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Reconstructive

Dressing Influence on Re-epithelialization Rate Following Split-thickness Skin Graft Harvest: Network Meta-analysis of Randomized Controlled Trials

Nawaf Alhindi, MBBS*
Sarah Qari, MBBS†
Houriah Nukaly, MBBS‡
Abdullah Althagafi, MBBS*
Sarah Alzolaibani, MBBS§
Mousa Akkour, MBBS¶
Kausar Ahmed, MBBS‖
Abdulaziz Samandar, MBBS**
Abdulaziz Alsuhaim, MBBS††
Hanin Banjer, MBBS‡‡
Feryal Alali, MBBS‡‡
Assal Hobani, MBBS†
Abdulaziz Altala, MBBS§§
Zainab Alasfour, MBBS¶¶
Khalid Arab, MD, FRCS(C)‖‖

Background: More than 160,000 skin grafts are performed annually in approximately 1 out of every 3 burn hospitalizations individually because they are primarily simple and quick. This network meta-analysis aimed to compare different conventional dressing options based on re-epithelialization time and side effects for split-thickness skin graft donor sites.

Methods: As per preferred reporting items for systematic reviews and meta-analysis guidelines, a thorough systematic review and network meta-analysis were conducted. A comprehensive search was performed using MEDLINE, Cochrane, and Embase databases, and all publications published before August 2023 were included without time restrictions.

Results: This study performed a network meta-analysis of 25 unique randomized controlled trials published between 1983 and 2022. We found that alginate is the most often used, followed by paraffin gauze. Nonetheless, povidone-iodine-impregnated foam (Betafoam) was the most effective (90.4%), followed by hydrocolloid (87.9%). Petrolatum (73.5%) is associated with faster re-epithelialization than alginate (40.6%) and paraffin (18.1%). Cotton gauze ranked as the worst modality for skin graft donor-site dressing (3.9%).

Conclusions: This study serves as a guide for the selection of proper dressing for patients undergoing partial-thickness skin graft harvest. Even though povidone-iodine-impregnated foam was the most effective, we recommend further research comparing other factors for selecting dressings, such as wound and patient characteristics, availability, and costs of dressings. *(Plast Reconstr Surg Glob Open 2025;13:e6748; doi: 10.1097/GOX.0000000000006748; Published online 9 May 2025.)*

*From the *Saudi Ministry of Health, Rabigh, Saudi Arabia; †Faculty of Medicine, Ibn Sina Medical College, Jeddah, Saudi Arabia; ‡Faculty of Medicine, Batterjee Medical College, Jeddah, Saudi Arabia; §Faculty of Medicine, Taibah University, Madinah, Saudi Arabia; ¶Division of Plastic Surgery, Department of Surgery, Prince Sultan Military Medical City, Riyadh, Saudi Arabia; ‖Faculty of Medicine, Fakeeh Medical College, Jeddah, Saudi Arabia; **Faculty of Medicine, Umm-AlQura University, Makkah, Saudi Arabia; ††Faculty of Medicine, King Saud University, Riyadh, Saudi Arabia; ‡‡Faculty of Medicine, King Abdulaziz University, Jeddah, Saudi Arabia; §§Faculty of Medicine, Dar AlUloom Medical College, Riyadh, Saudi Arabia; ¶¶Faculty of Medicine, King Faisal University, Alahsa, Saudi Arabia; and ‖‖Division of Plastic Surgery, Department of Surgery, College of Medicine, King Saud University, Riyadh, Saudi Arabia.*

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INTRODUCTION

More than 160,000 skin grafts are performed annually in approximately 1 out of every 3 burn hospitalizations individually, according to the Healthcare Cost and Utilization Project.[1] Split-thickness skin grafts (STSG) are widely used in reconstructive procedures to cover wounds resulting from burns, abrasions, trauma, diseases, and infections. They are also commonly used for the replacement of blemished and missing skin.[2,3] Upon harvesting of the STSG, the donor site's epidermal and dermal layers are sustainably damaged. Therefore, after extraction of an STSG, it is essential to maintain the integrity of the donor site as patients often experience more pain there than at the recipient site. Donor-site dressings aim to reduce patient discomfort, prevent infection, minimize leakage of wound exudate, and promote re-epithelialization within 7–10 days.[4] Effective management of the donor site can help prevent longer

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hospital stays, decrease the need for analgesics, and facilitate faster recovery and mobilization.[5] In recent years, the variety of dressings for STSG donor sites has increased commercially, along with various dressing techniques that have been applied to achieve earlier regeneration.[5–8] However, an ideal dressing that promotes healing, minimizes scarring, is affordable, and is easy to use has yet to be produced. There are variations in healing rates, prevalence of infections, and patient comfort depending on the type of dressing used for STSG donor sites. Each dressing has its unique characteristics but no single dressing has proven to be ideal.[9] To better understand the impact of various dressing types on STSG donor sites, we conducted a systematic review and network meta-analysis to evaluate the effects of the different dressings on the rate of re-epithelialization, occurrence of side effects, and complexity of care.

Takeaways

Question: What is the best dressing to achieve faster re-epithelialization of the skin graft donor site following partial-thickness skin harvest?

Findings: This review found a significant superiority of utilizing povidone-iodine-impregnated foam and hydrocolloid over other conventional dressings.

Meaning: Povidone-iodine-impregnated foam and hydrocolloid are highly recommended for partial-thickness skin donor-site management.

