Received: 5 February 2023 | Revised: 11 May 2023 | Accepted: 23 June 2023

DOI: 10.1002/micr.31081

REVIEW ARTICLE

MICROSURGERY WILEY

Supermicrosurgery with perforator-to-perforator anastomoses for lower limb reconstructions – A systematic review and meta-analysis

Federico Lo Torto MD, PhD[1] | Guido Firmani MD[1] | Luca Patanè MD[1] | Gianmarco Turriziani MD[1] | Arianna Di Rocco MD[2] | Annarita Vestri PhD[2] | Diego Ribuffo MD, PhD[1]

[1]Department of Surgery "P. Valdoni," Unit of Plastic and Reconstructive Surgery, Policlinico Umberto I, Sapienza University of Rome, Rome, Italy

[2]Department of Public Health and Infectious Diseases, Sapienza University of Rome, Rome, Italy

Correspondence
Federico Lo Torto, Department of Surgery "P. Valdoni," Unit of Plastic and Reconstructive Surgery, Policlinico Umberto I, Sapienza University of Rome, Piazzale Aldo Moro 5, 00185 Rome, Italy.
Email: federicolotorto@gmail.com

Abstract

Background: Supermicrosurgical flaps based on perforator-to-perforator microanastomoses have been described for lower limb reconstruction. This approach offers the benefit of raising short pedicles while sparing axial vessels, which effectively enables complex reconstructive techniques in comorbid patients at high risk of reconstructive failure. The aim of our study is to assess the surgical outcomes of perforator-to-perforator based flaps in comparison to conventional free flaps for reconstructions of the lower limb district, through a systematic review of literature and meta-analysis.

Methods: A search on PubMed, Embase, Cohrane, and Web of Science was performed between March–July 2022. No restrictions were placed on study date. Only English manuscripts were assessed. Reviews, short communications, letters, correspondence were excluded after reviewing their references for potentially relevant studies. A Bayesian approach was used to conduct the meta-analysis comparing flap-related outcomes.

Results: From 483 starting citations, 16 manuscripts were included for full-text analysis in the review, and three were included in the meta-analysis. Out of 1556 patients, 1047 received a perforator-to-perforator flap. Complications were reported in 119 flaps (11.4%), which included total flap failure in 71 cases (6.8%), partial flap failure in 47 cases (4.5%). Overall flap complications had a HR of 1.41 (0.94–2.11; 95% C.I.). Supermicrosurgical and conventional microsurgical reconstructions were not associated with statistically significant differences ($p = .89$).

Conclusion: Our evidence supports the safety of surgical outcomes, with acceptable flap complication rates. Nevertheless, these findings are limited by poor overall quality which must be addressed and used to encourage higher-level evidence in the field.

1 | INTRODUCTION

Lower limb soft tissue defects consistently overload plastic surgery practices, due to the heavy burden of trauma-related injuries, post-traumatic infections, diabetic foot-related issues, and oncologic outcomes for cancer resections. Microsurgery is now routinely performed for the treatment of these defects, having moved away from conventional workhorse flaps to sophisticated perforator-based free tissue transfers (May et al., 1981), including the antero-lateral thigh (ALT) flap and the superficial circumflex iliac perforator (SCIP) flap (Berner et al., 2020). The latest frontier in microsurgery is currently represented by the use of supermicrosurgical techniques (Koshima, 2008; Koshima et al., 2010). Microanastomosing vessels and single nerve fascicles as small as 0.3–0.8 mm in caliber is just one of the benefits (Badash et al., 2018), though this requires manipulation of 30–80 μm needles and micro-sutures as small as 13–0 (Yamamoto et al., 2017). The technical advancement of anastomosing <1-mm vessels has made possible what was previously considered unachievable within the field, cementing the success of microsurgery and setting the bar of satisfactory results higher than ever. Perforator-to-perforator supermicrosurgery is the next evolution of the technique, which consists in using perforators as the recipient vessels for microanastomoses, thus overcoming the need for dissecting axial vessels (Hong, 2009; Mureau & Hofer, 2008). The benefits of this approach include an easier flap dissection and the ability to spare main vascular pedicles in lower limbs, which is a considerable advantage since lower limb reconstruction patients commonly present impaired vascularity, either due to comorbidities and/or trauma-related injuries (de Laat et al., 2018). Nevertheless, the technical difficulties make these types of procedures particularly complex and place them beyond the reach of most routine plastic surgery practices and reconstructive units around the world.

The results of modern microsurgical procedures have improved over the years, with low donor site morbidity and high flap success rate (Park & Chang, 2016). It stands to reason whether supermicrosurgery procedures are associated with a higher rate of flap-related complications and are thus riskier than the more commonly performed, “standard” microsurgical procedures (with axial vessel anastomoses).

We conducted a systematic review summarizing the state of the art of scientific literature on supermicrosurgery using perforator-to-perforator anastomoses for reconstructions of lower limb defects, and performed a meta-analysis comparing the flap-related outcomes and complications of microsurgical flaps based on axial vessels versus perforator-to-perforator based flaps.

2 | MATERIALS AND METHODS

We performed a systematic review of literature in accordance with PRISMA guidelines. We searched for publications on PubMed, Embase, Web of Science (including Science Citation Index and Conference Proceedings Citation Index), and Cochrane Library databases to identify all publications regarding lower limb reconstructions using perforator-to-perforator supermicrosurgery techniques. For PubMed, the following search term strategy was used: (perforator-to-perforator [MeSH] OR supermicrosurgery [MeSH]). For Embase, we used: ((perforator AND to AND perforator/exp) OR (supermicrosurgery*) AND (lower AND limb [MeSH] OR (leg [MeSH]) OR (foot [MeSH]))). For Web of Science, we used: (Topic = (perforator AND to AND perforator*) OR Topic = (supermicrosurgery*)). Finally, for Cochrane Library ((perforator AND to AND perforator*) OR (supermicrosurgery*)) were used. All citations were screened through their titles and abstracts, duplicates were removed, and then full-text manuscripts were assessed according to the following inclusion criteria: only human-based topics and manuscripts written in English were to be taken into consideration. Case reports and case series with fewer than three patients, non-clinical articles addressing supermicrosurgery training or instrumentation and clinical cases addressing lymphedema treatment or treatment of anatomical districts other than the lower limb were used as exclusion criteria for this review. Review search started on March 2022 and ended in July 2022, and was conducted by G.F. and L.P. The two reviewers independently reviewed the titles and abstracts yielded by this comprehensive search and subsequently selected articles based on the predetermined inclusion and exclusion criteria. Disagreements were resolved by a third reviewer (P.P.) or through consensus-based discussion with a fourth reviewer (F.L.T.).

