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# Surgical Interventions for Patients With Vitiligo

## A Systematic Review and Meta-analysis

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**IMPORTANCE** Surgical interventions are a key part of the therapeutic arsenal, especially in refractory and stable vitiligo. Comparison of treatment outcomes between the different surgical procedures and their respective adverse effects has not been adequately studied.

**OBJECTIVE** To investigate the reported treatment response following different surgical modalities in patients with vitiligo.

**DATA SOURCES** A comprehensive search of the MEDLINE, Embase, Web of Science, and Cochrane Library databases from the date of database inception to April 18, 2020, was conducted. The key search terms used were *vitiligo*, *surgery*, *autologous*, *transplantation*, *punch*, *suction blister*, and *graft*.

**STUDY SELECTION** Of 1365 studies initially identified, the full texts of 358 articles were assessed for eligibility. A total of 117 studies were identified in which punch grafting (n = 19), thin skin grafting (n = 10), suction blister grafting (n = 29), noncultured epidermal cell suspension (n = 45), follicular cell suspension (n = 9), and cultured epidermal cell suspension (n = 17) were used.

**DATA EXTRACTION AND SYNTHESIS** Three reviewers independently extracted data on study design, patients, intervention characteristics, and outcomes. Random effects meta-analyses using generic inverse-variance weighting were performed.

**MAIN OUTCOMES AND MEASURES** The primary outcomes were the rates of greater than 90%, 75%, and 50% repigmentation response. These rates were calculated by dividing the number of participants in an individual study who showed the corresponding repigmentation by the total number of participants who completed the study. The secondary outcomes were the factors associated with treatment response to the surgical intervention.

**RESULTS** Among the 117 unique studies and 8776 unique patients included in the analysis, rate of repigmentation of greater than 90% for surgical interventions was 52.69% (95% CI, 46.87%-58.50%) and 45.76% (95% CI, 30.67%-60.85%) for punch grafting, 72.08% (95% CI, 54.26%-89.89%) for thin skin grafting, 61.68% (95% CI, 47.44%-75.92%) for suction blister grafting, 47.51% (95% CI, 37.00%-58.03%) for noncultured epidermal cell suspension, 36.24% (95% CI, 18.92%-53.57%) for noncultured follicular cell suspension, and 56.82% (95% CI, 48.93%-64.71%) for cultured epidermal cell suspension. The rate of repigmentation of greater than 50% after any surgical intervention was 81.01% (95% CI, 78.18%-83.84%). In meta-regression analyses, the treatment response was associated with patient age (estimated slope, -1.1418), subtype of vitiligo (estimated slope, 0.3047), and anatomical sites (estimated slope, -0.4050).

**CONCLUSIONS AND RELEVANCE** The findings of this systematic review and meta-analysis suggest that surgical intervention can be an effective option for refractory stable vitiligo. An appropriate procedure should be recommended based on patient age, site and size of the lesion, and costs.

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Vitiligo is a skin disease characterized by the chronic loss of functional melanocytes. The disease deeply affects quality of life in these individuals, and treatment options remain limited.<sup>1,2</sup> Medical treatments in vitiligo include phototherapy, topical corticosteroids, topical calcineurin inhibitors, and combination therapies. However, recent systematic reviews<sup>3-5</sup> have shown that these treatments provide only partial repigmentation in most treated individuals. Surgical interventions are an alternative therapeutic option in patients with stable vitiligo that is resistant to conventional medical approaches.<sup>6</sup>

Since thin split-thickness skin grafting was first reported to successfully repigment vitiliginous patches in 1947, various surgical methods have been developed for the treatment of vitiligo, including transplant and grafting techniques.<sup>7</sup> However, the efficacy and safety of these surgical interventions has not recently been investigated systematically. In the present study, we performed a systematic review and meta-analysis of all relevant prospective and retrospective studies to estimate the treatment responses following each type of surgical intervention for vitiligo.

