A systematic review on burn scar contracture treatment: searching for evidence

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Abstract

Introduction: Treating burn scar contracture remains a challenging problem for reconstructive surgeons. At present, no consensus exists on when to use what kind of technique. Therefore, a systematic review was performed on the effectiveness of the different surgical techniques after burn scar contracture release.

Materials and Methods: Electronic databases were searched using a predefined search strategy. Studies evaluating the outcome of surgical techniques for the treatment of burn scar contractures were included. The methodological quality was tested and data was summarized.

Results: 1649 papers were identified of which 17 met the inclusion criteria. Three papers reported on a controlled trial, 14 were cohort studies, including 10 of a pre-post operative design and 4 of a comparative design. The papers described outcomes of grafts, flaps with random or defined vascularization, and dermal substitutes. All studies had methodological shortcomings and most used inappropriate statistical methods.

Conclusions: The current evidence on the effectiveness of reconstruction techniques for burn scar contractures was summarized. Due to the scarcity and low quality of the included studies, no definitive conclusions could be reached about the effectiveness of different techniques. Therefore, no direct implications for daily practice could be made. However, recommendations could be given for improvement of the quality of further primary research on the effectiveness of surgical treatment strategies for burn scar contracture release.

Introduction

Patients with burn scars often experience functional problems because of scar contractures1. A contracture describes the condition in which contraction of scar tissue results in a decrease in range of motion and/or instability of the scar. This problem is considerable in burn patients because burns often cover large areas. Although various efforts have been made to prevent the development of contractures in the acute phase of burn treatment, the contraction rate of burn scars is still a poorly controlled process and reconstructive surgery is often indicated.

The purpose of surgery is releasing the contracture to improve the function of an underlying joint by incising a scar in such a way that it allows optimal mobility. This often leads to a defect that needs closure for which various techniques are available. Many established surgical techniques are available such as split thickness skin grafts (STSG), full thickness grafts (FTG), V-Y plasties, V-M plasties, dermal substitution and free flaps. Also, new techniques mainly in the field of defined vascular supplied flaps and dermal substitution are rapidly developing, gaining importance in the treatment of burn scar contractures.

Worldwide many types of reconstructive procedures are performed for scar contractures every day, yet there is still no systematic review on the effectiveness of different treatment techniques. Therefore, we performed a systematic review on this relevant topic. We looked at the methodological and statistical quality of the available primary studies and summarized the evidence to clarify the efficacy of different techniques and the outcome parameters used.

Materials and Methods

Types of studies

All types of studies that evaluated the effect of different types of reconstruction techniques after burn scar contracture release were included. Also, studies that evaluated the effect of a single intervention (a pre-post comparison) were eligible next to studies that compared two interventions (cohort studies and RCTs). This was done because we expected it to be unlikely to find a sufficient number of randomized controlled trials concerning this subject. We realized that, as a consequence, potential biases were likely to be greater and therefore careful assessment of the risk of biases, especially the potential for selection bias and confounding, was performed.
**Types of participants**
All studies concerning reconstructive procedures for burn scar contractures were included.

**Types of interventions**
Studies examining the effect of any type of reconstruction technique after burn scar contracture release were included. If a comparator intervention was described, it could be any other reconstruction technique, placebo intervention or no intervention.

**Types of outcome measures**
Only studies that described long-term outcomes i.e. ≥ 3 months were included, because we were interested in lasting functional results. Studies with a shorter follow-up period predominantly describe the direct effect of the operation such as survival rate and percentage of necrosis of the intervention. Typical outcome measures were functional improvement, surface area measurements and scar quality. As outcomes are often described in different ways, this broad term strategy was chosen in order to include all articles concerning this subject.

**Other aspects of eligibility**
Studies were excluded if they were not (only) on burns or (only) on the treatment of contractures, there was no abstract available or it concerned a narrative description instead of an outcome description of a reconstructive technique. We decided to include studies with an inclusion number of at least 15 procedures to avoid inclusion of small, possibly selective patient series.

**Search methods for identification of studies**

**Electronic searches**
The following databases were searched until November 2012:
- Cochrane CENTRAL Trial register;
- PubMed; from inception;
- Ovid EMBASE - 1980 to date; and
- Clinical Trials Registry Platform Search Portal (www.who.int/trialsearch).