The following data were extracted from the manuscripts included in the final tally: number of patients, gender, mean age, comorbidities, indication for surgery, location of defect, size of defect, type of flap used for reconstruction, recipient vessels used, flap complications, donor-site complications and follow-up. In the meta-analysis, the following outcomes were evaluated: flap survival rate (total flap losses to total number of flaps ratio) and partial flap loss rate. Studies with a sample size of four or more flaps and that directly compared the outcomes for perforator-to-perforator anastomosis versus axial vessel anastomosis were included in the meta-analysis. The level of evidence for included studies was evaluated using the Oxford Centre for Evidence-Based Medicine (OCEBM) (Howick et al., 2011), and the Oxford quality scoring system (Jadad Score) (Jadad et al., 1996).

2.1 | Statistical analysis

When available, hazard ratios (HRs) were recorded from each study. When not available, hazard ratios and their standard errors were computed according to the methods described by Tierney et al. (2007). All data was provided with a confidence interval (C.I.) of 95%. Statistical significance was considered at *p*-value <.05. Several separate meta-analyses were performed for each outcome. Given the small number of studies involved, it was not possible to reasonably assess study heterogeneity. Considering that, a hierarchical Bayesian approach with heterogeneity and informative priors was used, according to guidelines (Higgins et al., 2009), and as previously published in articles under similar circumstances (Iocca et al., 2017; Proietti et al., 2018, 2020).

TABLE 1 Quality assessment of included studies and overview of patient population and outcomes.

Author	OCEBM	Jadad score	Number of p-2-p flaps	Location of defect	Type of flap	Flap success (%)	Flap complications	Donor site complications	Follow-up (days)
Iocca et al. (2017)	4	0	176	N/A	• SCIP: 176 (100%)	94.3	Total failure: 10 Partial failure: 14	Wound dehiscence: 1 Seroma: 1	400 [30–1690]
Proietti et al. (2020)	4	0	42	• Knee and upper 1/3 of leg: 17 • Middle 1/3 of leg: 25	• ALT: 38 (90.5%) • UMT: 4 (9.5%)	97.6	Total failure: 1 Partial failure: 0	None	150 [30–420]
Egger et al. (1997)	3	0	25	• Knee and upper 1/3 of leg: 25	N/A	100	Total failure: 0 Partial failure: 0	Wound dehiscence: 1	[30–390]
Goh et al. (2015)	4	0	79	• Thigh: 3 • Knee and upper 1/3 of leg: 11 • Middle 1/3 of leg: 26 • Lower 1/3 of leg and foot: 39	• SCIP: 79 (100%)	94.9	Total failure: 4 Partial failure: 1	Wound dehiscence: 1	360 [20–780]
Hong (2009)	4	0	27	• Thigh: 1 • Middle 1/3 of leg: 3 • Lower 1/3 of leg and foot: 23	• SGAP: 22 (81.5%) • IGAP: 5 (18.5%)	100	Total failure: 0 Partial failure: 2	None	390 [60–1050]
Hong and Koshima (2010)	3	0	18	• Lower 1/3 of leg and foot: 18	• PEaP: 16 (88.9%) • SoP: 2 (11.1%)	94.4	Total failure: 1 Partial failure: 0	Wound dehiscence: 2	249 [210–480]
Hong et al. (2013)	4	0	21	• Lower 1/3 of leg and foot: 21	• LDP: 21 (100%)	95.2	Total failure: 1 Partial failure: 0	Hematoma: 1	228
Hong et al. (2014)	3	0	50	• Thigh: 2 • Knee and upper 1/3 of leg: 35 • Middle 1/3 of leg: 13	• ALT: 29 (58.0%) • SCIP: 21 (42.0%)	98.0	Total failure: 1 Partial failure: 4	None	780
Kim et al. (2010)	4	0	323	• Thigh: 13 • Knee and upper 1/3 of leg: 37 • Middle 1/3 of leg: 32 • Lower 1/3 of leg and foot: 241	• SCIP: 183 (56.7%) • ALT: 91 (28.2%) • TDAP: 3 (0.9%) • Others: 46 (14.2%)	89.0	Total failure: 36 Partial failure: 0	None	365
Kim and Kim (2012)	4	0	109	• Thigh: 9 • Knee and upper 1/3 of leg: 11 • Middle 1/3 of leg: 1 • Lower 1/3 of leg and foot: 67	• SCIP: 65 (59.6%) • ALT: 26 (23.9%) • Others: 18 (16.5%)	94.5	Total failure: 6 Partial failure: 13	None	855

(Continues)

TABLE 1 (Continued)

Author	OCEBM	Jadad score	Number of p-2-p flaps	Location of defect	Type of flap	Flap success (%)	Flap complications	Donor site complications	Follow-up (days)
Kim et al. (2015)	4	0	21	• Thigh: 2 • Knee and upper 1/3 of leg: 2 • Lower 1/3 of leg and foot: 17	• SCIP: 6 (28.6%) • ALT: 8 (38.1%) • MSA: 4 (19.0%) • UMT: 2 (9.5%) • RF: 1 (4.8%)	95.2	Total failure: 1 Partial failure: 0	Wound dehiscence: 3 Infection: 2	270
Koh et al. (2018)	4	0	22	• Knee and upper 1/3 of leg: 9 • Middle 1/3 of leg: 6 • Lower 1/3 of leg and foot: 7	N/A	95.5	Total failure: 1 Partial failure: 1	None	N/A
Power et al. (2022)	4	0	5	• Knee and upper 1/3 of leg: 2 • Lower 1/3 of leg and foot: 3	• PAP: 2 (40.0%); • SCIP: 2 (40.0%); • ALT: 1 (20.0%)	100	Total failure: 0 Partial failure: 0	Wound dehiscence: 1	N/A
Scaglioni et al. (2021)	3	0	95	• Lower 1/3 of leg and foot: 95	• SCIP: 57 (60%) • ALT: 21 (22.1%) • PIAp: 10 (10.5%) • SGAP: 5 (5.3%) • ATAp: 1 (1.1%)	90.5	Total failure: 9 Partial failure: 12	None	1305
Seo et al. (2015)	4	0	20	• Thigh: 11 • Lower 1/3 of leg and foot: 9	N/A	100	Total failure: 0 Partial failure: 0	None	N/A
Seo et al. (2018)	3	0	14	• Lower 1/3 of leg and foot: 14	N/A	100	Total failure: 0 Partial failure: 0	Hematoma: 2	540