## Methods

### Protocol and Registration

This systematic review and meta-analysis was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guideline and reviewed and approved by the institutional review board of St Vincent's Hospital, Seoul, Korea. The study was registered with PROSPERO, an international database of prospectively registered systematic reviews.<sup>8</sup>

### Databases

We performed a comprehensive search using predefined search terms (eTable 1 in the Supplement) in the MEDLINE, Embase, Web of Science, and Cochrane Library databases from inception to April 18, 2020. The main search terms were *autologous, melanocyte, surgery, suspension, transplantation, transplant, graft, grafting, blister, punch, thin, split thickness, and vitiligo*. All prospective and retrospective studies were included with no language restriction, and the reference lists in relevant review articles were scanned manually as well. All articles identified by this search were screened independently by 3 reviewers for study eligibility and data extraction (H.J.J., R.W.L., and S.H.K.).

### Study Selection

Study selection was based on the following inclusion criteria: (1) prospective and retrospective studies; (2) participants of all age groups with a diagnosis of vitiligo; (3) at least 1 surgical intervention group; (4) at least 10 participants in each treatment arm, regardless of the dropout rate; (5) outcomes measured based on all vitiligo lesions on the patient's whole body or each target patch; and (6) outcomes measured according to the percentage of repigmentation. Exclusion criteria consisted of the following: (1) not a clinical study; (2) outcomes

## Key Points

**Question** What are the treatment outcomes and adverse effects of surgical interventions for patients with vitiligo?

**Findings** In this systematic review and meta-analysis that included 117 unique studies and 8776 unique patients, the rates of repigmentation above 90% and above 50% after a single session of all surgical interventions were 52.69% and 81.01%, respectively.

**Meaning** These findings suggest that surgical intervention can be an effective and safe option for managing refractory stable vitiligo; selection of appropriate patients in terms of disease stability and suitable surgical procedure is important.

measured according to criteria other than percentage of repigmentation; (3) other intervention or combination with other intervention; (4) more than a single session of surgery; and (5) the inability to contact the corresponding authors.

Three reviewers (H.J.J., R.W.L., and S.H.K.) independently identified relevant articles by searching titles and abstracts. If the abstract did not provide enough information to determine inclusion or exclusion of the study, the reviewers performed a full-text evaluation to determine eligibility. The reviewers compared the results, and discrepancies were resolved through discussion.

### Data Extraction and Outcome Measures

For the meta-analysis, the 3 independent reviewers extracted the following predefined variables: authors, country, year of publication, study type, numbers of treated patients or lesions, treatment protocols, and outcome. We performed data extraction in duplicate, and any discrepancies were resolved by consensus.

### Treatment Response Following Surgical Interventions and Safety Profiles

The outcome of repigmentation was evaluated as greater than 90%, greater than 75%, and greater than 50%. The treatment response rates were calculated as the number of participants or lesions who achieved the corresponding degree of repigmentation divided by the total number of participants or lesions who completed the individual study. Patients with unstable vitiligo, piebaldism, or other types of leukoderma were excluded from the analysis, whenever possible. We investigated all reported adverse events for each surgical intervention in the included studies.

### Meta-regression of Age, Vitiligo Subtype, and Body Sites

Meta-regression was performed to investigate factors associated with the achievement of greater than 90% repigmentation. Selective moderating variables, such as the type of surgical intervention, age, vitiligo subtype, and the body site were investigated for that purpose. We collected the mean age of patients, proportion of segmental vitiligo, and proportion of treated lesions on the acral and joint areas in the enrolled participants for each study, whenever this was possible.

## Statistical Analysis

The rates of the corresponding treatment responses of the included studies were pooled by generic inverse variance weighting and were combined using a random-effects model. In each subgroup analysis, heterogeneity was assessed using the Cochran Q test and  $I^2$  value. Influence of variables on the outcome were analyzed using meta-regression. Publication bias was evaluated using the contoured funnel plot (eFigure 1 in the Supplement). Statistical analyses were conducted using R software, version 3.6.1 (R Foundation for Statistical Computing) with the metagen and metafor packages. Two-sided  $P < .05$  indicated significance.

