Domain</th>
<th>T</th>
<th>N</th>
<th>Search methods stateda</th>
<th>Comprehensive searchb</th>
<th>Inclusion criteria reportedc</th>
<th>Selection bias avoidedd</th>
<th>Validity assessment reportede</th>
<th>Appropriate validity criteriaf</th>
<th>Methods of combining results reportedg</th>
<th>Combining of findingsh</th>
<th>Conclusions consistent with resultsi</th>
<th>Outcomesj</th>
<th>Overall quality ratingk</th>
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<tbody>
<tr>
<td>Azzopardi [15]</td>
<td>2009</td>
<td>Fluids</td>
<td>3</td>
<td>89</td>
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<td>no</td>
<td>no</td>
<td>moderate</td>
<td>yes</td>
<td>no</td>
<td>no</td>
<td>no</td>
<td>S</td>
<td>unacceptable</td>
</tr>
<tr>
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<td>2004</td>
<td>Fluids</td>
<td>3</td>
<td>72</td>
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<td>yes</td>
<td>yes</td>
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<td>yes</td>
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<td>yes</td>
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<tr>
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<td>3</td>
<td>1340</td>
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<td>no</td>
<td>no</td>
<td>no</td>
<td>no</td>
<td>no</td>
<td>no</td>
<td>no</td>
<td>no</td>
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<td></td>
</tr>
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<td>no</td>
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</tr>
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<td>266</td>
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<td>yes</td>
<td>yes</td>
<td>moderate</td>
<td>n/a</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>PC</td>
<td>unacceptable</td>
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<td>Analg</td>
<td>4</td>
<td>67</td>
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<td>moderate</td>
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<td>n/a</td>
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<td>n/a</td>
<td>n/a</td>
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<td>0</td>
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<td>yes</td>
<td>yes</td>
<td>n/a</td>
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<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>n/a</td>
<td>n/a</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>PC</td>
<td>acceptable</td>
</tr>
<tr>
<td>Parizc [42]</td>
<td>2016</td>
<td>Haemo</td>
<td>20</td>
<td>566</td>
<td>Yes moderate</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
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<tr>
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<td>11</td>
<td>102</td>
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<td>no</td>
<td>no</td>
<td>n/a</td>
<td>n/a</td>
<td>moderate</td>
<td>yes</td>
<td>yes</td>
<td>S</td>
<td>unacceptable</td>
</tr>
</tbody>
</table>

a. Were the search methods used to find the evidence on the primary question(s) stated?
b. Was the search for evidence reasonably comprehensive?
c. Were the criteria used for deciding which studies to include in the overview reported?
d. Was bias in the selection of studies avoided?
e. Were the criteria used for assessing the validity of the included studies reported?
f. Was the validity of all the studies referred to in the text assessed using appropriate criteria?
g. Were the methods used to combine the findings of the relevant studies (to reach a conclusion) reported?
h. Were the findings of the relevant studies combined appropriately relative to the primary question of the overview?
i. Were the conclusions made by the author(s) supported by the data and/or analysis reported in the overview?
j. What type of outcomes were used (patient centred or surrogate)?
k. See Section 2 for definitions of 'acceptable' and 'unacceptable'.
### Table 2 – Randomised controlled trial assessment—based on Cochrane collaboration tool for assessing risk of bias [12].

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Domain</th>
<th>N</th>
<th>single or mult centre</th>
<th>Random sequence generation*</th>
<th>Allocation concealment*</th>
<th>Blinding of participants*</th>
<th>Blinding of assessors*</th>
<th>Incomplete outcome data*</th>
<th>Selective reporting*</th>
<th>Other bias*</th>
<th>Conclusion consistent with results*</th>
<th>Outcomes*</th>
<th>Overall quality rating</th>
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<tr>
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<td>Haemo</td>
<td>50</td>
<td>single</td>
<td>low risk</td>
<td>low risk</td>
<td>low risk</td>
<td>low risk</td>
<td>low risk</td>
<td>low risk</td>
<td>low risk</td>
<td>high risk</td>
<td>No</td>
<td>S</td>
</tr>
<tr>
<td>Tokarik [65]</td>
<td>2013</td>
<td>Haemo</td>
<td>21</td>
<td>single</td>
<td>low risk</td>
<td>low risk</td>
<td>low risk</td>
<td>low risk</td>
<td>low risk</td>
<td>low risk</td>
<td>low risk</td>
<td>high risk</td>
<td>No</td>
<td>S</td>
</tr>
<tr>
<td>Reper [70]</td>
<td>2002</td>
<td>Vent</td>
<td>36</td>
<td>single</td>
<td>mod risk</td>
<td>mod risk</td>
<td>mod risk</td>
<td>high risk</td>
<td>high risk</td>
<td>high risk</td>
<td>high risk</td>
<td>yes</td>
<td>S</td>
<td>unacceptable</td>
</tr>
</tbody>
</table>