Abbreviations: ALT, antero-lateral thigh flap; ATAp, anterior tibial artery perforator flap; IGAP, inferior gluteal artery perforator; LDP, latissimus dorsi perforator flap; MSA, medial sural artery perforator flap; p-2-p, perforator-to-perforator; PAP, profunda artery perforator flap; PEaP, peroneal artery perforator flap; PIAp, posterior interosseous artery perforator flap; RF, radial flap; SGAP, superior gluteal artery perforator; SoP, soleus perforator flap; TDAP, thoraco-dorsal artery perforator flap; UMT, upper medial thigh (gracilis) flap.

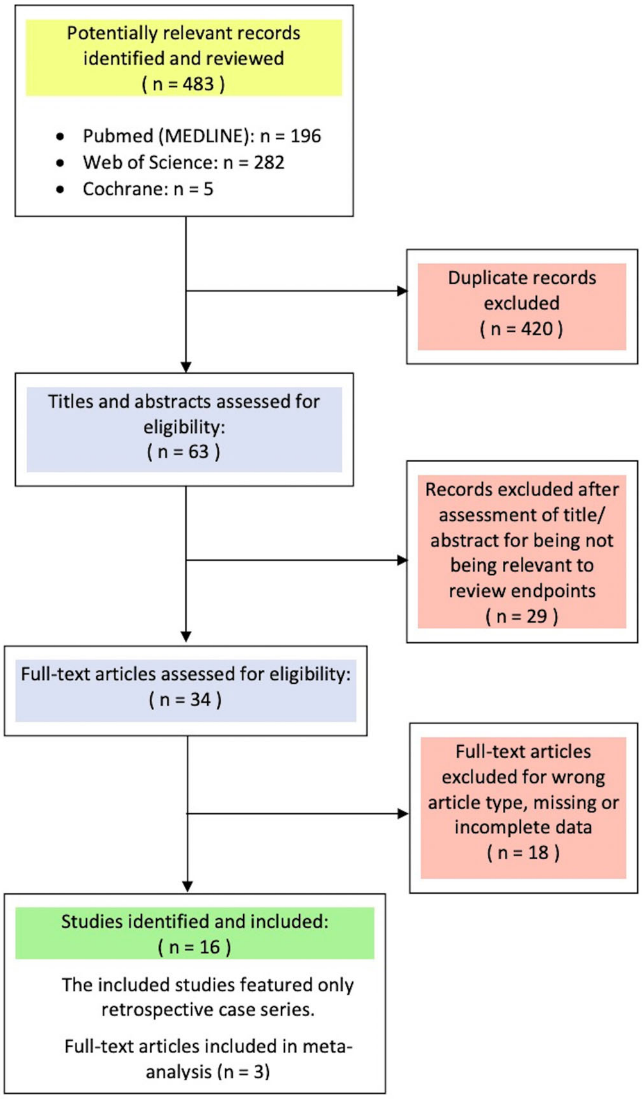

FIGURE 1 Flow diagram representation of the search strategy used for the systematic review and meta-analysis, in accordance with PRISMA guidelines.

Funnel-plots, Egger's regression test were used to assess publication bias for the flap success rate (Egger et al., 1997). All analyses were conducted with R version 4.0.4, using the metafor and adaptMCMC packages.

3 | RESULTS

3.1 | Study selection

From 483 starting citations, we identified 63 articles following the first screening based on the assessment of titles and abstracts. Any citation deemed not relevant to the systematic review endpoints was excluded. During the second screening, duplicates were excluded and manuscripts not meeting the inclusion criteria or meeting the exclusion criteria were discarded, only leaving 34 articles. After full-text

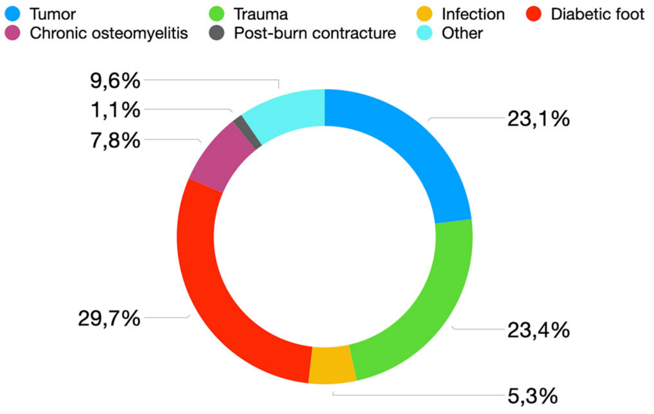

FIGURE 2 Distribution of various indications for p-2-p supermicrosurgery for soft tissue coverage of the lower limbs.

assessment, any manuscript that did not provide clinical data of a patient population undergoing supermicrosurgical free flaps for lower limb reconstruction, and namely data on flap-related outcomes, was excluded. Thus, 16 manuscripts remained and are listed in Table 1 (Goh et al., 2015; Hong, 2009; Hong et al., 2013, 2014; Hong & Koshima, 2010; Kim et al., 2010, 2015; Kim & Kim, 2012; Koh et al., 2018; Power et al., 2022; Scaglioni et al., 2021; Seo et al., 2015, 2018; Suh et al., 2016; Tashiro et al., 2014; Yoon et al., 2014). Flow-chart representation of the search strategy with the included and excluded articles is depicted in Figure 1.