## Results

### Search Results

We initially identified 1365 records through database searching; 656 duplicates were removed and 351 were deleted after reviewing the titles and abstracts (Figure 1). A total of 358 full-text articles were assessed for eligibility, of which 241 were excluded for the following reasons: (1) not a clinical study ( $n = 23$ ); (2) less than 10 participants included ( $n = 61$ ); (3) abstract only or not enough information about the methods ( $n = 31$ ); (4) outcomes measured according to criteria other than percentage of repigmentation ( $n = 61$ ); (5) not a single-session surgery ( $n = 16$ ); (6) other intervention used with surgery ( $n = 7$ ); (7) duplicated studies ( $n = 14$ ); and (8) the inability to reach corresponding authors at least twice by email ( $n = 28$ ). The remaining 117 studies fulfilled the inclusion criteria and were included in the final analysis.

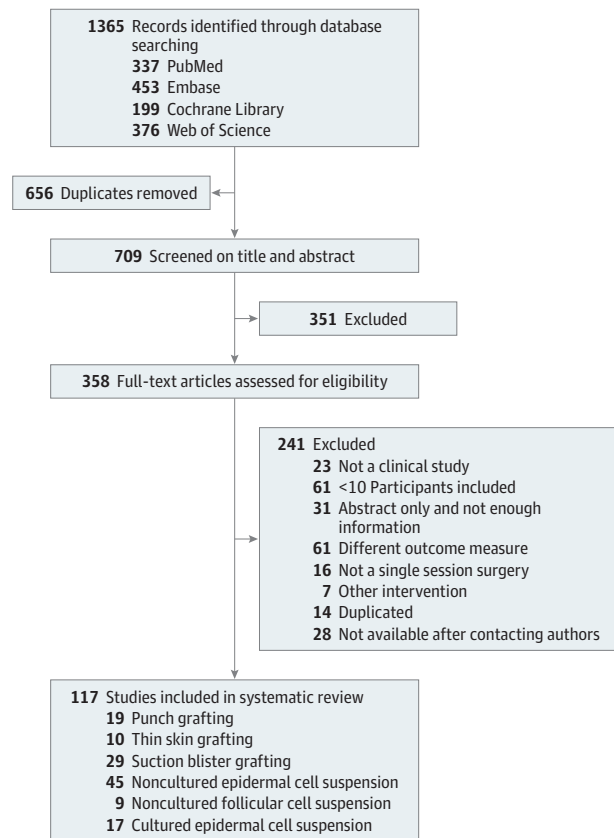
### Characteristics of Included Studies

We analyzed a total of 117 unique studies with 8776 unique patients (eTable 1 in the Supplement), including 19 studies<sup>9-27</sup> with 1631 patients in the punch grafting group, 10 studies<sup>15,20,28-35</sup> with 718 patients in the thin skin grafting group, 29 studies<sup>10,24,36-62</sup> with 2652 patients in the suction blister grafting group, 45 studies<sup>21,51,56,63-104</sup> with 2209 patients in the noncultured epidermal cell suspension (NCES) group, 9 studies<sup>75,87,93,105-110</sup> with 185 patients in the noncultured follicular cell suspension (NCFs) group, and 17 studies<sup>56,81,111-125</sup> with 1381 patients in the cultured epidermal cell suspension (CES) group; 11 studies included more than 1 procedure type. The median follow-up duration was 7 (range, 2-108) months. The Methodological Index for Non-randomized Studies<sup>126</sup> criteria scoring was used to assess the methodological quality for included studies (eTable 2 in the Supplement).