We conducted the PubMed, EMBASE and Cochrane search using the search strategy illustrated in Table 1 of the Appendix. No date or language restrictions were applied and citation lists within all studies were checked in an effort to identify additional relevant studies.

**Data collection and analysis**
Two authors (Carlijn Stekelenburg and Roos Marck) independently screened the titles and abstracts identified from the search against the inclusion criteria. The full text articles were reviewed; data extraction and quality assessment were performed independently by the same two authors (Carlijn Stekelenburg and Roos Marck). As different types of studies were included, different types of criteria based on different assessment forms were applied. For (randomized) controlled trials the Cochrane Risk of Bias criteria² were used (Table 2, Appendix), for cohort studies the Newcastle-Ottawa quality assessment scale¹ was used (Figure 1, Appendix). The studies were judged on three broad perspectives: selection, comparability and outcome. Any discrepancies in judgment between the two authors were again resolved by discussion between the review authors.

**Statistical analysis**
The included studies were summarised using a structured narrative description. The studies were grouped according to their primary outcome parameter. Of each study effect sizes (with 95% confidence intervals) were calculated if possible using the standardised response mean⁴. For this analysis, comprehensive meta-analysis Version 2, Biostat, Englewood NJ (2005) was used. Statistical pooling of the data per outcome would only be undertaken for studies that are comparable (concerning study design, type of intervention, outcome description and statistical analysis) and that present sufficient data to perform pooling.

**Results**

**Search results**
After de-duplication 1649 references were identified from electronic databases. Checking titles and abstracts on the inclusion and exclusion criteria resulted in 327 papers. The exclusion of studies with an insufficient outcome description and studies with a sample size of less than 15 persons left only 17 studies for full evaluation⁵-21. Figure 1 illustrates the flow of studies throughout the review process.

**Main description of studies**
No randomized controlled trials were identified. Three manuscripts, describing the follow-up of the same controlled trial⁷,18,19, and 14 cohort studies met the review inclusion criteria. Of the included cohort studies 4 compared different therapies⁵,6,9,16 and 10 had a pre-post operative design⁸,10-15,17,20,21. The patients were measured before operation and at a predefined time period after operation. The follow-up period varied from 3 months to 12 years. The controlled trial analyzed the same cohort at multiple time points, so each parameter could only be evaluated once⁷,18,19. The same was true for 2 cohorts which were analyzed twice in different papers⁵,6,10,11. Overall, the patient groups studied in the different papers were small with a median of 27 patients (range 10-103).

The included articles describe different operative techniques that could be divided in 4 main groups: skin grafts, flaps based on random vascularization (such as Z-plasties and
V-Y plasties flaps), flaps based on defined vascularization (perforator based flaps, free flaps), and dermal substitutes. This division seemed to cover the different treatment modalities best.

**Outcome measures**

Methods for measuring the effect of surgical interventions included goniometry, planimetry, scar assessment scales and 3D video-based goniometry (Table 1). Most studies that used range of motion as outcome measure, used goniometric measurements, but did not describe the measurement technique. Only one study used a semi-validated system to measure different movements. Planimetric measurements were performed by tracing (surface area) and/or measuring (width). In the dermal substitutes group scar scales were used to measure the scar quality as outcome measure. The Vancouver scar scale and the POSAS (Patient and Observer Scar Assessment Scale) were used.

**Effect of Interventions**

**Skin grafts**

Four studies assessed the outcome of skin grafts after burn scar contracture release, of which 3 used the range of motion (ROM) as primary outcome parameter to assess the functional results. The detailed descriptions of the outcomes can be found in Table 1.

**Flaps with random vascularization**

All papers that studied the effectiveness of plasties used ROM as outcome parameter. Table 1 gives a detailed description of the different flaps and their outcome.