3.2 | Patient characteristics

This study features 1556 patients out of which 1047 received a supermicrosurgical perforator-to-perforator flap. The mean age was 48.9 years (range: 38.0–64.0), while BMI was 24.2 kg/m^2 (range: 15.4–38.4). The average follow-up period was of 16.4 months (range: 1 month–7.2 years). The most common indications for surgery were diabetic foot in 311 cases (29.7%), followed by trauma in 245 cases (23.4%) and tumor resection in 242 cases (23.1%), chronic osteomyelitis in 82 cases (7.8%), then infections in 55 cases (5.3%), and release of post-burn contractures/scars in 12 cases (1.1%). Other less common indications include implant exposure, amputation stumps, vascular malformations and immune disorders, which were reported in 100 cases (9.6%) (Figure 2). Defects were most commonly located in the lower third of leg and/or foot, which was reported in 554 patients (52.9%). Other less common locations include the knee and upper third of leg (14.2%) followed by the middle third of leg (10.1%). The least common location was the thigh, which was reported in just 41 cases (3.9%), but location was unknown in 197 cases (18.9%). Most defect sizes were moderate (between 10 and 50 cm^2), and were covered with flaps which were 84 cm^2 in mean size. Reconstructive flaps included the SCIP, the ALT, the Upper Medial Thigh (UMT), the Inferior Gluteal Artery Perforator (IGAP), the Superior Gluteal Artery Perforator (SGAP), the Peroneal Artery

TABLE 2 Patient demographics and surgical characteristics.

Patient characteristics	Values and percentages
Mean age	48.9 (range: 38–64)
Gender	Males = 615 (58.7%)
	Females = 432 (41.3%)
Mean BMI (in kg/m^2)	24.2 (range: 15.8–38.4)
Comorbidities	Total: 794
High blood pressure	95 (12.0%)
Diabetes mellitus	373 (43.0%)
Ischemic heart disease	41 (5.2%)
Peripheral vascular disease	115 (14.5%)
Chronic renal failure	41 (5.2%)
Smoking history	112 (14.1%)
History of radiotherapy	17 (2.1%)
Location of lower limb defects	
Thigh	41 (3.9%)
Knee and upper third of leg	149 (14.2%)
Middle third of leg	106 (10.1%)
Lower third of leg and foot	554 (52.9%)
Unknown/not reported	197 (18.9%)
Mean defect size	Moderate (10–50 cm^2)
Mean flap size	84 cm^2 (range: 4–1000)
Median flap thickness	5.5 mm (range: 2.5–12.0)
Median pedicle length	4.1 cm (range: 1.0–8.0)
Type of free flaps used	
SCIP	589 (56.3%)
ALT	214 (20.4%)
Peroneal artery perforator flap	40 (3.8%)
SGAP	27 (2.6%)
PIAP	24 (2.3%)
TDAP	23 (2.2%)
LD	21 (2.0%)
UMT	6 (0.6%)
IGAP	5 (0.5%)
MSA	4 (0.3%)
Soleus perforator flap	2 (0.2%)
ATAP	1 (0.1%)
Radial forearm	1 (0.1%)
Unknown/not reported	90 (8.6%)

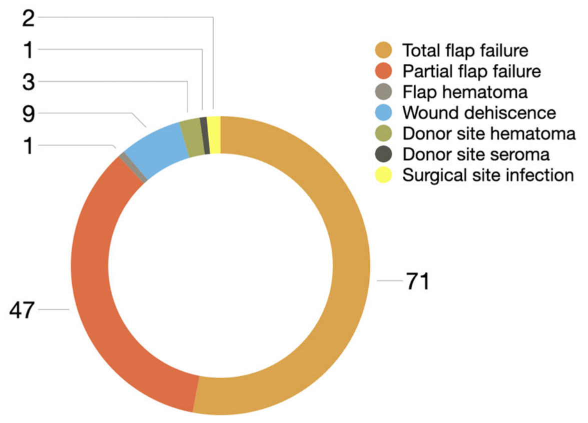

FIGURE 3 Distribution of all complications in p-2-p supermicrosurgical procedures.

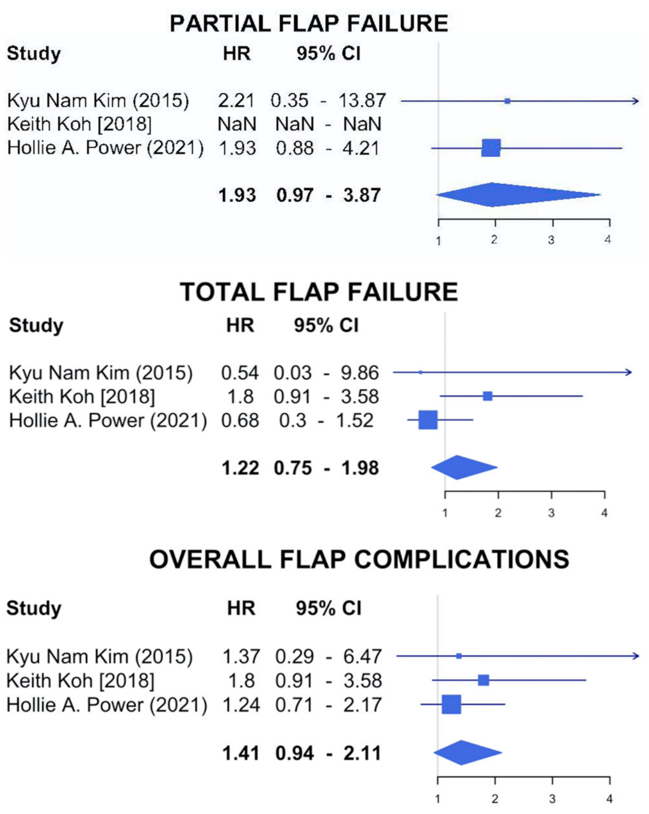

FIGURE 4 Forest plot depicting partial, total and overall flap-related complications.