### Treatment Response Following Surgical Intervention and Meta-regression

Overall, the rate of repigmentation achieved by patients after 1 session of any surgical intervention included greater than 90% in 52.69% (95% CI, 46.87%-58.50%) in 106 studies with 6586 patients ( $I^2 = 97.2%$ ) (eFigure 2 in the Supplement); greater than 75% in 64.72% (95% CI, 59.52%-69.92%) in 100 studies with 3400 patients ( $I^2 = 95.7%$ ); and greater than 50% in 81.01% (95% CI, 78.18%-83.84%) in 92 studies with 5462 patients

Figure 1. Flow Diagram Showing Identification of Eligible Studies



( $I^2 = 90.7%$ ). According to the surgical intervention type, greater than 90% repigmentation was achieved in 72.08% (95% CI, 54.26%-89.89%) of patients undergoing thin skin grafting (670 patients in 8 studies<sup>20,28-33,35</sup>), 61.68% (95% CI, 47.44%-75.92%) of patients undergoing suction blister grafting (2349 patients in 21 studies<sup>36-42,46-52,54-56,58-61</sup>), 56.82% (95% CI, 48.93%-64.71%) of patients undergoing CES (1138 patients in 14 studies<sup>56,111-123</sup>), 47.51% (95% CI, 37.00%-58.03%) of patients undergoing NCES (907 patients in 29 studies<sup>51,56,63-66,69-71,75-77,79,82,83,85,87,89,91,93-98,100-103</sup>), 45.76% (95% CI, 30.67%-60.85%) of patients undergoing punch grafting (1354 patients in 11 studies<sup>9,11-14,16,17,19,20,23,26</sup>), and 36.24% (95% CI, 18.92%-53.57%) of patients undergoing NCFs (160 patients in 8 studies<sup>75,87,93,105-107,109,110</sup>) after 1 session of each surgery (eFigure 2 in the Supplement and Table 1). In our meta-regression analysis, for greater than 90% repigmentation, the estimate of the slopes for mean age of patients was  $-1.1418$  ( $P = .02$ ); for the proportion of segmental vitiligo,  $0.3047$  ( $P = .01$ ); and for the proportion of treated lesions on the acral and joint areas,  $-0.4050$  ( $P = .002$ ) (Figure 2).

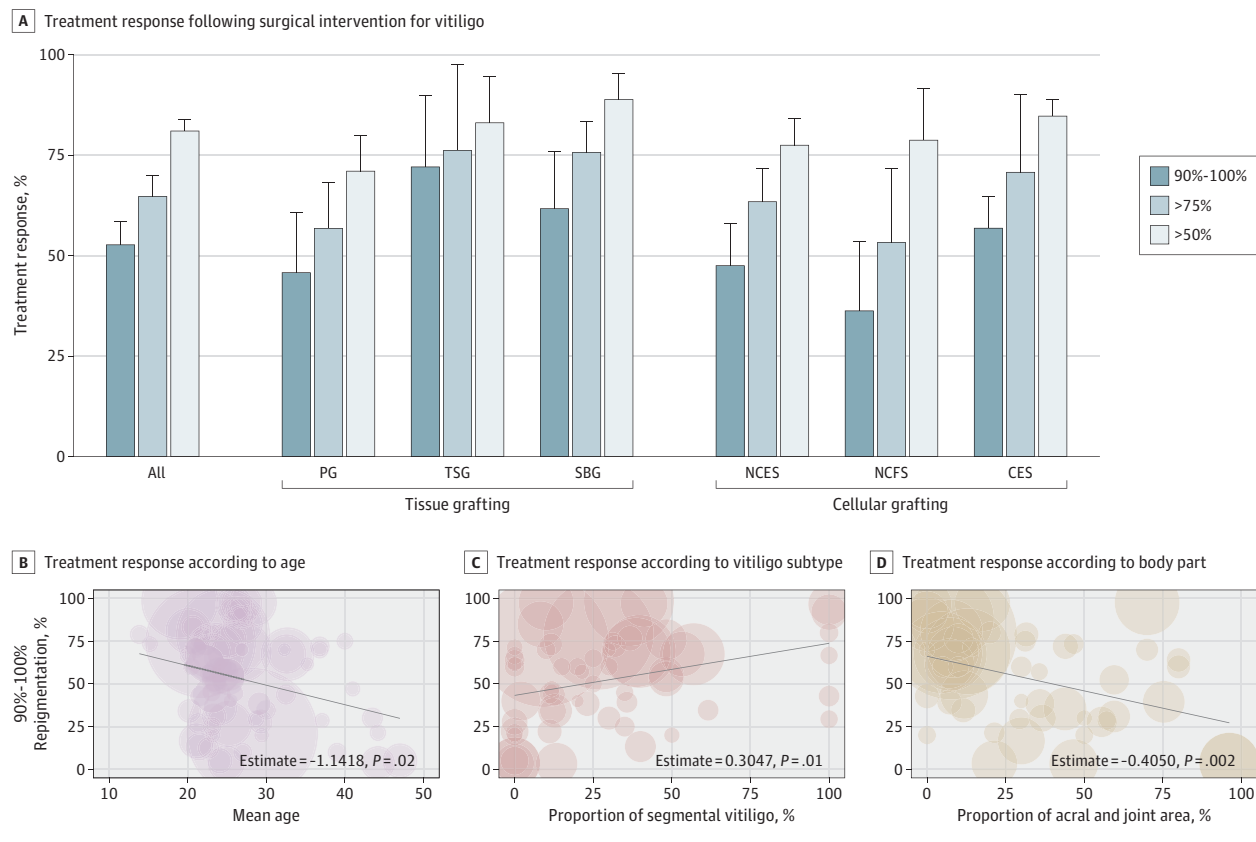
### Safety of Each Surgical Intervention