METHODS AND MATERIALS

Literature Search

A thorough systematic review and network meta-analysis were carried out following preferred reporting items for systematic reviews and meta-analysis guidelines; the study protocol was prospectively registered in PROSPERO with the identification number (CRD42023449798).[10] Using the most important databases, including MEDLINE, Cochrane, and Embase, a comprehensive search for published articles reporting the rate of re-epithelialization in skin graft donor-site dressings was conducted with no time constraints up to August 2023.

Study Selection

Articles were initially screened according to the title and abstract using Rayyan web,[11] followed by full-text screening to ensure accuracy with the following inclusion criteria: (1) published without time frame limitations up to August 2023; (2) published in English language; (3) reported randomized controlled trials (RCT); (4) patients

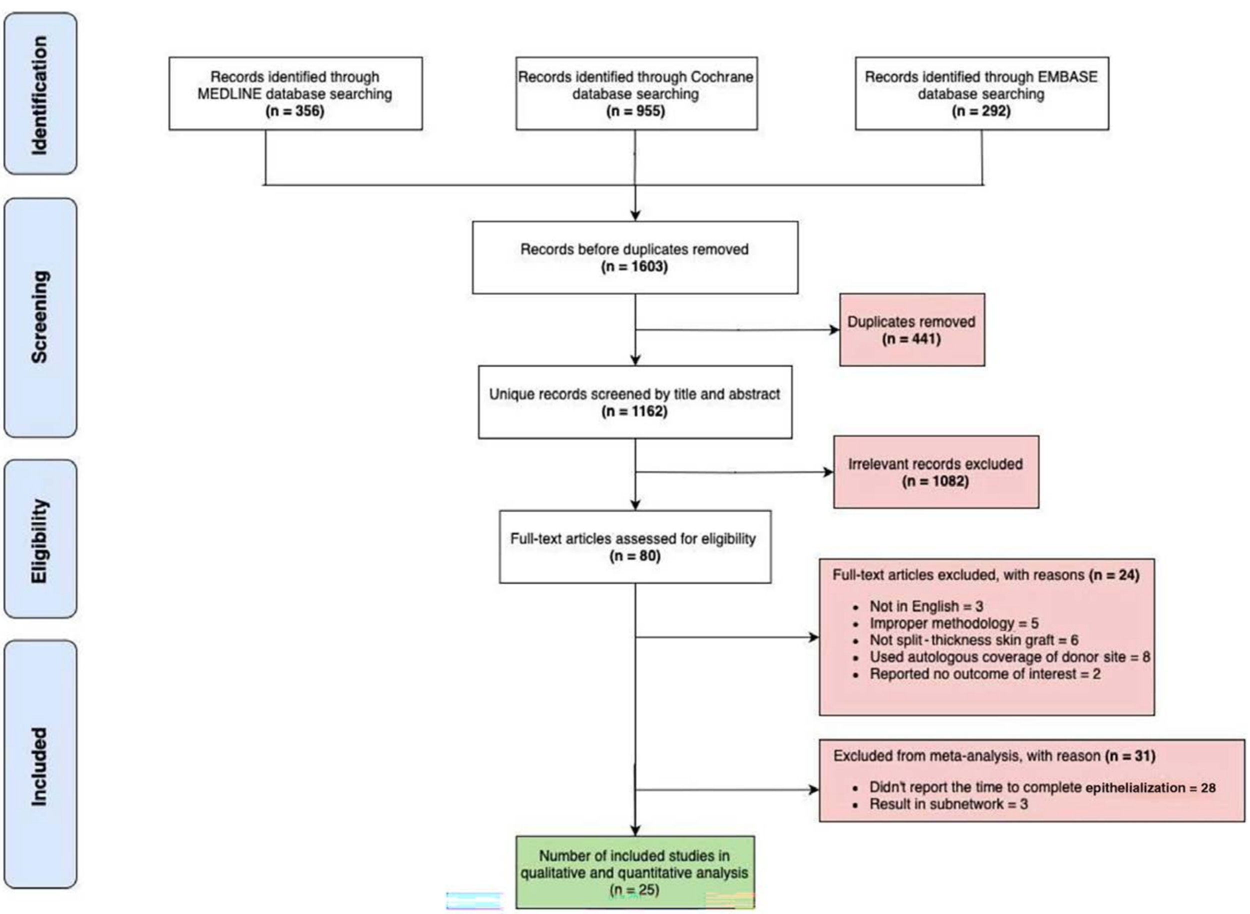

Fig. 1. PRISMA flowchart. PRISMA, preferred reporting items for systematic reviews and meta-analysis.

who underwent STSG harvest with donor sites managed by any dressing; and (5) reported outcomes of interest for the clinical question. Meanwhile, studies were excluded due to improper methodology or included a sample of flap or full-thickness skin graft coverage. The review process involved an independent review of all studies by 6 authors. In case of any disagreements, 3 other authors intervened to resolve the inconsistencies through discussion.

Screening and Data Extraction

A team of 13 authors began working on the data extraction table. An Excel sheet (Microsoft 365) was utilized, with different columns representing various aspects of interest. These columns included the following information: characteristics of the studies, sample details, characteristics of the donor site, intervention details, complications and side effects related to the donor site, and outcomes (including the time of complete healing).

Assessment of Methodological Quality

A comprehensive evaluation of RCTs was conducted by 2 independent parties simultaneously using the Cochrane Collaboration risk-of-bias instrument,[12] which focuses on 6 critical methodological domains that are key determinants of bias. The likelihood of bias was categorized as high, low, or unclear. To ensure consensus and resolve any exceptional disagreement, a third party was involved in the evaluation process.