Perforator, the Soleus Perforator, the Medial Sural Artery (MSA), the Posterior Interosseous Artery Perforator (PIAP), the Anterior Tibial Artery perforator (ATAP), the Thoraco-Dorsal Artery Perforator (TDAP), the Latissimus Dorsi (LD), and the Radial Forearm flaps. The most commonly reported reconstructive option was the SCIP flap, followed by the ALT flap. Median flap thickness was 5.5 mm (range: 2.5–12.0 mm), while pedicle length was 4.1 cm (range: 1.0–8.0 cm). Patient comorbidities and other demographics and surgical characteristics are reported in Table 2. Regarding surgical outcomes, flap complications were reported in 119 flaps (11.4%), which included total flap failure in 71 cases (6.8%), partial flap failure in 47 cases (4.5%) and one case of hematoma (0.1%). Donor-site complications were reported in 15 flaps (1.4%), including 9 cases of wound dehiscence (0.9%), 1 seroma (0.1%), 3 hematomas (0.3%), and 2 surgical site infections (0.2%) (Figure 3).

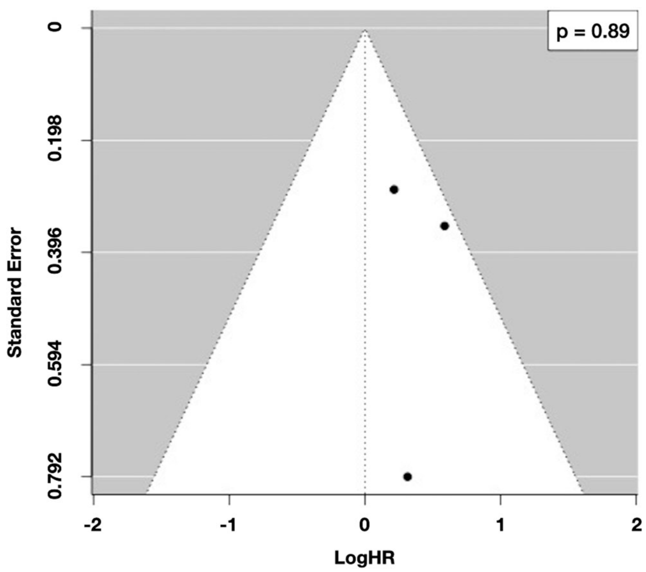

FIGURE 5 Funnel plot for flap-related complications.

3.3 | Meta-analysis

Among the 16 identified articles from the systematic review, 5 had an OCEBM level of 3 (i.e., non-randomized controlled cohort/follow-up studies) and 11 had a level of 4 (i.e., case-series, case–control, or historically controlled studies). No study had a Jadad score above 0 as none of the featured articles met the methodological requirements of a clinical trial by objective criteria. While all 16 articles were initially considered for the meta-analysis, only three were included after review of full-text manuscripts in accordance with inclusion and exclusion criteria, as they were the only manuscripts to successfully compare perforator-to-perforator and regular microsurgical anastomoses in lower limb reconstructions. The meta-analysis compared 482 perforator-2-perforator flaps to 451 conventional free flaps, assessing flap-related complications. Overall flap complications had a HR of 1.41 (0.94–2.11; 95% C.I.). Supermicrosurgical and conventional microsurgical reconstructions were not associated with statistically significant differences ($p = .89$) (Figure 4). Egger's test did not demonstrate presence of publication bias (Figure 5).

4 | DISCUSSION

Supermicrosurgery has been gradually adopted worldwide in cases where adequate major vessels are not available as recipient vessels, only leaving small caliber vessels and nerves for anastomosis. The surgical innovation that is supermicrosurgery has made certain advancements possible, including improved nerve coaptation (Iida et al., 2014), secondary free flap salvage (Cereceda-Monteoliva et al., 2018), and lymphatico-venular bypasses in lymphatic surgery (van Mulken et al., 2018). The potential of supermicrosurgery shines particularly bright with the implementation of perforator-to-perforator free tissue transfers (Zeiderman & Pu, 2021). A perforator-to-perforator approach has been proven to be a reliable and safe technical approach to soft tissue defect coverage (Escandón et al., 2023). The most relevant finding from our study is that no statistically significant differences could be found between flap complications in conventional and perforator-to-perforator anastomoses, despite the notorious technical difficulties of the latter. A relevant advantage of perforator-to-perforator based flaps in lower limbs is related to the infamously complex nature of the lower limb reconstruction population, which if often characterized by either comorbidities which damage peripheral blood vessels and microcirculation, or by impaired limb vascularity caused by injury to one of the main lower limb vessels which is typical in patients with a history of trauma and/or amputation. In fact, our study population was characterized by diabetes mellitus in as many as 43.0% of patients, followed by peripheral vascular disease in 14.5% and high blood pressure in 12.0%. The study is however limited by the fact that neither the vascularity of the affected limb in trauma cases nor the effect of comorbidities on flap-related complications could be assessed due to a lack of data provided by the full-text manuscripts selected for analysis. Nevertheless, having optimal recipient vessels can be challenging, and a perforator-to-perforator technique can overcome the need for intact axial vessels, especially in circumstances where their blood supply supports the vascularity of the entire limb and thus cannot be expendable. Additionally, its overcomes the need for tedious dissections of long pedicles which is ought to reduce morbidity associated with long and delicate dissections. We speculate that a perforator-to-perforator approach might also help avoiding the risk of avascular complications to the distal segment related to thrombosis of the anastomosis. Furthermore, clinical appearance of the perforator (good pulsation) and blood velocity in its lumen (>15 cm/s with duplex scans) have been recognized as the best predictors of success for a super-microanastomosis, thus more invasive pre-operative diagnostic tests (i.e., angiography) could be avoided and applied only for selected cases. With these two factors, in fact, flap survival rate is reported to be more than 90% in patients with peripheral vascular disease (Hong, 2009; Hong et al., 2014).