The occurrence of adverse events was reported in 56 studies. Common adverse events included pain, hyperpigmentation at the recipient site, and hypopigmentation at the donor site regardless of the type of the procedure. In punch grafting, cobblestone appearance, milia, and color mismatch were the most

Table 1. Summary of Findings for Surgical Interventions for Vitiligo

Intervention	Treatment response rate, % (95% CI)			Included studies
	>90% Repigmentation	>75% Repigmentation	>50% Repigmentation	
Punch grafting	45.76 (30.67-60.85)	56.78 (45.35-68.22)	71.02 (62.23-79.80)	1631 Patients in 19 studies <sup>9-27</sup>
Thin skin grafting	72.08 (54.26-89.89)	76.17 (54.77-97.57)	83.06 (71.47-94.65)	718 Patients in 10 studies <sup>15,20,28-35</sup>
Suction blister grafting	61.68 (47.44-75.92)	75.69 (68.09-83.39)	88.85 (82.47-95.23)	2652 Patients in 29 studies <sup>10,24,36-62</sup>
Noncultured epidermal cell suspension	47.51 (37.00-58.03)	63.42 (55.21-71.62)	77.47 (70.90-84.05)	2209 Patients in 45 studies <sup>21,51,56,63-104</sup>
Noncultured follicular cell suspension	36.24 (18.92-53.57)	53.25 (34.81-71.69)	78.73 (65.86-91.60)	185 Patients in 9 studies <sup>75,87,93,105-110</sup>
Cultured epidermal cell suspension	56.82 (48.93-64.71)	70.73 (51.49-89.98)	84.72 (80.67-88.77)	1381 Patients in 17 studies <sup>56,81,111-125</sup>
All	52.69 (46.87-58.50)	64.72 (59.52-69.92)	81.01 (78.18-83.84)	8776 Patients in 117 studies <sup>9-125</sup>

Figure 2. Summary of Treatment Response Following Surgical Interventions for Vitiligo



CES indicates cultured epidermal cell suspension; NCES, noncultured epidermal cell suspension; and NCFS, noncultured follicular cell suspension.

common and critical adverse events.<sup>9-13,15-18,20,22-24,26,27</sup> In suction blister grafting, perigraft halo, variegated appearance, and color mismatch were frequently reported.<sup>10,24,36-38,40,43,45,46,48-50,54,55,57,60</sup> Thin skin grafting was associated with graft contracture, overhanging margin, wrinkles over the graft surface, and perigraft halo.<sup>15,20,28-31,33-35</sup> In cellular grafting techniques, pain, discomfort, and burning sensation were more commonly reported when compared with tissue grafting,<sup>84,104</sup> which was likely owing to multiple injections of local anesthetic performed over a large area in the former. Mottled pigmentation, marginal halo, and scarring were also reported in all the evaluated surgical interventions.