Data Synthesis and Analysis

RStudio (R version 4.1.1), a programming language used for statistical computing, was utilized to perform network meta-analysis of 16 different interventions. The author used a standardized mean difference effect measure for the mean time taken to achieve complete wound healing or epithelialization with a 95% confidence interval (CI). Multiple packages including netmeta, forestplot, and grid were used. The reference treatment in the meta-analysis is alginate. All results are presented in the form of a network graph, league table, and surface under the cumulative ranking curve (SUCRA), which is a statistical method to rank interventions based on the probability of being the best for management. However, a publication bias was also utilized using the Egger test.

RESULTS

Literature Findings

A thorough review of the prevailing literature revealed 1603 articles overall. The articles included 356 from MEDLINE, 955 from Cochrane, and 292 from Embase. For this study, the authors initially included 80 full-text published articles. However, after implementing the inclusion/exclusion criteria, only 56 articles were initially selected. Then, 55 articles were further excluded. In the end, only 25 unique RCTs published between 1983 and 2022 were included (Fig. 1).

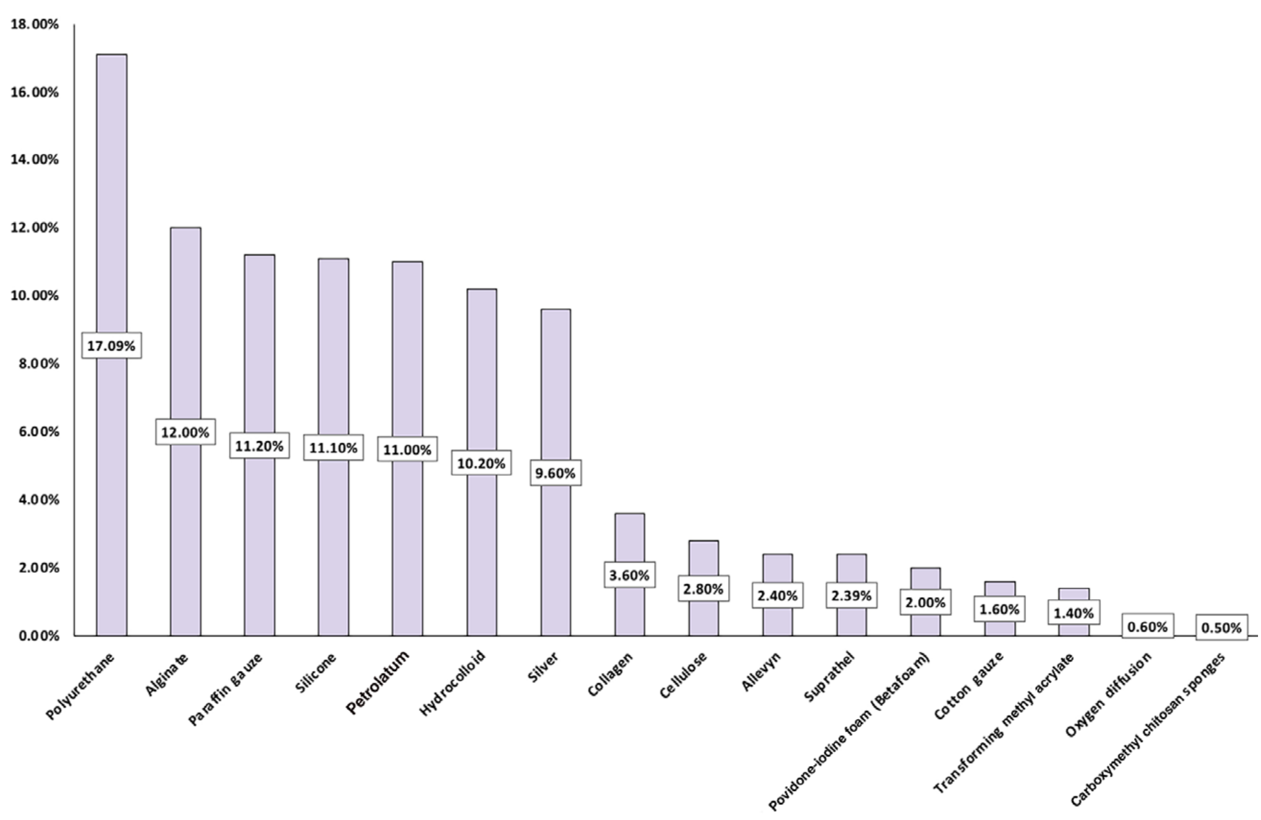

Fig. 2. Bar chart represents the complete sample distribution according to the interventions.

Characteristics of Included Studies

This network meta-analysis included a total of 25 RCTs involving 1541 participants, published in the time frame of 1983 and 2023.[3,4,9,13–34] The majority of the studies were conducted in Europe (10 studies),[14,17,18,21–23,27–30,33] followed by North America (6 studies),[4,9,15,16,25,34] Asia (6 studies),[13,19,20,24,26,31] and Australasia (2 studies).[3,32] These studies assessed the efficacy of different STSG donor-site dressings. The primary outcome of interest in this network meta-analysis was re-epithelialization time. (**See table, Supplemental Digital Content 1**, which summarizes the characteristics of the studies included, **http://links.lww.com/PRSGO/E4**.)