Cereceda-Monteoliva et al. (2018) conducted a meta-analysis counting 47 manuscripts to assess success rate of reconstructive supermicrosurgery in various anatomical districts. Out of 698 flaps, 69.2% were used for soft tissue coverage of the lower limb. They reported 3.84% of cumulative partial flap loss rate and an overall vascular complication rate 5.93% which resulted in complete or partial flap loss. When specifically addressing lower limb complications, they found that 22 flaps experienced partial flap loss (4.6%) while 18 had complete flap loss (3.7%). These findings are in line with our own, based on 1047 perforator-to-perforator flaps, where total flap failure occurred in 71 cases (6.8%) and partial flap failure in 47 cases (4.5%). Escandón et al.'s findings resonate with our own, as the main takeaway from their study suggests that case series of supermicrosurgical procedures used in lower limb reconstructions have a success rate comparable to that which can be found in standard microsurgical procedures. Even so, our findings are limited by the fact that they could not highlight disadvantages directly related to technical aspects of supermicrosurgical perforator-to-perforator flaps. This is particularly relevant since several authors have addressed some concerns with the technique and its possible limitations. In fact, the ability to raise perforator-to-perforator flaps and to successfully revascularize them requires long learning curves, experience and very specific training (Liu, 2013), all of which are neither accounted for nor addressed by any of the included manuscripts, in which surgeries were performed by senior surgeons with recognized expertise in the field. We believe that expertise is the mother of success in microsurgery, as in surgery overall. It is likely that the high flap success rate and low flap complication rates have been achieved by the authors of the manuscripts assessed in this review through their expertise and surgical capabilities honed over the years.

Additionally, Badash et al. (2018) discussed an alleged increased inherent risk of thrombosis in small-caliber perforator thrombosis which ultimately leads to flap necrosis. This could be due to several reasons: a higher risk of caliber mismatch due to uneven lumens (Fensterer et al., 2014; Zhou et al., 2010), turbulent blood flow due to vessel wall irregularity leading to turbulence-induced thrombogenicity (Doh et al., 2021; Krijgh et al., 2021), or vessel wall collapse due to low inner lumen pressures, since blood flow rate proportionally decreases with reduction in vessel diameter (Drzewiecki et al., 1997). Finally, another concern has been raised by Kim et al. (2015), according to whom the use of perforator-to-perforator should be limited to small-sized flaps, as a single low-caliber vessel may not be adequate to perfuse across large flap areas. While these concerns have not been properly substantiated, as demonstrated by the fact that flaps in our meta-analysis had a mean size of 84 cm^2, we still believe that the relevance of these concerns should be weighed in future evidence regarding the use of perforator-to-perforator flaps.

Finally, while our findings were characterized by relatively a short follow-up period of 16.4 months on average. We believe that this was still enough to assess the surgical safety of perforator-to-perforator technique since most free flap failures occur within the first 48 h from surgery (Novakovic et al., 2009). Late failures (defined as vascular compromise occurring after the first 48 h) are mainly linked to infection or mechanical stress/pressure on the pedicle and around the anastomosis (Wax & Rosenthal, 2007). Our study was conclusive in proving the safety of perforator-to-perforator supermicrosurgery for lower limb reconstructive surgery. Nevertheless, we believe that the meta-analysis was also limited by the low quality of overall evidence, as suggested by OCEBM and Jadad Score results, summarized in Table 1. This is purportedly due to lack of high-level evidence in this specific field of plastic surgery, which will hopefully be addressed by implementing clinical trials in research to come.

5 | CONCLUSION

The use of perforator-to-perforator supermicrosurgery has been compared to conventional free flap transfers for soft tissue reconstruction of the lower limbs. Our evidence supports the safety of surgical outcomes, with acceptable flap complication rates. Nevertheless, these findings are limited by poor overall quality which must be addressed and used to encourage higher-level evidence in the field.

CONFLICT OF INTEREST STATEMENT

Nothing to disclose.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ORCID

Federico Lo Torto https://orcid.org/0000-0001-8901-3614
Guido Firmani https://orcid.org/0000-0002-5806-1530
Arianna Di Rocco https://orcid.org/0000-0003-1043-0103
Diego Ribuffo https://orcid.org/0000-0002-1844-7850

REFERENCES

Badash, I., Gould, D. J., & Patel, K. M. (2018). Supermicrosurgery: History, applications, training and the future. *Frontiers in Surgery*, *5*, 23. https://doi.org/10.3389/fsurg.2018.00023

Berner, J. E., Nikkhah, D., Zhao, J., Prousskaia, E., & Teo, T. C. (2020). The versatility of the superficial circumflex iliac artery perforator flap: A single surgeon's 16-year experience for limb reconstruction and a systematic review. *Journal of Reconstructive Microsurgery*, *36*(2), 93–103. https://doi.org/10.1055/s-0039-1695051

Cereceda-Monteoliva, N., Izadi, D., & Wilson, S. (2018). Salvage of free flaps following vascular pedicle avulsion using "supermicrosurgery" techniques: A case report of DIEP free flap salvage and review of the literature. *Eplasty*, *18*, ic9.

de Laat, F. A., Dijkstra, P. U., Rommers, G. M., Geertzen, J. H. B., & Roorda, L. D. (2018). Prevalence of comorbidity and its association with demographic and clinical characteristics in persons wearing a prosthesis after a lower-limb amputation. *Journal of Rehabilitation Medicine*, *50*(7), 629–635. https://doi.org/10.2340/16501977-2336

Doh, G. H., Kim, B. S., Lee, D. Y., Yoon, J. S., Lim, S. A., Han, Y. S., & Eo, S. R. (2021). Hemodynamic principles in free tissue transfer: Vascular changes at the anastomosis site. *Archives of Hand and Microsurgery*, *26*(4), 285–292. https://doi.org/10.12790/ahm.21.0118

Drzewiecki, G., Field, S., Moubarak, I., & Li, J. K. (1997). Vessel growth and collapsible pressure-area relationship. *The American Journal of Physiology*, *273*(4), H2030–H2043. https://doi.org/10.1152/ajpheart.1997.273.4.H2030

Egger, M., Davey Smith, G., Schneider, M., & Minder, C. (1997). Bias in meta-analysis detected by a simple, graphical test. *BMJ*, *315*(7109), 629–634. https://doi.org/10.1136/bmj.315.7109.629

Escandón, J. M., Ciudad, P., Mayer, H. F., Pencek, M., Mantilla-Rivas, E., Mohammad, A., Langstein, H. N., & Manrique, O. J. (2023). Free flap transfer with supermicrosurgical technique for soft tissue reconstruction: A systematic review and meta-analysis. *Microsurgery*, *43*(2), 171–184. https://doi.org/10.1002/micr.30894

Fensterer, T. F., Miller, C. J., Perez-Abadia, G., & Maldonado, C. (2014). Novel cuff design to facilitate anastomosis of small vessels during cervical heterotopic heart transplantation in rats. *Comparative Medicine*, *64*(4), 293–299.