**Flaps with defined vascularization**

Five studies described the outcome of different flaps on various anatomic locations. Tsai et al, Woo et al, and Er et al found an increased postoperative range of motion. Although all the 3 studies measured an increased range of motion, unfortunately, none used statistical analysis to evaluate this effect. Three of the authors used planimetric measurements to evaluate the effect of treatment strategies; surface area or width during surgery was compared to the surface area or width at follow-up. However, only Verhaegen et al performed statistical analysis and found no statistical difference. See Table 1.

**Dermal substitutes**

Six manuscripts describing the outcome of 3 trials assessed the effect of dermal substitutes in combination with an STSG. Different dermal substitutes are used across studies: Integra, Matriderm prototype, and Alloderm. All the studies that measured scar quality before and after surgical procedures showed a significant decrease in Vancouver Scar Scale score. Furthermore, no difference in surface area was found for the use of skin grafts with or without dermal substitution; both show a considerable contraction after a mean follow-up period of more than one year. Table 1 describes in detail the outcomes of the different studies relating dermal substitutes.

**Effect sizes and meta-analysis**

The studies were subdivided according to the way the outcome was measured, i.e. planimetry, range of motion or scar quality. The effect sizes were calculated and plotted to allow for a comparison between the treatments per outcome parameter. Calculation of effect sizes was only done when comparison with another independent study that measured the outcome similarly was possible. Figure 2 visualizes the effect sizes with corresponding 95% confidence intervals of different interventions. No meta-analysis of these data could be performed because this was incorrect for both clinical and statistical heterogeneity of the studies. Calculation of the effect sizes was done using mean differences, standard deviations, sample sizes and p-values retrieved from the result sections of the articles. Corresponding authors were contacted in case studies did not contain sufficient information. After repeated requests we were only able to calculate effect sizes for a small amount of studies.
### Table 1. Summary of outcome in included studies.

<table>
<thead>
<tr>
<th>Study</th>
<th>Intervention</th>
<th>Number</th>
<th>Primary outcome parameter</th>
<th>Effect of intervention</th>
<th>Use of validated outcome measures?</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Controlled trials</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Van Zuijlen et al (2000 and 2001)(^{18,19})</td>
<td>Dermal substitution +STSG vs. STSG</td>
<td>44</td>
<td>Scar quality and surface area</td>
<td>Surface area: no significance diff between with or without dermal substitute</td>
<td>Planimetry</td>
</tr>
<tr>
<td>Bloemen et al (2010)(^{7})</td>
<td></td>
<td>34</td>
<td></td>
<td>VSS: no significance diff between with or without dermal substitute</td>
<td>Vancouver scar scale</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>POSAS: 12 years: significant better result for pliability, relief and general</td>
<td>POSAS</td>
</tr>
<tr>
<td><strong>Cohort studies - Comparative design</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alexander et al (1982)(^{5})</td>
<td>Skin grafts, Z plasties, Rotation flaps</td>
<td></td>
<td>ROM</td>
<td>NS differences between Graft, z-plasty and rotational flap</td>
<td>Goniometry: retrospective chart review</td>
</tr>
<tr>
<td>Alexander et al (1983)(^{6})</td>
<td>V-M plasty</td>
<td>36</td>
<td>ROM</td>
<td>Significant differences in ROM and cosmetic appearance between V-M plasty and control group</td>
<td>Goniometry: retrospective chart review</td>
</tr>
<tr>
<td>Stern et al (1985)(^{14})</td>
<td>Flaps (Z-plasty, X-Y advancement, rotation flap) and STSG’s</td>
<td>78</td>
<td>ROM</td>
<td>Decrease in extension contracture for Flaps and STSG’s. No statistical analysis</td>
<td>Goniometry: retrospective chart review</td>
</tr>
<tr>
<td>Iwuagwu et al (1999)(^{9})</td>
<td>STSG vs. FTSG</td>
<td>75</td>
<td>Rereleases</td>
<td>Significant more rereleases in of STSG’s than for FTSG’s</td>
<td>Documentation: retrospective chart review</td>
</tr>
<tr>
<td><strong>Cohort studies - Pre-post operative design</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moiemen et al (2000 and 2006)(^{10,11})</td>
<td>Integra + STSG</td>
<td>30</td>
<td>Scar quality</td>
<td>Significant improvement in VSS pre-op vs. post-op</td>
<td>Vancouver scar scale</td>
</tr>
<tr>
<td>Woo et al (2001)(^{13})</td>
<td>Free flap</td>
<td>18</td>
<td>ROM</td>
<td>Increase in range of motion pre-op vs. post-op. No statistical analysis</td>
<td>Goniometry: retrospective chart review</td>
</tr>
<tr>
<td>Peker et al (2003)(^{16})</td>
<td>Y-V plasty combined with Z-plasty</td>
<td>98</td>
<td>ROM</td>
<td>Significant increase in ROM arc</td>
<td>Goniometry: retrospective chart review</td>
</tr>
<tr>
<td>Er et al (2005)(^{21})</td>
<td>Thoracodorsal perforator based cutaneous island flap</td>
<td>15</td>
<td>ROM</td>
<td>Increase in ROM pre-op vs. post-op. No statistical analysis</td>
<td>Goniometry: retrospective chart review</td>
</tr>
<tr>
<td>Tsai et al (2006)(^{17})</td>
<td>Flaps</td>
<td>40</td>
<td>ROM and Flap width</td>
<td>Increase in ROM for different areas in the neck. Increase in flap width. No statistical analysis</td>
<td>Goniometry: retrospective chart review</td>
</tr>
<tr>
<td>Rashid et al (2006)(^{19})</td>
<td>Supraclavicular flap</td>
<td>27</td>
<td>Flap width</td>
<td>Increase in flap width pre-op vs. post-op. No statistical analysis</td>
<td>Planimetry: measuring</td>
</tr>
<tr>
<td>Verhaegen et al (2010)(^{20})</td>
<td>Perforator based flaps</td>
<td>22</td>
<td>Flap width and area</td>
<td>No statistical differences in flap width and area directly postoperative and at follow-up</td>
<td>Planimetry</td>
</tr>
<tr>
<td>Oh et al (2011)(^{17})</td>
<td>Alloderm + STSG</td>
<td>27</td>
<td>Scar quality</td>
<td>Significant improvement in VSS pre-op vs. post-op</td>
<td>Vancouver scar scale</td>
</tr>
<tr>
<td>Sison-Williamson et al (2012)(^{22})</td>
<td>STSG</td>
<td>16</td>
<td>ROM</td>
<td>Significant improvement in most motions that are needed for high reach, hand to head and hand to back tasks</td>
<td>3D-videobased technique using retroreflective markers attached to the patient</td>
</tr>
</tbody>
</table>