Results of Individual Studies

Twenty-five RCTs including a total of 1541 patients who underwent skin graft donor-site dressing were analyzed in this study. Among the studies that reported the sex of participants, 63% (657 of 1042) of patients were men and 37% (385 of 1042) were women, which is differentiation in numbers; 7 articles did not give any information about the sex of the participants.[3,9,15,16,23,26,30] The mean patient age was 48.76. In 2 articles, the mean age was not mentioned.[9,23] The most included dressing type was polyurethane (n = 529 of 3088; 17.09%) followed by alginate (n = 369 of 3088; 12%), paraffin gauze (n = 348 of 3088; 11.2%), and silicone (n = 344 of 3088; 11.1%) (Fig. 2).

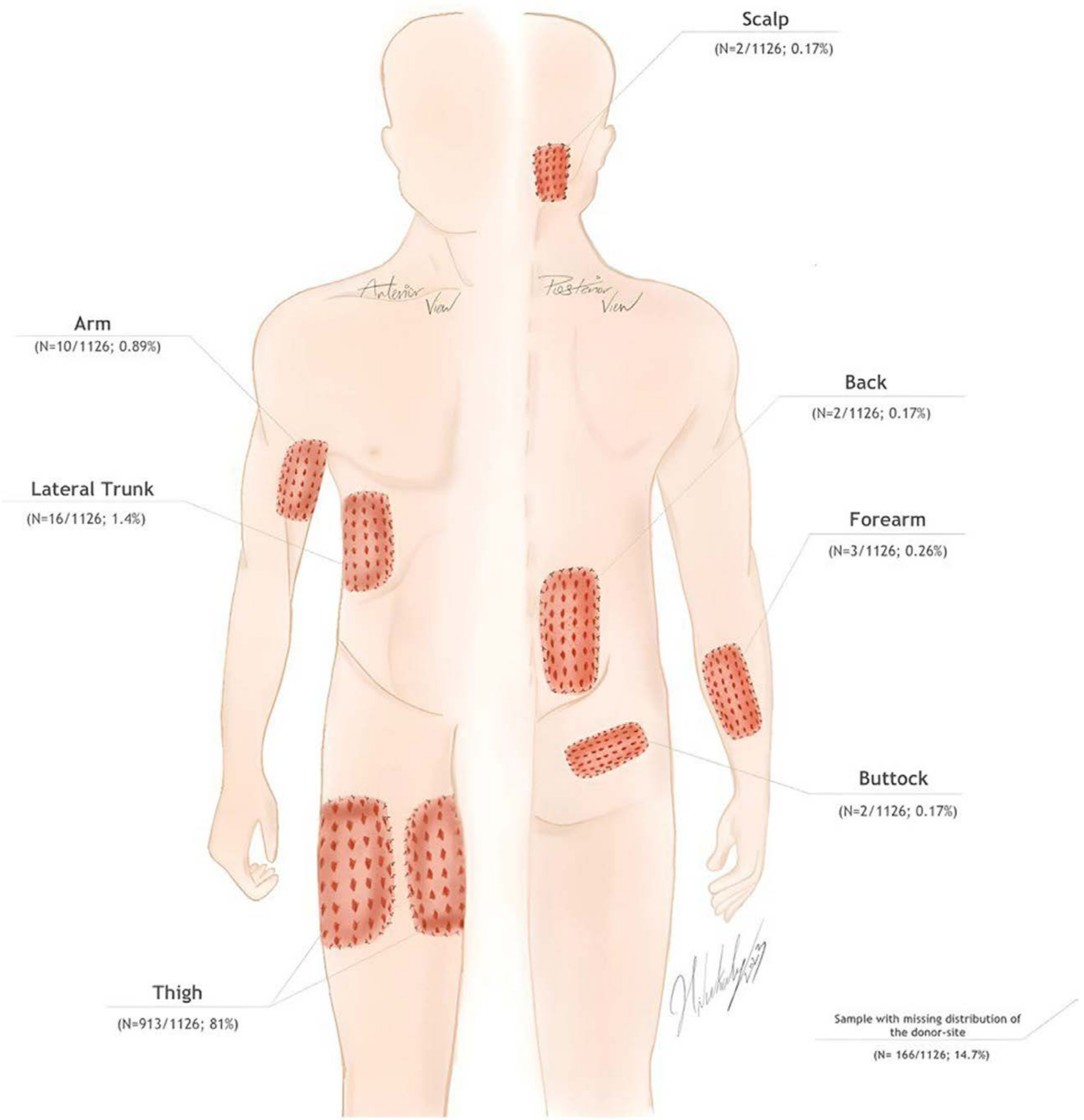

Fig. 3. Illustration representing the most common donor-site distribution of included sample.

In our analysis of donor-site utilization in skin graft harvest, the thigh emerged as the most common site, with specific distributions as follows: overall thigh usage was 81% (n = 913 of 1126), followed by the lateral trunk (16 of 1126; 1.4%), lower leg (6 of 1126; 0.5%), and other undetermined location (14.7%, 166 of 1126). Notably, a significant number of studies did not specify either the donor site or the number of lesions.[9,15,16,31] Regarding graft thickness, the average measured across different donor sites was 0.013 inches. Notably, however, many studies did not provide data on graft thickness[9,14–17,19,21,23,26–29,34] (Fig. 3) (**Supplemental Digital Content 1**, **http://links.lww.com/PRSGO/E4**).