* Selection bias (biased allocation to interventions) due to inadequate generation of a randomised sequence.

b Selection bias (biased allocation to interventions) due to inadequate concealment of allocations prior to assignment.

c Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.

d Detection bias due to knowledge of the allocated intervention by the assessors.

e Attrition bias due to amount, nature and handling of incomplete outcome data.

f Reporting bias due to selective outcome reporting.

g Bias due to problems not covered elsewhere in the tool.

h Were the conclusions made by the author(s) supported by the data and/or analysis reported?

i What type of outcomes were used (patient centred or surrogate)?

j See Section 2 for definitions of ‘acceptable’ and ‘unacceptable’. 
Table 3 – Cohort study assessment—based on NHLBI quality assessment tool for observational cohort and cross sectional studies [13].

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Domain</th>
<th>N</th>
<th>Single/multicentre</th>
<th>Research question clearly stated(^a)</th>
<th>Study population clearly defined(^a)</th>
<th>Participation rate &gt;50%(^c)</th>
<th>Subject selection consistent(^d)</th>
<th>Sample size justification(^e)</th>
<th>Exposure measured pre outcome(^f)</th>
<th>Timeframe sufficient?(^g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bechir [35]</td>
<td>2010</td>
<td>Fluids</td>
<td>30</td>
<td>Single</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>NA</td>
<td>Yes</td>
</tr>
<tr>
<td>Bocneegra [36]</td>
<td>1998</td>
<td>Fluids</td>
<td>308</td>
<td>Single</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>NA</td>
<td>Not stated</td>
</tr>
<tr>
<td>Murphy [37]</td>
<td>1999</td>
<td>Fluids</td>
<td>18</td>
<td>Partial</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>NA</td>
<td>Yes</td>
</tr>
<tr>
<td>Förtsch [54]</td>
<td>1995</td>
<td>Analg</td>
<td>106</td>
<td>Multicentre (2)</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>N/A</td>
<td>Yes</td>
</tr>
<tr>
<td>Nilsson [59]</td>
<td>2008</td>
<td>Analg</td>
<td>11</td>
<td>Single</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>N/A</td>
<td>Yes</td>
</tr>
<tr>
<td>Cartotto [66]</td>
<td>2003</td>
<td>Haemo</td>
<td>38</td>
<td>Single</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
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</tr>
<tr>
<td>Holm [67]</td>
<td>2001</td>
<td>Haemo</td>
<td>23</td>
<td>Single</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>N/A</td>
<td>Yes</td>
</tr>
<tr>
<td>Kuntscher [64]</td>
<td>2002</td>
<td>Haemo</td>
<td>14</td>
<td>Single</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>N/A</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Levels of exposure examined\(^h\), Independent variables well applied\(^i\), Exposure measured >1 time, Dependant variables well applied\(^k\), Assessors blinded\(^l\), Loss to follow up <50\(^m\), Confounders accounted for?\(^n\), Conclusion consistent with results?\(^o\), Overall quality rating\(^p\).

\(^{a}\) Was the research question or objective in this paper clearly stated?

\(^{b}\) Was the study population clearly specified and defined?

\(^{c}\) Was the participation rate of eligible persons at least 50%?

\(^{d}\) Were the subjects selected or recruited from the same or similar populations (including the same time period)? Were the inclusion and exclusion criteria for being in the study prespecified and applied uniformly to all participants?

\(^{e}\) Was a sample size justification, power description, or variance and effect estimates provided?

\(^{f}\) For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured?

\(^{g}\) Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed?

\(^{h}\) For the exposures that can vary in amount or level, did the study examine different levels of the exposure as related to the outcome (e.g. categories of exposure, or exposure measured as continuous variable)?

\(^{i}\) Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?

\(^{j}\) Was the exposure(s) assessed more than once over time?

\(^{k}\) Were the outcomes measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?

\(^{l}\) Were the outcomes assessors blinded to the exposure status of the participants?

\(^{m}\) Was loss to follow up after baseline 20% or less?

\(^{n}\) Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s)?

\(^{o}\) Were the conclusions made by the author(s) supported by the data and/or analysis reported?

\(^{p}\) What type of outcomes were used (patient centered or surrogate)?