Goh, T. L. H., Park, S. W., Cho, J. Y., Choi, J. W., & Hong, J. P. (2015). The search for the ideal thin skin flap: Superficial circumflex iliac artery perforator flap – A review of 210 cases. *Plastic and Reconstructive Surgery*, *135*(2), 592–601. https://doi.org/10.1097/PRS.0000000000000951

Higgins, J. P., Thompson, S. G., & Spiegelhalter, D. J. (2009). A re-evaluation of random-effects meta-analysis. *Journal of the Royal*

Statistical Society. Series A, Statistics in Society, *172*(1), 137–159. https://doi.org/10.1111/j.1467-985X.2008.00552.x

Hong, J. P. (2009). The use of supermicrosurgery in lower extremity reconstruction: The next step in evolution. *Plastic and Reconstructive Surgery*, *123*(1), 230–235. https://doi.org/10.1097/PRS.0b013e3181904dc4

Hong, J. P., & Koshima, I. (2010). Using perforators as recipient vessels (supermicrosurgery) for free flap reconstruction of the knee region. *Annals of Plastic Surgery*, *64*(3), 291–293. https://doi.org/10.1097/SAP.0b013e3181ac4263

Hong, J. P., Sun, S. H., & Ben-Nakhi, M. (2013). Modified superficial circumflex iliac artery perforator flap and supermicrosurgery technique for lower extremity reconstruction: A new approach for moderate-sized defects. *Annals of Plastic Surgery*, *71*(4), 380–383. https://doi.org/10.1097/SAP.0b013e3182503ac5

Hong, J. P., Yim, J. H., Malzone, G., Lee, K. J., Dashti, T., & Suh, H. S. (2014). The thin gluteal artery perforator free flap to resurface the posterior aspect of the leg and foot. *Plastic and Reconstructive Surgery*, *133*(5), 1184–1191. https://doi.org/10.1097/PRS.0000000000000127

Howick, J., Chalmers, I., Glasziou, P., Greenhalgh, T., Heneghan, C., Liberati, A., Moschetti, I., Phillips, B., & Thornton, H. (2011). *OCEBM levels of evidence – Centre for Evidence-Based Medicine (CEBM)*. University of Oxford. https://www.cebm.ox.ac.uk/resources/levels-of-evidence/ocebm-levels-of-evidence

Iida, T., Narushima, M., Hara, H., Yamamoto, T., Yoshimatsu, H., Morizaki, Y., Uehara, K., & Koshima, I. (2014). Supermicrosurgical free sensate intercostal artery perforator flap based on the lateral cutaneous branch for plantar reconstruction. *Journal of Plastic, Reconstructive & Aesthetic Surgery*, *67*(7), 995–997. https://doi.org/10.1016/j.bjps.2014.01.001

Iocca, O., Farcomeni, A., Pardiñas Lopez, S., & Talib, H. S. (2017). Alveolar ridge preservation after tooth extraction: A Bayesian network meta-analysis of grafting materials efficacy on prevention of bone height and width reduction. *Journal of Clinical Periodontology*, *44*(1), 104–114. https://doi.org/10.1111/jcpe.12633

Jadad, A. R., Moore, R. A., Carroll, D., Jenkinson, C., Reynolds, D. J. M., Gavaghan, D. J., & McQuay, H. J. (1996). Assessing the quality of reports of randomized clinical trials: Is blinding necessary? *Controlled Clinical Trials*, *17*(1), 1–12. https://doi.org/10.1016/0197-2456(95)00134-4

Kim, C. Y., & Kim, Y. H. (2012). Supermicrosurgical reconstruction of large defects on ischemic extremities using supercharging techniques on latissimus dorsi perforator flaps. *Plastic and Reconstructive Surgery*, *130*(1), 135–144. https://doi.org/10.1097/PRS.0b013e318254b128

Kim, C. Y., Naidu, S., & Kim, Y. H. (2010). Supermicrosurgery in peroneal and soleus perforator-based free flap coverage of foot defects caused by occlusive vascular diseases. *Plastic and Reconstructive Surgery*, *126*(2), 499–507. https://doi.org/10.1097/PRS.0b013e3181df64c2

Kim, K. N., Hong, J. P., Park, S. W., Kim, S. W., & Yoon, C. S. (2015). Overcoming the obstacles of the Ilizarov device in extremity reconstruction: Usefulness of the perforator as the recipient vessel. *Journal of Reconstructive Microsurgery*, *31*(6), 420–425. https://doi.org/10.1055/s-0035-1548549

Koh, K., Goh, T. L. H., Song, C. T., Suh, H., Rovito, P., Hong, J. P., & Hallock, G. (2018). Free versus pedicled perforator flaps for lower extremity reconstruction: A multicenter comparison of institutional practices and outcomes. *Journal of Reconstructive Microsurgery*, *34*(8), 572–580. https://doi.org/10.1055/s-0038-1639576

Koshima, I. (2008). Atypical arteriole anastomoses for fingertip replantations under digital block. *Journal of Plastic, Reconstructive & Aesthetic Surgery*, *61*(1), 84–87. https://doi.org/10.1016/j.bjps.2006.11.023

Koshima, I., Yamamoto, T., Narushima, M., Mihara, M., & Iida, T. (2010). Perforator flaps and supermicrosurgery. *Clinics in Plastic Surgery*, *37*(4), 683–689, vii-iii. https://doi.org/10.1016/j.cps.2010.06.009

Krijgh, D. D., Tellier, B., Teunis, T., Maarse, W., & Coert, J. H. (2021). Is there a difference in venous thrombosis rate in free flap anastomoses based on coupler diameter? A systematic review. Does size really matter? *JPRAS Open*, *30*, 74–83. https://doi.org/10.1016/j.jpra.2021.07.005

Liu, H. L. (2013). Microvascular anastomosis of submillimeter vessels-a training model in rats. *Journal of Hand and Microsurgery*, *5*(1), 14–17. https://doi.org/10.1007/s12593-013-0089-z

May, J. W., Jr., Lukash, F. N., & Gallico, G. G., 3rd. (1981). Latissimus dorsi free muscle flap in lower-extremity reconstruction. *Plastic and Reconstructive Surgery*, *68*(4), 603–607. https://doi.org/10.1097/00006534-198110000-00022