Methodological Quality and Risk of Bias

The majority of the included studies were deemed to have a low risk of bias based on the Cochrane risk-of-bias assessment. Almost all of the included publications are associated with a low risk of bias in the aspect of randomization and allocation concealment. However, we found that several studies concerning blinding were either associated with high risk or the risk was not clear. Most of the studies had not excluded any patient after starting the intervention; therefore, almost all of the included studies have a low attrition bias, thus increasing the reliability of the data collected (Fig. 4).

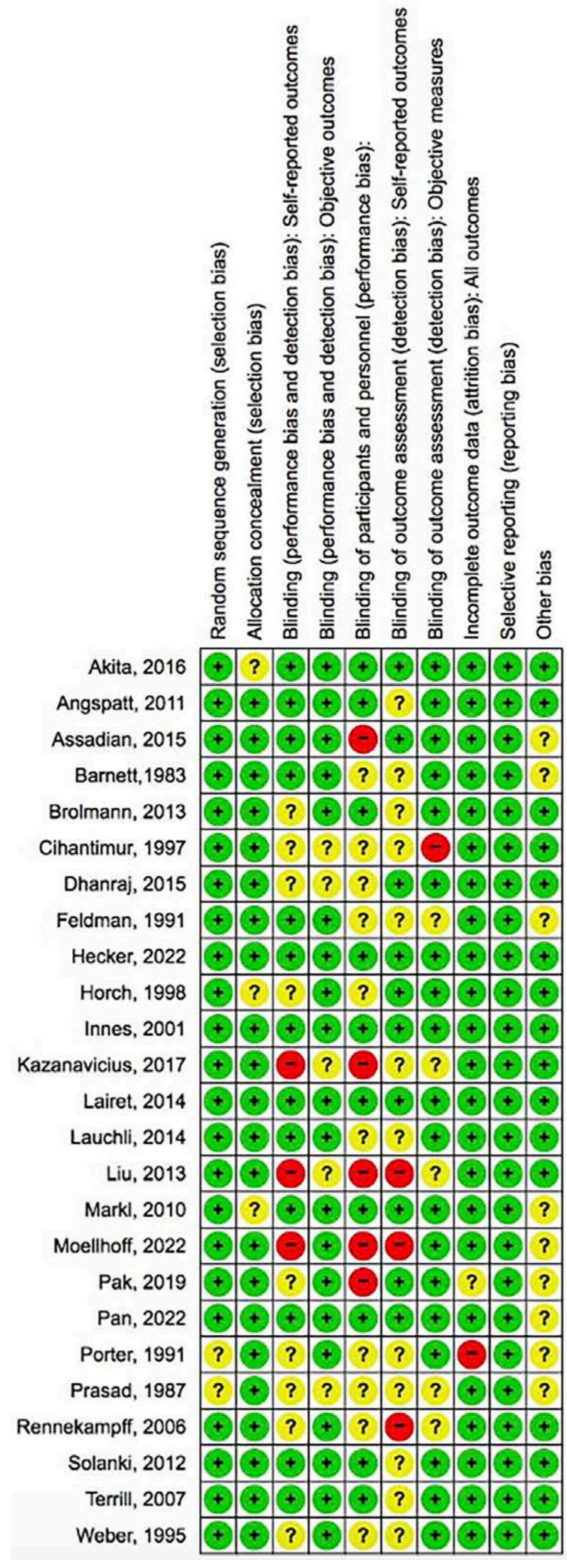

Fig. 4. Cochrane bias assessment tool summary.

Results of the Network Meta-analysis

In our comprehensive systematic review study, we identified 25 studies that met the rigorous inclusion criteria for participation in the network meta-analysis. Among these selected studies, 1 featured a comparison of 6 distinct arms, and another study comprised a comparison of 5 arms. Additionally, 7 studies contributed to the analysis by presenting comparisons involving 3 arms, whereas 16 studies focused on dual-arm comparisons (Fig. 5).

The outcomes of direct comparison showed a significant superiority in the rate of epithelialization using hydrocolloid compared with collagen (inverse variance [IV] = 4.66, 95% CI 0.2–9.1), alginate (IV = 6.44, 95% CI 1.7–11.1), silicon (IV = −10.20, 95% CI −19.3 to −1.0), and paraffin (IV = −8.90, 95% CI −17.0 to −0.7). The rest of the outcomes of the network meta-analysis are shown in Supplemental Digital Content 2. (**See table, Supplemental Digital Content 2**, which displays the league table representing summary estimates from the network meta-analysis, **http://links.lww.com/PRSGO/E5**.)

Results of SUCRA Ranking Probability

In the context of our systematic review study, where we evaluated the efficacy of 16 distinct skin graft donor-site dressings in terms of their ability to facilitate re-epithelialization and complete wound healing, we used the SUCRA probability method to gauge their performance. Notably, povidone-iodine (PI)-impregnated foam (Betafoam) emerged as the most advantageous choice, boasting a remarkable SUCRA score of 89.7%. Immediately following this top-performing option were hydrocolloid dressings at 87.3%, oxygen diffusion dressings at 85.8%, cellulose dressings at 74.1%, and petrolatum dressings at 71.6%. Subsequently, our rankings unfolded as follows: Allevyn (70%), silver-coated dressing (53%), collagen (43.2%), transforming methacrylate (43.2%),