\(^{q}\) See Section 2 for definitions of 'acceptable' and 'unacceptable'.

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hemodynamic monitoring end points and was of acceptable quality [61]. The other investigated the use of transoesophageal echo to guide resuscitation targets [60]. This second review had significant methodological weaknesses including no clear validity assessment of included studies, poorly defined inclusion criteria, surrogate outcomes and conclusions not supported by the reported data [60].

3.3.2. Randomised controlled trials (RCTs): Table 2

Four RCTs were found which all compared traditional end points of hourly urine output and mean arterial pressure (MAP) to invasive haemodynamic monitor parameters to guide fluid resuscitation [62-65]. None of these manuscripts were of acceptable overall quality. All had surrogate outcomes, high risk of bias through inadequate binding of outcomes assessors and the conclusions were not consistent with reported results.

3.3.3. Cohort studies with concurrent controls: Table 3

Three studies of this type on the topic of haemodynamic monitoring and targets were identified [66-68]. Two compared the use of the pulmonary artery catheter to other invasive haemodynamic monitors [67,68], the other investigated the use of baseline deficit as a marker of poor outcome [66]. One study was of acceptable overall quality [66]. The weaknesses of the other cohort studies included small numbers with no sample size justification, surrogate outcomes and no binding of assessors.

3.4. Ventilation

3.4.1. Randomised controlled trials (RCTs): Table 2

Only two RCTs on the topic of ventilation of the acute burn patient were found with no systematic reviews, meta-analyses or cohort studies with concurrent controls identified.
during our search [69,70]. Both compared high frequency percussive ventilation (HFPV) to conventional ventilation and both were of unacceptable overall quality. Methodological weaknesses included small numbers (<100 participants) with no sample size justification or power calculations, surrogate outcomes and non-blinded assessors.

3.5. Transfusion

No articles fulfilling the inclusion criteria on the topic of blood transfusion in acute burn injury were found. Seven studies were identified in the initial search but three were retrospective observational studies [71–73], one was a cohort study with no concurrent controls [74], two had paediatric subjects [75,76] and one was not written in English [77].

3.6. Overall quality ratings: Tables 1–3

A summary of the overall quality ratings revealed that 11 out of 56 or just under one fifth of the reviewed acute burn care literature was of acceptable methodological quality with low risk of bias.

4. Discussion

This systematic review of current evidence regarding the early management of severe burn patients found there is little high quality evidence to guide clinical practice.

Validated assessment tools were used to examine the quality of available literature. These tools were useful to structure an approach to identifying areas of potential bias or deficiencies in study design, however, only the Overview Quality Assessment Questionnaire had a component for overall assessment of manuscript quality. The aim of the study was to review the quality of the evidence and its applicability to clinical practice, therefore, it was necessary to assign a global quality rating to every study so that a definitive judgement and conclusion could be reached. The tools were modified to include outcome type (patient-centred vs surrogate) and whether the conclusions were consistent with the reported results (already a question of OQAQ) because these are additional important criteria for good quality, clinically applicable evidence.

The global assessment was not reached by merely tallying the results and seeing if a pass mark was achieved, as this would have been an oversimplification of the complex process of critical appraisal. Instead, when a flaw was identified the assessor determined whether the amount and type of bias were significant enough to affect the validity of the results and clinical applicability. Similar types of bias have the potential to affect studies results differently depending on study characteristics and outcomes [13].

The small numbers of randomised controlled trials (RCTs) in the burn literature has been previously noted [78]. Sixty one RCTs were published in the major journal, Burns, in the 23 years from first publication until 1995. Not only were the overall number of RCTs small but the proportion on the topic of resuscitation/fluid therapy was particularly deficient (5 RCTs). The majority (62%) were on the subject of wound dressing and healing [78]. This trend continued in another major journal, Journal of Burn Care and Rehabilitation, with 50 RCTs, mostly covering wound healing and dressings, published between 1985 and 1995 [78]. Only two systematic reviews of RCTs were found reflecting the paucity of grade I evidence in 1998 [78].

Since then, the quantity of trials has grown with over 1000 peer-reviewed articles on burn care published in 2013 [6]. The results of our study also reflect an increase in quantity of burns research over time. All ten systematic reviews [15–18,38–41,61] and 21 of 38 RCTs [19,20,22,28,30,31,33,42,45,47–49,51,54–57,62,63,65,69] were published in the last 10 years. This is encouraging, however, in a similar time period (1971–2013) 11,623 critical care RCTs were indexed on PubMed compared to 38 found in this study [79]. While the total number of RCTs related to burn critical care will be higher than we found in the five specific areas covered, the figures highlight that critical care management of burns is a neglected area of research.