Table 1. Continued.
**Assessment of the risk of bias**

Information on the methodological quality of the included studies is summarized in Table 2. The overall risk of biases was high in all cohort studies. One of the most frequent encountered problems included insufficient description of the cohort. Only two studies satisfactorily described the cohort; a representative cohort and the presence of a comparable cohort\(^5\),\(^9\). One study performed most favorably by controlling for differences between cohorts on the basis of the design. In terms of outcome assessment, the weaknesses were mainly found in an insufficient outcome measurement\(^8\),\(^12\),\(^13\),\(^14\),\(^15\),\(^16\),\(^17\),\(^18\),\(^19\),\(^20\). The key concern for the controlled trials was the absence of randomization and blinding resulting in selection, performance, and detection bias. The description of the outcome however, was done adequately with the use of reliable and valid measurement instruments\(^7\),\(^18\),\(^19\).

**Discussion**

As far as we have been able to establish, this is the first systematic review on the effectiveness of reconstructive techniques after burn scar contracture release revealing that the current literature is of low methodological quality. We analyzed 1649 articles on the subject of which only 17 described a surgical treatment regimen in a sample of ≥15 patients. Considering the fact that we applied mild inclusion criteria regarding the year of publication and study type, this is a particularly low number of studies.

The included studies were evaluated using standardized assessment scales and found to be of low overall quality. Because of these limitations, we were not able to provide sufficient evidence to draw conclusions on the effectiveness of reconstructive techniques after burn scar contracture release and developing a standardized treatment algorithm remains a challenge. Probably, the most important conclusion of this review is that there is definitely a need for more adequate research.