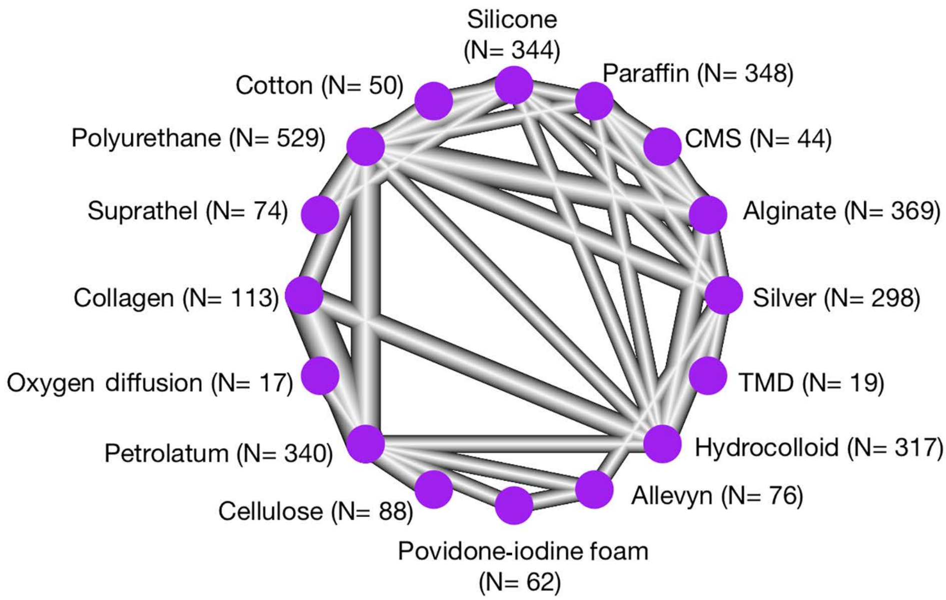

Fig. 5. Network graph representing the included sample size. Each node represents an intervention, and the edges represent the comparison. CMS, carboxymethyl chitosan sponges, TMD, transforming methacrylate dressing.

carboxymethyl chitosan sponges (42.7%), alginate (38.7%), silicone (31.4%), polyurethane (24.2%), Suprathel (22.3%), paraffin gauze (17.9%), and cotton gauze (3.1%) (Fig. 6). Notably, cotton gauze ranked as the least effective dressing for skin graft donor sites. These conclusive findings were derived from our comprehensive SUCRA ranking analysis, unequivocally designating PI-impregnated foam (Betafoam) as the preeminent dressing option for expediting the processes of wound healing and re-epithelialization.

Publication Bias

The assessment of publication bias did not show evidence of a significant risk of bias in the outcomes of the re-epithelialization rate. This was confirmed by the results of the Egger test ($P = 0.377$, Fig. 7) (**Supplemental Digital Content 1**, **http://links.lww.com/PRSGO/E4**).

DISCUSSION

Skin grafting was first performed in India 2000 years ago, but widespread interest did not develop until the 19th century. Skin grafting currently represents the most rapid and effective method of reconstructing large skin defects.[35] The choice of dressing for the donor site can significantly affect the healing and satisfaction of the patient. Effective and appropriate dressing of skin graft donor sites is vital for optimal wound healing, pain management, prevention of complications, and ensuring successful outcomes in grafting procedures. To evaluate and distinguish the range of dressings used for the care of the STSG donor site, in the perception of healing span and occurrence of side effects and complexity, we thus carried out a systematic review and network meta-analysis. According to the results of this meta-analysis, the most commonly utilized dressing type was polyurethane, followed closely by alginate, and paraffin. After estimating the effectuality by SUCRA of 16 skin graft donor-site dressings regarding their capacity to promote full wound healing and re-epithelialization, we determined that cotton gauze was the least effective option and that PI-impregnated foam (Betafoam) was the most beneficial, closely followed by hydrocolloid. To date, there is no consensus on the optimal STSG donor-site dressing, despite numerous RCTs implemented to reach such an option. In Australia and the United Kingdom, alginates made of ribbons, ropes, and sheets are the most common donor-site wound dressing used for STSG by surgeons.[36,37] It has been reported that alginate dressing accelerates the donor's STSG healing.[38,39] On the other hand, an RCT comparing paraffin versus a combination of alginate and polyurethane reported that dressing with alginate and polyurethane film had no pain-free or healing time advantages over paraffin gauze with a P value of 0.29. Furthermore, they preferred paraffin gauze dressings because of their lower cost and patient preference.[40] A recent systematic review and meta-analysis reported insignificant pain differences between polyurethane and calcium alginate for STSG donor sites. However, patients who underwent polyurethane had a significant level of comfort (IV = 3.08, 95% CI 0.09–4.28).[41]

Healing of the donor site for STSG is obtained only through re-epithelialization, as it lacks the entire epidermis and a variable dermis depth.[42] Regarding re-epithelialization and complete wound healing, in this study, PI-impregnated foam (Betafoam) ranked as the most favorable type of dressing according to SUCRA, with a score of 89.7%, and was found to be highly significant in comparison to paraffin (IV = 8.36, 95% CI 2.36–14.35) and other dressings, including TMD, silicone,