The second major finding in our study is the poor methodological quality of the published manuscripts. The majority of RCTs and cohort studies were single centre with small numbers of subjects (often <100) with no reporting of sample size calculation or power.

In a systematic review published in 2009 methodological quality was assessed as less than optimal with highly variable reporting standards [80]. Only 16% of RCTs had appropriate randomisation and 9.3% allocation concealment [80]. In our study 39% reported adequate randomisation and 32% allocation concealment with 75% of these studies published since the systematic review in 2009 thus reflecting a quality improvement in study design and reporting over time.

5. Limitations

The areas covered in the search are believed to be the clinically important domains for acute burn care and therefore the results and conclusions should be generally applicable to literature on critical care burn management even though all available evidence was not examined.

The study reviewed only prospective cohort studies with concurrent controls or evidence levels above. Retrospective, unmatched, observational and case–control studies were excluded because even if well designed, these have significant potential for bias meaning the results are only hypothesis generating and not directly applicable to clinical practice.

Only published manuscripts were included in the study which reflects the practical aim of this study to find readily available evidence. Papers not written in English were excluded.

Assigning a single judgement of quality to a study may be viewed as an oversimplification of the complex process of critical appraisal. However, the aim of this review was to assess the applicability of evidence, so it was necessary to reach a practical conclusion about each paper. Combining the quality of evidence into an overall summary assessment reflects the GRADE working group approach. This sorts evidence into high, moderate, low or very low quality groups and has been adopted by over twenty organisations including the WHO, ACP and NICE in the UK [81,82].
6. Recommendations

Only a small number of papers passed assessment as being of acceptable methodological quality but each still had considerable weaknesses. Therefore what recommendations, if any, can be made for clinical practice from the papers with acceptable method?

In the fluid resuscitation papers the conclusions included:

1. Albumin may be beneficial but the meta-analysis was based on just four small RCTs (129 subjects) and four non-randomised trials with significant heterogeneity. Three RCTs were published more than 30 years ago [18].

2. Hypertonic crystalloid resuscitation may decrease fluid requirements and overall net fluid accumulation but multiple endpoints were measured, weakening the significance of the findings [20].

3. Hyperoncotic hydroxyethyl starch may increase mortality and incidence of renal failure based on retrospectively analysed data collected 10 years earlier on 30 patients [35].

In the analgesics papers the conclusions included:

1. The only alternative agent to traditional opioid analgesia that provided clinical benefit was pregabalin. It reduced procedural pain, elements of neuropathic pain and was well tolerated but pain intensity, the majority of neuropathic pain components, opioid use, length of hospital stay or incidence of chronic pain were unchanged [47].

2. Gabapentin and lignocaine (based on one RCT of 45 patients [41,51]) showed no clinical benefit of reduction in pain scores or opioid consumption [56].

3. Patient controlled intranasal fentanyl was similar in efficacy to oral morphine but the study excluded burns >25% TBSA and those receiving intravenous analgesia [46].

In the papers addressing haemodynamic monitoring the conclusions included:

1. Alternative endpoints to urine output and haemodynamic monitoring may improve outcomes but the article relied heavily on one cohort study with weak methodology [61].

2. A proportion of patients may benefit from resuscitation targeted at oxygen delivery and uptake goals because of a persisting malperfusion state despite conventional resuscitation. However, only five patients were in the base deficit <−6 group and a total of 38 subjects in the study [66].

Overall, no clear recommendations for clinical practice can be made from these limited conclusions, instead the results should only be a consideration in clinical decision making.

7. Conclusion

There is very little high quality evidence to guide clinical practice in acute burn care. The number of meta-analyses, RCTs and controlled cohort studies is small and less than one fifth (11 of 56) are of acceptable methodological quality with low risk of bias. The vast majority are single centre studies with small numbers of subjects, surrogate outcomes and high risk of bias affecting the validity of the results.

The study provides a platform from which to direct and guide future research. The aim should be to obtain an in-depth description of current burn care practice and outcomes to guide much needed large multicentre trials looking at patient centred outcomes. Well-designed, large-scale, multinational databases with specific definitions provide a wealth of information about burn care and allow significant differences in outcome and clinical practice to be identified. From this information, future RCTs can be conducted in a targeted, strategic manner to guide best practice, reduce variability and ultimately improve patient outcomes.

Conflict of interest

None declared.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.burns.2016.02.025.

REFERENCES