Mureau, M. A., & Hofer, S. O. (2008). Perforator-to-perforator musculocutaneous anterolateral thigh flap for reconstruction of a lumbosacral defect using the lumbar artery perforator as recipient vessel. *Journal of Reconstructive Microsurgery*, *24*(4), 295–299. https://doi.org/10.1055/s-2008-1080532

Novakovic, D., Patel, R. S., Goldstein, D. P., & Gullane, P. J. (2009). Salvage of failed free flaps used in head and neck reconstruction. *Head and Neck Oncologia*, *1*, 33. https://doi.org/10.1186/1758-3284-1-33

Park, J. E., & Chang, D. W. (2016). Advances and innovations in microsurgery. *Plastic and Reconstructive Surgery*, *138*(5), 915e–924e. https://doi.org/10.1097/PRS.0000000000002715

Power, H. A., Cho, J., Kwon, J. G., Abdelfattah, U., Pak, C. J., Suh, H. P., & Hong, J. P. (2022). Are perforators reliable as recipient arteries in lower extremity reconstruction? Analysis of 423 free perforator flaps. *Plastic and Reconstructive Surgery*, *149*(3), 750–760. https://doi.org/10.1097/PRS.0000000000008873

Proietti, M., Farcomeni, A., Romiti, G. F., di Rocco, A., Placentino, F., Diemberger, I., Lip, G. Y. H., & Boriani, G. (2020). Association between clinical risk scores and mortality in atrial fibrillation: Systematic review and network meta-regression of 669,000 patients. *European Journal of Preventive Cardiology*, *27*(6), 633–644. https://doi.org/10.1177/2047487318817662

Proietti, M., Romiti, G. F., Romanazzi, I., Farcomeni, A., Staerk, L., Nielsen, P. B., & Lip, G. Y. H. (2018). Restarting oral anticoagulant therapy after major bleeding in atrial fibrillation: A systematic review and meta-analysis. *International Journal of Cardiology*, *261*, 84–91. https://doi.org/10.1016/j.ijcard.2018.03.053

Scaglioni, M. F., Meroni, M., & Fritsche, E. (2021). Free tissue transfer with supermicrosurgical perforator-to-perforator (P-to-P) technique for tissue defect reconstruction around the body: Technical pearls and clinical experience. *Journal of Plastic, Reconstructive & Aesthetic Surgery*, *74*(8), 1791–1800. https://doi.org/10.1016/j.bjps.2020.12.025

Seo, S. W., Kim, K. N., Ha, W., & Yoon, C. S. (2018). Validity of the use of a subfascial vessel as the recipient vessel in a second free flap transfer: A retrospective clinical review. *Medicine*, *97*(5), e9819. https://doi.org/10.1097/MD.0000000000009819

Seo, S. W., Kim, K. N., & Yoon, C. S. (2015). Extended scope of the use of the peroneal perforator flap in lower limb reconstruction. *Journal of Reconstructive Microsurgery*, *31*(9), 654–659. https://doi.org/10.1055/s-0035-1558462

Suh, H. S., Oh, T. S., Lee, H. S., Lee, S. H., Cho, Y. P., Park, J. R., & Hong, J. P. (2016). A new approach for reconstruction of diabetic foot wounds using the angiosome and supermicrosurgery concept. *Plastic and Reconstructive Surgery*, *138*(4), 702e–709e. https://doi.org/10.1097/PRS.0000000000002401

Tashiro, K., Harima, M., Yamamoto, T., Narushima, M., & Koshima, I. (2014). Locating recipient perforators for perforator-to-perforator anastomosis using color doppler ultrasonography. *Journal of Plastic, Reconstructive & Aesthetic Surgery*, *67*(12), 1680–1683. https://doi.org/10.1016/j.bjps.2014.08.047

Tierney, J. F., Stewart, L. A., Ghersi, D., Burdett, S., & Sydes, M. R. (2007). Practical methods for incorporating summary time-to-event data into meta-analysis. *Trials*, *8*, 16. https://doi.org/10.1186/1745-6215-8-16 van Mulken, T. J. M., Schols, R. M., Qiu, S. S., Brouwers, K., Hoekstra, L. T., Booi, D. I., Cau, R., Schoenmakers, F., Scharmga, A. M. J., & van der Hulst, R. R. W. J. (2018). Robotic (super) microsurgery: Feasibility of a new master-slave platform in an in vivo animal model and future directions. *Journal of Surgical Oncology*, *118*(5), 826–831. https://doi.org/10.1002/jso.25195

Wax, M. K., & Rosenthal, E. (2007). Etiology of late free flap failures occurring after hospital discharge. *The Laryngoscope*, *117*(11), 1961–1963. https://doi.org/10.1097/MLG.0b013e31812e017a

Yamamoto, T., Yamamoto, N., & Ishiura, R. (2017). Thirty-micron needle for precise supermicrosurgery. *Microsurgery*, *37*(6), 735–736. https://doi.org/10.1002/micr.30165

Yoon, C. S., Noh, H. J., Malzone, G., Suh, H. S., Choi, D. H., & Hong, J. P. (2014). Posterior interosseous artery perforator-free flap: Treating intermediate-size hand and foot defects. *Journal of Plastic, Reconstructive & Aesthetic Surgery*, *67*(6), 808–814. https://doi.org/10.1016/j.bjps.2014.03.007

Zeiderman, M. R., & Pu, L. L. Q. (2021). Free-style free perforator flaps in lower extremity reconstruction. *Clinics in Plastic Surgery*, *48*(2), 215–223. https://doi.org/10.1016/j.cps.2020.12.001

Zhou, Y., Gu, X., Xiang, J., Qian, S., & Chen, Z. (2010). A comparative study on suture versus cuff anastomosis in mouse cervical cardiac transplant. *Experimental and Clinical Transplantation*, *8*(3), 245–249.

How to cite this article: Lo Torto, F., Firmani, G., Patanè, L., Turriziani, G., Di Rocco, A., Vestri, A., & Ribuffo, D. (2023). Supermicrosurgery with perforator-to-perforator anastomoses for lower limb reconstructions – A systematic review and meta-analysis. *Microsurgery*, 1–10. https://doi.org/10.1002/micr.31081