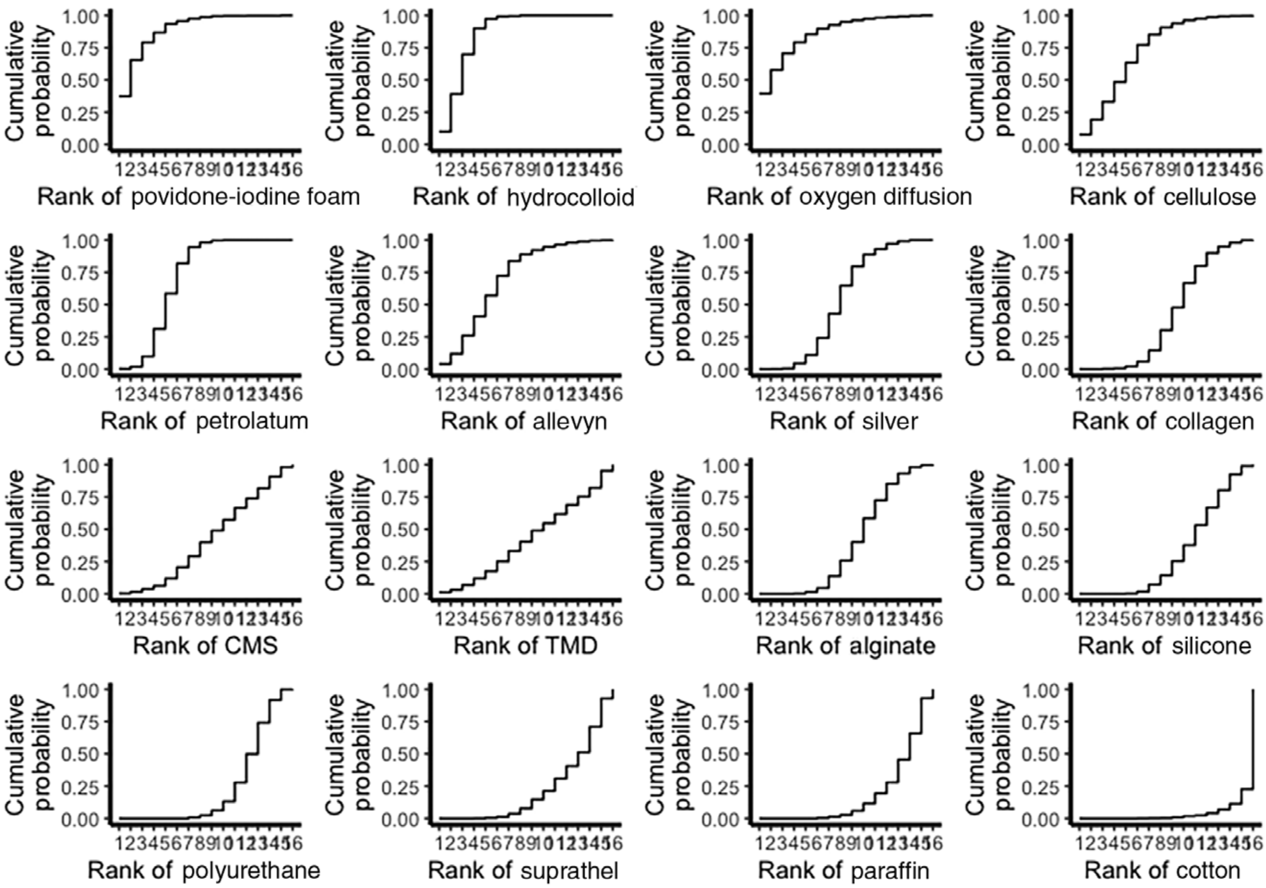

Fig. 6. Ranking cumulative probabilities (SUCRA) of each intervention. The value represents the probability of being the best intervention among those included in the network (larger the value, higher the ranking). CMS, carboxymethyl chitosan sponges, TMD, transforming methacrylate dressing.

polyurethane, collagen, alginate, and cotton. A relatively recent systematic review and meta-analysis study that included 22 articles showed that re-epithelialization rates, expressed as a percentage of total wound area at a predetermined follow-up time point, were higher in moist dressings than in nonmoist dressings, and this was associated with improved wound healing.[43] A more recent systematic literature review included 77 studies that revealed that the mean time to donor-site epithelialization, after harvesting STSGs, ranged between 4.7 and 35 days. However, the range of re-epithelialization was not computed in the present study for comparison, whereas the rate of complete re-epithelialization ranged between 11.0% and 99.5%.[44] Although PI is well documented for its antimicrobial efficacy, it can exhibit cytotoxic effects on fibroblasts, keratinocytes, and endothelial cells, particularly at higher concentrations, as highlighted by Burks et al.[45] In the context of PI-impregnated foam dressings, the foam structure likely plays a crucial role in regulating the release of PI, thereby reducing cytotoxicity while maintaining antimicrobial activity. This controlled release mechanism may explain the enhanced re-epithelialization observed with these dressings in this study.[46]

Overall, comparison between studies in this regard is not a practical issue, as the wound re-epithelialization was inconsistently defined and assessed across the studies; whereas some studies relied on photographic wound assessment by surgeons, others depended on spontaneous separation of wound dressings.[47] Donor-site wounds, after harvesting STSGs, are expected to heal within 2–3 weeks.[48] When wound epithelialization takes longer than 2–3 weeks, abnormal scarring is much more likely to occur[49] (**Supplemental Digital Content 1, http://links.lww.com/PRSGO/E4; Supplemental Digital Content 2, http://links.lww.com/PRSGO/E5**). (**See table, Supplemental Digital Content 3**, which displays the article's results summary, **http://links.lww.com/PRSGO/E6**.)

Limitations and Future Recommendations

Although this network meta-analysis synthesized the best available evidence on the preferred dressing protocol for skin graft donor sites, there were some encountered limitations. First, studies that used autologous dressing for coverage of the donor site were excluded from this study, including amniotic membrane, skin graft, and cell suspension. Also, studies that used electromechanical methods to enhance wound healing were excluded, as the current study focuses on comparing only conventional dressing; a combination of 2 different dressings in the management of a single wound was excluded from this study.