Koebner phenomenon at the donor site or disease progression was reported in several studies as well,<sup>9,13,36,37,40,49,54,65,96,114,115</sup> indicating a need for carefully assessing disease stability before performing surgery (Table 2).

## Discussion

Surgical interventions are essential for the management of refractory stable vitiligo, which can be classified into tissue grafting and cellular grafting according to the nature of the grafts. Tissue grafting, including thin skin grafting, suction blister

grafting, and punch grafting, has been traditionally performed for a long time, whereas cellular grafting has made a great advance in recent years. For many reasons, including ease of use and safety, NCES has greatly contributed to the reduced costs of surgical interventions for vitiligo, globally. A systematic review on surgical interventions for vitiligo was published in 2013,<sup>127</sup> and the present study further includes all the articles published since then and derives the response rate for each surgical method.

In the present study, we systematically reviewed the treatment response following different types of surgical interventions for vitiligo, including punch grafting (19 studies), thin skin grafting (10 studies), suction blister grafting (29 studies), NCES (45 studies), NCFS (9 studies), and CES (17 studies). In meta-analysis, regardless of the type of intervention, 52.69% of the patients achieved greater than 90% repigmentation after a single surgical procedure. However, when evaluating this specific outcome according to the type of intervention, the highest response rate (for >90% repigmentation) was achieved in patients undergoing thin skin grafting (72.08%), followed by suction blister grafting (61.68%), CES (56.82%), NCES (47.51%), punch grafting (45.76%), and NCFS (36.24%).

The oldest reported surgical procedure performed in patients with vitiligo, thin skin grafting, encompasses all methods of transplanting ultrathin or thin skin grafts measuring 0.125 to 0.275 mm harvested using a manual or electronic dermatome.<sup>128</sup> Various modifications have been added to the initially published method such as Thiersch,<sup>129</sup> smash,<sup>130</sup> and flit-top<sup>20</sup> grafting. However, this technique is difficult to use on a large surface area and requires experienced skill to harvest the graft with a constant thickness.

Because thin skin grafting commonly leads to uneven pigmentation and scarring of the donor site, a surgical method to precisely harvest the epidermal graft has been attempted.<sup>131</sup> Suction blister grafting, first described by Falabella<sup>132</sup> in 1971, has decreased the risk of scarring of the donor site by raising subepidermal blisters with clear noninflammatory transudate and low suction pressures maintained for sufficient periods. It is safe and effective for vitiligo on junctional areas or curved areas such as lips or eyelids.<sup>133</sup> Several studies<sup>46,58,61</sup> reported that 87% to 90% of the lip vitiligo and 85.7% of vitiligo on the nipple and areolar showed complete repigmentation after suction blister grafting at 6 to 24 months.

Punch grafting is another well-established surgical method in vitiligo. Several motorized punch grafting devices have been put on the market in recent years, making this method more convenient and cost-effective with increased favorable outcomes.<sup>23</sup> Moreover, repeated procedures can be easily performed in an outpatient setting. Despite the low overall treatment response following punch grafting shown in our meta-analysis, recent studies describe motorized micropunch grafting has a greatly increased response rate and reduced cobblestone appearance.<sup>23,134</sup>

Transplant of NCES is the most commonly performed cellular grafting technique for vitiligo. The procedure can treat large areas covering a ratio of donor to recipient of as much as 1:10. However, processing of the grafts is time-consuming, and the procedure itself is lengthy. In our study, greater than 90%