Several reasons may explain the difficulty in stating conclusions on the effectiveness of reconstructive techniques for burn scar contracture release. The first relates to the design of the studies: most were of a pre-post operative design without the presence of a comparative cohort. These studies reported an improvement in range of motion or scar...
quality, but only a few compared the technique of interest with another technique. As can be seen in Figure 2, the effect sizes of the studies with a comparative cohort are smaller than the studies of a pre-post operative design. This means that besides the improvement that was established by means of an operation, the difference between reconstructive techniques is moderate. The pre-post operative design is informative, but does not allow for strong conclusions in terms of effectiveness of one treatment method over another. Three papers reported on the same controlled trial. These papers had a superior design and used reliable and validated measurements. As these 3 papers were based on the same patient population, we could not pool the results. A second reason may relate to the considerable amount of studies that failed to perform an adequate data presentation and statistical analysis, preventing a full interpretation of the presented results. Effect sizes were only calculated in case the same construct was measured by a comparable measurement technique (Figure 2). Because of both the statistical and methodological heterogeneity, no meta-analysis could be performed.

Although most of the interventions have some evidence for the effectiveness in burn scar contracture release, the included studies used different outcome parameters limiting comparisons between treatments and making a meta-analysis impossible to perform. Therefore, only a rough division could be made between functional outcome parameters and scar quality parameters. Furthermore, most studies did not describe the type of contracture. This is important because broad contractures reasonably need a different treatment than linear contractures. A final difficulty relates to the fact that burn scar reconstruction options are not completely interchangeable because they are subject to many different variables, such as width, location and extensiveness of the scars. This may put challenges on systematically reviewing the literature on the treatment of burn scar contractures.

This review has limitations. The methodological quality of the included studies was assessed using the New Castle Ottawa quality assessment tool in order to address the quality of non randomized studies. Because this tool presumes the presence of a comparable cohort, all studies except for one were not awarded any stars for comparability. Other tools for assessing the risk of biases were considered; however, to our knowledge no validated tools for assessing the methodological quality of pre-post design studies were available. Second, we chose to use a broad search strategy to include all types of treatment modalities. Although this offers an overview of the available literature on burn scar contracture release, it also results in an inability to compare data because of the heterogeneity of the included studies.

Despite the low number of eligible studies and the poor quality of the included studies, strength of this study is the profundness of reviewing the data: an extensive search of 4 databases, no restriction regarding language and year and study type, and the independent reviewing by two researchers. Hereby, this review uncovers the weaknesses of the currently available scientific literature offering a starting point for future research. We believe this to be a unique opportunity to bundle all the lessons learnt so far in the field of treating burn scar contractures and more specifically in the hurdles and challenges that one faces when performing studies in this field. Therefore it is paramount that we make good use of these lessons when setting up future studies.

We make a plea to use the findings of this review and its implication for future research. The first step is the design of a sound study set up; preferably a design that uses a comparator intervention. Only then the treatment effect can be distinguished from the clinical course and from the treatment with other surgical techniques. Also, a relevant sample size should be chosen. Comparative studies with a too small sample size are not informative and a realistic power calculation is needed for determining the numbers required in a trial, depending on the expected effect of the intervention in a specific patient population. Studies should include a clear description of the patient groups including the type of contracture. The outcome assessment should be carefully linked to a relevant clinically expected outcome. Reliable and valid measurement techniques should be used to assess the outcome, which allows for comparison between study results. The introduction of new measurement tools without validating them is not preferred. Finally, an adequate data presentation and statistical analysis should be considered. Of the studies included in our review, many contain information to perform statistical analysis, but fail to present statistical important information such as standard deviations, p-values and confounders. Further primary research in collaboration with experts in research methodology and biostatistics is highly recommended. This review aims to encourage and inspire research initiatives on reconstruction techniques after burn scar contracture release.