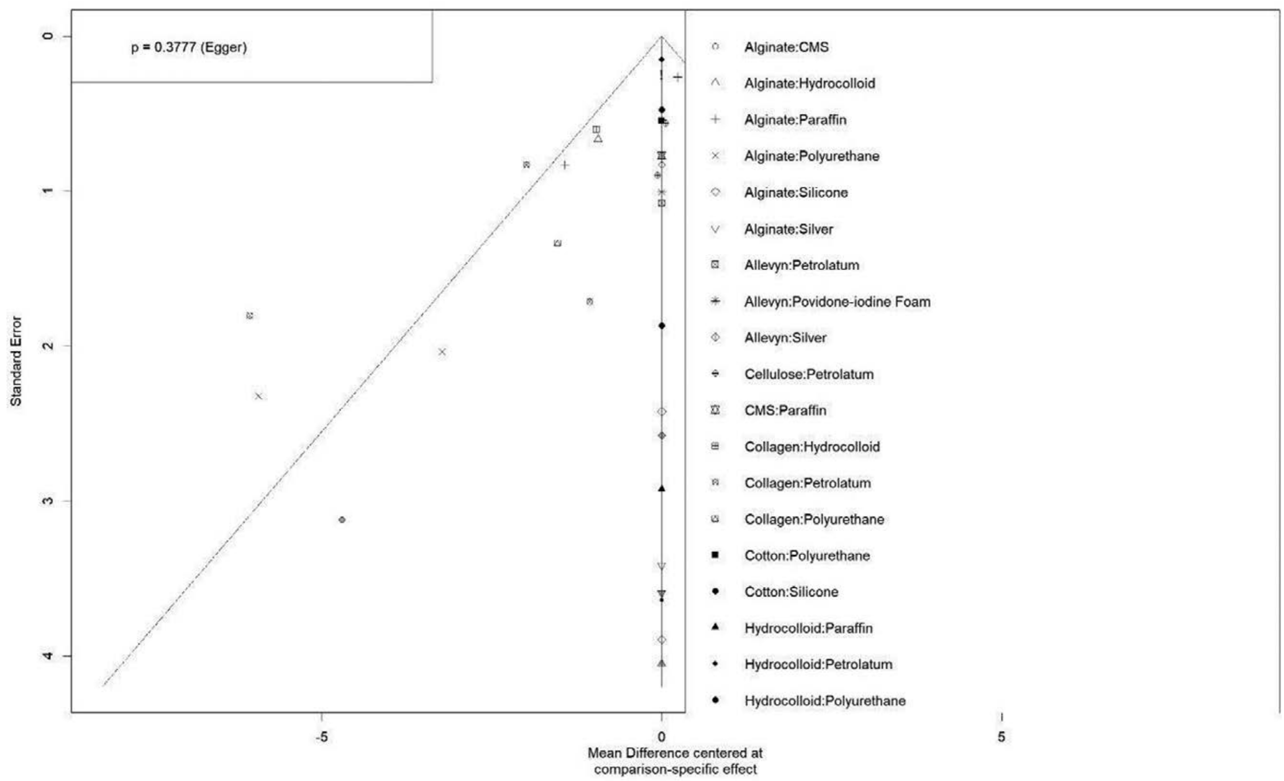

Fig. 7. The Egger test of the publication bias. CMS, carboxymethyl chitosan sponges.

A key limitation of this study was the inability to evaluate pain scores. Although re-epithelialization rates were the primary focus, the absence of pain data limits our understanding of the overall effects of different dressings. Future research should include pain assessment of dressing choices on patient comfort and overall healing. Another limitation relates to the methodology of network meta-analysis. Although we strongly emphasize the power and conclusiveness of this statistical method, the analysis is only as good as the underlying data. Inconsistency in a network meta-analysis occurs when the effect size from direct evidence differs substantially from that of indirect evidence, which can lead to significant inconsistency values and heterogeneity at the single-study level. However, the authors recommend future studies comparing combinations of more than one dressing for possible faster or scarless outcomes, drawing a connection between multiple factors that influence the selection of dressing, including wound size, characteristics, and comorbidity affecting wound healing. The cost of each dressing is highly challenging to be standardized, as it depends on specific economic conditions and market dynamics of each country, which can only be standardized individually on a national level. It is noteworthy that several factors, including patient age, overall health condition, the surface area of the harvested STSG, and the thickness of the graft, may have introduced variability in donor-site healing outcomes. These variables are potential confounders that could independently influence the healing process, making it challenging to isolate the specific effects of each dressing.

CONCLUSIONS

The STSG is a simple technique that has been widely used in the field of plastic surgery for the treatment of severe burns, chronic wounds, and to cover areas of skin loss. This systematic review and network meta-analysis aimed to analyze and compare different conventional dressing options based on re-epithelialization time and side effects for STSG donor sites. Our findings show that the most often used dressing type is polyurethane, followed by alginate dressing. However, based on SUCRA probability, PI-impregnated foam dressing was the most effective, followed by hydrocolloid dressings. The score of petrolatum dressings was higher than that of alginate and paraffin gauze. Cotton gauze dressings ranked as the least effective.

Nawaf Alhindi, MBBS
Faculty of Medicine
King Abdulaziz University
Rabigh 25727, Saudi Arabia
E-mail: inawafalhindi@gmail.com

DISCLOSURE

The authors have no financial interest to declare in relation to the content of this article.

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