**Table 2. Common Adverse Events of Surgical Interventions**

Intervention	Adverse events
Punch grafting	Recipient site: cobblestone appearance, variegated appearance, polka dots, color mismatch, infection, perilesional halo, insufficient repigmentation, hyperpigmentation Donor site: Koebner phenomenon, scarring, infection
Thin skin grafting	Recipient site: perigraft halo, milia, hypertrophic scarring, graft displacement, overhanging margin, partial graft loss, wrinkles over the graft surface, hyperpigmentation, reactivation or progression Donor site: pain, hypertrophic scarring, hyperpigmentation, infection
Suction blister grafting	Recipient site: hyperpigmentation, hypertrophic scar, perigraft halo, infection, color mismatch, reactivation or progression Donor site: Koebner phenomenon, hyperpigmentation
Noncultured epidermal cell suspension	Recipient site: color mismatch, hyperpigmentation, marginal halo, infection, mottled pigmentation, burning pain and discomfort Donor site: Koebner phenomenon, infection, hypertrophic scar, hyperpigmentation
Noncultured follicular cell suspension	Recipient site: color mismatch, hyperpigmentation, infection, pruritus, xerosis Donor site: hyperpigmentation, hypertrophic scar, infection
Cultured epidermal cell suspension	Recipient site: marginal halo, burning pain and pruritus

repigmentation was achieved in 47.51%, and greater than 75% repigmentation was achieved in 63.42% after 1 session of NCES, which is slightly less than the previously reported success rate.<sup>63</sup> Of note, treatment outcome in NCES is strongly related to the experience and skill of the surgeon and proper processing of the cell suspension. The initially reported method<sup>135</sup> has undergone several modifications over time to improve repigmentation rates. For example, the use of hyaluronic acid instead of the patient's serum was added to increase the viscosity and facilitate adherence of the cell suspension grafts.<sup>65</sup> Furthermore, oral pulse betamethasone therapy started as early as 2 months after initial NCES procedure has been shown to enhance repigmentation in patients who underwent additional transplant.<sup>136</sup>

The hair follicle is an attractive reservoir, given its high density of melanocytes and melanocyte stem cells; however, NCFS was shown to be inferior to other surgical interventions in our study. Singh et al<sup>75</sup> reported that greater than 90% repigmentation was observed in 83% of the NCES group and 65% of the NCFS group. The success rate of cellular grafting can be optimized as demonstrated in another randomized controlled study<sup>87</sup> in which the combination of NCES and NCFS improved repigmentation rates compared with NCES alone (76% vs 57%).

Cultured epidermal cell suspension has been performed to expand the amount of autologous cell suspensions, allowing for wider graft areas. Cultured melanocytes at a density of 70 000 to 100 000 melanocytes/cm<sup>2</sup> are transplanted to an area covering as much as 500 cm<sup>2</sup>. Hong et al<sup>116</sup> reported that CES could provide the highest donor-to-recipient ratio to 1:60. However, melanocyte culture is time-consuming and costly and requires a laboratory specialized in cell culture and a highly

stimulatory media.<sup>111</sup> Basic fibroblast growth factor is an effective and safe media commonly used,<sup>137</sup> but long-term safety of melanoma risk remains to be addressed.<sup>138</sup>

In our meta-regression analyses, successful outcome (>90% repigmentation) was associated with younger age, segmental vitiligo, and nonacral area ( $P < .05$  for all). Therefore, selection of appropriate candidates would be a critical factor when considering the surgical intervention of vitiligo.

Phototherapy may also play an adjuvant role in surgical interventions for vitiligo by stimulating melanocyte spreading, inhibiting T lymphocytes, and suppressing the various cytokines to create a favorable environment for the transplanted melanocytes. Several studies reported narrow-band UV-B phototherapy before and after CES-accelerated repigmentation<sup>121</sup> and adjuvant narrow-band UV-B phototherapy after NCES-enhanced repigmentation.<sup>97</sup> In our study, subgroup analysis according to adjuvant phototherapy showed no significant difference in repigmentation rates. The large heterogeneity of these studies may limit the interpretation of the results; thus, randomized clinical trials to estimate the effect of adjuvant phototherapy are necessary.