Conclusions

This review has brought to light that the current literature on the effectiveness of reconstructive techniques after burn scar contracture release is below par in both quantity and quality of the studies performed. Due to the lack of evidence we were not able to provide definitive conclusions on the effectiveness of different techniques or make specific recommendations on treatment algorithms. However, in view of the currently available literature future research initiatives are strongly encouraged. It is of the essence that such studies include methods of high quality, use of comparative outcome measures and adequate statistical analysis to ensure they contribute to a better understanding in the optimal treatment of burn scar contractures.
References


### Appendix

#### Table 1. Detailed search strategy for MEDLINE and EMBASE.

<table>
<thead>
<tr>
<th>Nr</th>
<th>Subject</th>
<th>PubMed</th>
<th>EMBASE</th>
<th>Cochrane</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Burns</td>
<td>Mesh descriptor Burns [explode all trees]</td>
<td>burn/</td>
<td>(burn OR burns OR scald* OR postburn* OR (thermal AND injur*)):ti,ab,kw</td>
</tr>
<tr>
<td>2</td>
<td>Burn OR burns OR burned OR scald* [tiab]</td>
<td>burn or burns or burned or scald* or postburn,ti,ab,kw.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Thermal AND injur* [tiab]</td>
<td>thermal and injur*:ti,ab,kw.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Scar/ Contracture</td>
<td>Mesh Cicatrix [noexp]</td>
<td>skin scar/ or scar/</td>
<td>(contractur* OR scar* OR cicatri* OR hypertroph*):ti,ab,kw</td>
</tr>
<tr>
<td>5</td>
<td>Mesh cicatrix, hypertrophic</td>
<td>burn contraction/ or contracture/ or flexion contracture/ or joint contracture/or (contractur* OR scar* OR cicatri* OR hypertroph*):ti,ab,kw</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Contractur* OR scar* OR cicatri* OR hypertroph* [tiab]</td>
<td>exp SCAR FORMATION/ or exp BURN SCAR/ or exp HYPERTROPHIC SCAR/or</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>Reconstruction</td>
<td>Mesh descriptor Reconstructive Surgical Procedures [explode all trees]</td>
<td>reconstruct* or releas*:ti,ab,kw.</td>
<td>(axial OR perforator OR random OR rotation OR advancement OR transposition OR free) AND flap* OR reconstructive surg*:ti,ab,kw</td>
</tr>
<tr>
<td>8</td>
<td>Mesh descriptor Surgical Flaps [explode all trees]</td>
<td>exp island flap/ or exp transverse rectus abdominis musculocutaneous flap/ or exp vertical rectus abdominis musculocutaneous flap/ or exp perforator flap/ or exp forehead flap/ or exp skin island flap/ or exp radial forearm flap/ or exp anterolateral thigh flap/ or exp adipofascial flap/ or exp thoracodorsal artery perforator flap/ or exp latissimus dorsi flap/ or exp scapular flap/ or exp superior gluteal artery perforator flap/ or exp skin transposition flap/ or exp skin flap survival/ or exp superficial inferior epigastric artery flap/ or exp deep inferior epigastric perforator flap/ or exp inferior gluteal artery perforator flap/ or exp lateral arm flap/ or exp muscle flap/ or exp myocutaneous flap/ or exp pedicled skin flap/ or exp gracilis flap/ or exp deltopectoral flap/ or exp skin flap/ or exp inguinal flap/ or exp paraumbilical perforator flap/ or exp tissue flap/ or exp fasciocutaneous flap/</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>reconstructive surg* [tiab]</td>
<td>Reconstructive surg*:ti,ab,kw.</td>
<td>(reconstruct* OR releas*):ti,ab,kw</td>
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<tr>
<td>10</td>
<td>z plasty OR y plasty OR y v plasty</td>
<td>z plasty or y plasty or y v plasty,ti,ab,kw</td>
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<tr>
<td>11</td>
<td>Axial OR perforator OR random OR rotation OR transposition OR advancement OR transposition OR free AND flap* [tiab]</td>
<td>axial or perforator or random or rotation or transposition or advancement or pedicled or free) and flap*,ti,ab,kw.</td>
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<td>skin or dermal or full thickness and graft*:ti,ab,kw.</td>
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<td>split thickness OR split-thickness OR split skin AND graft* [tiab]</td>
<td>split skin or split thickness and graft*:ti,ab,kw.</td>
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<tr>
<td>14</td>
<td>STSG OR FGT [tiab]</td>
<td>STSG or fgt,ti,ab,kw.</td>
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<tr>
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<td>16</td>
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<td>artificial skin or matriderm or integra or alloderm or dermagraft or oasis,ti,ab,kw.</td>
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<td></td>
</tr>
<tr>
<td>17</td>
<td>#12 OR #13 OR #14 OR #15 OR #16 AND (reconstruct* OR releas*)</td>
<td>#12 OR #13 OR #14 OR #15 OR #16 AND #7</td>
<td>(#8 AND #9)</td>
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<tr>
<td>18</td>
<td>(#7 OR #8 OR #9 OR #10 OR #11) OR #17</td>
<td>#8 OR #9 OR #10 OR #11 OR #17</td>
<td>(#1 AND #4 AND (#7 OR #17))</td>
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<tr>
<td>19</td>
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<td>(#1 OR #2 OR #3) AND (#4 OR #5 OR #6) AND #18</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Appendix, Table 1. Continued.
### Domain | Description | Review authors’ judgment
--- | --- | ---
Sequence generation | Describe the method used to generate the allocation sequence in sufficient detail to allow an assessment of whether it should produce comparable groups. | Was the allocation sequence adequately generated? |
Allocation concealment | Describe the method used to conceal the allocation sequence in sufficient detail to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment. | Was allocation adequately concealed? |
Blinding of participants, personnel and outcome assessors | Describe all measures used, if any, to blind study participants and personnel from knowledge of which intervention a participant received. Provide any information relating to whether the intended blinding was effective. | Was knowledge of the allocated intervention adequately prevented during the study? |
Incomplete outcome data | Describe the completeness of outcome data for each main outcome, including attrition and exclusions from the analysis. State whether attrition and exclusions were reported, the numbers in each intervention group (compared with total randomized participants), reasons for attrition/exclusions where reported, and any re-inclusions in analyses performed by the review authors. | Were incomplete outcome data adequately addressed? |
Selective outcome reporting | State how the possibility of selective outcome reporting was examined by the review authors, and what was found. | Are reports of the study free of suggestion of selective outcome reporting? |
Other sources of bias | State any important concerns about bias not addressed in the other domains in the tool. If particular questions/entries were pre-specified in the review’s protocol, responses should be provided for each question/entry. | |