The assessment of disease stability is critical when selecting appropriate candidates for surgical interventions in patients with vitiligo. Evaluation with digital photographs during a 12-month period in addition to a scoring system such as the Vitiligo Area Scoring Index<sup>139</sup> or the Vitiligo European Task Force<sup>140</sup> assessment score is recommended.<sup>141</sup> However, many studies were performed before the publication of these recommendations, and a great heterogeneity of definition of the length of stability was observed ranging from 3 to 12 months. The most commonly used scoring system, the Vitiligo Disease Activity Score,<sup>142</sup> could also lead to recall bias. As a result, Koebner phenomenon at the donor site after surgery was commonly reported. This reflects how the adequate assessment of disease stability would be essential when considering surgical options; therefore, test grafting or patient-reported Vitiligo Noticeability Scale scores<sup>143</sup> could be useful options because they are quick, simple, and readily interpreted in the outpatient clinic.<sup>28</sup>

Long-term treatment outcomes are also an important aspect for patients deciding to undergo surgical treatments. Patients expect not only repigmentation but also maintenance of gained repigmentation, expectations that were validated by international e-Delphi consensus.<sup>144</sup> However, vitiligo often recurs after successful repigmentation, and prospective studies reporting the long-term outcome in surgical interventions are lacking. Fongers et al<sup>17</sup> reported that at least 65% repigmentation was maintained in 51% and 89% of the patients with

vitiligo vulgaris and segmental vitiligo, respectively, after several sessions of punch grafting (mean follow-up, 5.2 years). Al-Mutairi et al<sup>30</sup> reported that the thin skin grafting with adjuvant excimer laser treatment led to long-lasting repigmentation for as long as 4 years. Jin et al<sup>49</sup> observed that repigmentation significantly decreased over time, especially starting from 2 years after epidermal grafting. Altalhab et al<sup>88</sup> reported that 103 of 553 patients who underwent a single session of melanocyte-keratinocyte transplant (18.6%) showed a relapse after 6-year follow-up; focal and segmental vitiligo showed a significantly lower recurrence rate.

Each surgical intervention for vitiligo has advantages and disadvantages. Therefore, the appropriate procedure should be recommended based on the patient's age, economic status, the location and extent of vitiligo, and the facilities available at the clinic. Because complete repigmentation is rarely achieved after 1 session, multiple sessions are necessary to improve treatment outcome and patient satisfaction. Lesions of large areas can first be treated by cellular grafting, followed by tissue grafting for smaller remaining areas.<sup>145</sup>

### Limitations

Our systematic review has limitations. First, there was considerable heterogeneity in study designs, demographic information, and protocols regarding preoperative and postoperative procedures. In particular, we observed a great heterogeneity of definition of outcome measures because the studies were published before the international consensus was reached. Repigmentation has currently reached consensus to use percentage of repigmentation quartiles, including 0 to 25%, 26% to 50%, 51% to 79%, and 80% to 100%.<sup>146</sup> Second, limited evidence was available from randomized clinical trials or systematic reviews. Last, because the outcome of surgical interventions largely depends on the skill and experience of the clinician, actual outcomes may vary among the studies.

### Conclusions

The findings of this systematic review and meta-analysis confirm that surgical interventions are essential for the management of refractory stable vitiligo. Maximizing treatment outcomes requires the selection of appropriate patients in terms of disease stability and suitable surgical technique. In the future, we should categorize patients for the surgical procedure that is performed. Consensus among physicians should also be reached on preoperative evaluations and postoperative assessments.

#### ARTICLE INFORMATION

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**Author Contributions:** Drs Ju and Bae contributed equally to this study. Drs Ju and Bae had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

**Concept and design:** Bae, Kim, Parsad, Shourick. **Acquisition, analysis, or interpretation of data:** Ju, Bae, Lee, Kim, Pourang, Hamzavi, Ezzedine.



*Drafting of the manuscript:* Ju, Lee, Kim.

*Critical revision of the manuscript for important intellectual content:* Bae, Lee, Parsad, Pourang, Hamzavi, Shourick, Ezzedine.

*Statistical analysis:* Ju, Bae.

*Administrative, technical, or material support:* Ju, Bae, Lee, Pourang.

*Supervision:* Bae, Parsad, Hamzavi, Ezzedine.

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