**NEWCASTLE - OTTAWA QUALITY ASSESSMENT SCALE**

**COHORT STUDIES**

**Note:** A study can be awarded a maximum of one star for each numbered item within the Selection and Outcome categories. A maximum of two stars can be given for Comparability

**Selection**
1) **Representativeness of the exposed cohort**
   a) truly representative of the average ___________ (describe) in the community *
   b) somewhat representative of the average ___________ in the community *
   c) selected group of users e.g. nurses, volunteers
   d) no description of the derivation of the cohort
2) **Selection of the non exposed cohort**
   a) drawn from the same community as the exposed cohort *
   b) drawn from a different source
   c) no description of the derivation of the non exposed cohort
3) **Ascertainment of exposure**
   a) secure record (e.g. surgical records) *
   b) structured interview *
   c) written self report
   d) no description
4) **Demonstration that outcome of interest was not present at start of study**
   a) yes *
   b) no

**Comparability**
1) **Comparability of cohorts on the basis of the design or analysis**
   a) study controls for ___________ (select the most important factor) *
   b) study controls for any additional factor * (This criteria could be modified to indicate specific control for a second important factor.)

**Outcome**
1) **Assessment of outcome**
   a) independent blind assessment *
   b) record linkage *
   c) self report
   d) no description
2) **Was follow-up long enough for outcomes to occur**
   a) yes (select an adequate follow-up period for outcome of interest) *
   b) no
3) **Adequacy of follow-up of cohorts**
   a) complete follow-up - all subjects accounted for *
   b) subjects lost to follow-up unlikely to introduce bias - small number lost - > ____ % (select an adequate %) follow-up, or description provided of those lost) *
   c) follow-up rate < ____% (select an adequate %) and no description of those lost
   d) no statement

**Appendix, Table 2. The Cochrane Collaboration’s tool for assessing risk of bias**.

**Appendix, Figure 1. The Newcastle-Ottawa quality assessment scale**.
References
