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Comparing the Clinical Effects of Free and Pedicled Flap in Repairing Small Area of Distal Lower Limb Soft Tissue Defects: A Retrospective Comparative Study

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Keywords: free perforator flap | lower limb | pedicled perforator flap | soft tissue defects

ABSTRACT

Background and Aims: The exposure of tendons, blood vessels, nerves, and bone due to soft tissue defects in the foot poses a significant challenge for microsurgeons. Free perforator flaps and pedicled perforator flaps are currently the most common methods used for repairing small areas of soft tissue defects in the distal lower limb.

Methods: A retrospective analysis was carried out on 124 patients with small soft tissue defects in the distal lower limb from January 2009 to December 2021. The evaluation criteria encompassed the patient's intraoperative condition, the occurrence of short-term and long-term postoperative complications, as well as the esthetic and functional outcomes.

Results: In this study, two groups of patients with similar soft tissue defects were included. However, the free perforator flap group showed more severe wound damage compared to the pedicled perforator group. Intraoperatively, the pedicled perforator group needed a larger flap area for wound repair, and the free perforator group had higher intraoperative blood loss and longer operation time. Postoperatively, the incidence of complications was significantly higher in the pedicled perforator group, while the esthetic outcomes were poorer, but the functional evaluation results were better.

Conclusion: For small soft tissue defects in the distal lower limb, both free perforator flap and pedicled perforator flap are effective in wound repair. The free perforator flap has the advantage of being able to handle more complex wounds with less limitation by location. In cases where the microsurgical expertise is relatively limited and the injuries are minor, pedicled perforator can be considered as the primary choice.

Level of Evidence: III, case-control study.

Abbreviations: ALTP, anterolateral thigh perforator; AOFAS, American Orthopaedic Foot and Ankle Society; BMI, body mass index; CSAP, circumflex scapular artery perforator flap; DIEP, deep inferior epigastric perforator flap; PPF, free perforator flaps; LD, latissimus dorsi musculocutaneous flap; PAP, peroneal artery perforator flap; PPF, pedicled perforator flap; PTAP, posterior tibial artery perforator flap.

Zhe-Ming Cao and Yan Yang contributed equally to this work.

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1 | Introduction

Distal lower extremity soft tissue defects with exposed tendons, vessels, nerves, and bone tissue pose a significant challenge for microsurgeons. These wounds come in different sizes and depths, often leading to delayed healing or complications such as infection, which can result in deformities during the recovery process. Therefore, these complications not only have a profound impact on the esthetics of the foot but also affect the movement function of the foot and ankle. In severe cases, amputation may be necessary [1, 2]. Relevant studies have indicated that perforator flap technology remains a common choice in clinical practice, including pedicled perforator flap (PPF) and free perforator flap (FPF) [3–7]. However, repairing the specific area around the distal lower limb often requires thin, flexible, and wear-resistant flap tissue; thus, selecting a suitable flap is particularly crucial.

Many relevant literature reports the clinical efficacy of FPF or PPF in repairing distal limb defects. Among them, the anterolateral thigh perforator (ALTP) flap and circumflex scapular artery perforator (CSAP) flap are the most commonly used FPFs for lower limb distal reconstruction. Due to their relatively concealed donor site, reliable blood supply, and large cutting area, they can be used to design composite flaps using the vastus lateralis or muscle tissue to repair deep structures such as the foot and sensory nerves to resume sensations [8, 9]. PPFs, such as those derived from the peroneal artery perforator (PAP) flap and the posterior tibial artery perforator (PTAP) flap, offer numerous advantages including a large rotational arc, skin texture and color congruence with the recipient site, obviating the need for vascular anastomosis, minimal trauma, and favorable cosmetic outcomes [10]. They have found extensive application in addressing cutaneous and soft tissue deficiencies in the proximal lower limb resulting from trauma, posttraumatic scar release, and tumor excision [11, 12].

However, only a few retrospective studies have compared the postoperative complications and flap survival rates between FPF and PPF. However, the injuries of the patients included in these studies were not consistent (such as wound size, location, and severity). Therefore, there is still insufficient evidence to distinguish the differences between FPF and PPF in lower limb soft tissue reconstruction. To enhance the reliability of this study, strict control was implemented over the fundamental injury conditions of patients in both groups, ensuring their comparability.

2 | Patients and Methods

This study is a retrospective analysis of 124 patients with distal lower extremity small soft tissue defects caused by trauma from January 2009 to December 2021. A total of 68 patients underwent FPF repair (of which 28 were caused by traffic accidents, 23 by crush injuries, and 17 by other injuries), while 56 patients underwent PPF repair (of which 25 were caused by traffic accidents, 16 by crush injuries, and 15 by other injuries). Detailed records of preoperative, intraoperative, and postoperative data as well as long-term follow-up results were recorded. All patients were operated on by the same surgeon and team.

This retrospective observational study was approved by the Medical Ethics Committee of Xiangya Hospital of Central South

University on January 5, 2024. It only collected clinical data of patients without interfering with their treatment plan and would not bring risks to their physiology. Patients themselves or their families provide informed consent to participate in the study and consent to the disclosure of their anonymous details and images. The protocol was in accordance with the ethical standards of the Helsinki Declaration of 1975 and all subsequent revisions.

Inclusion criteria include: (1) the location of soft tissue defect in the lower limb distal end (including the distal 1/3 of the tibia, the area around the ankle joint, and 1/2 of the foot); (2) the repair method used is FPF (ALTP or CSAP) or PPF (PAP or PTAP); and (3) the area of soft tissue defect is less than 60 cm². Exclusion criteria include: (1) soft tissue defect caused by tuberculosis, tumors or other chronic diseases; (2) the pedicle flap with deficiency or insufficiency of perforator supply; and (3) the follow-up time is less than 12 months.

2.1 | Surgical Technique

Upon admission, all patients underwent thorough debridement before scheduling flap repair.

In the FPF group, ALTP (Figure 1) or CSAP (Figure 2) was used to repair the wound according to the size of the wound, and a chimeric perforator flap was designed for patients with deep dead space. Before the flap is dissected, the location of the perforator vessel supplying the flap is identified using color Doppler ultrasound. The flap is then dissected using the retrograde tetrahedral anatomy technique, and thorough hemostasis is done before direct closure of the donor site. The detailed surgical method has been described in previous studies [8, 9, 13].

In the PPF group, the PAP flap (Figure 3) was located at 1–10 cm above the lateral malleolus and the PTAP flap (Figure 4) was located at 4–7 cm above the medial malleolus using a Doppler detector. The perforator points were chosen near the edge of the wound and healthy skin tissue. The other two perforator points were determined as a backup in case of possible anatomical variations. Small skin flaps were usually closed directly at the donor site; if the tension was too high and the donor site could not be closed directly, a skin graft (second donor site) was used to repair the donor site. The detailed surgical method was consistent with previous studies [10].

2.2 | Evaluation of Outcomes

The intraoperative conditions and postoperative complications of both patient groups were observed. At the 12th month, subjective and objective assessments were conducted to evaluate the appearance of the donor site and recipient site [14–16], along with ankle function using the AOFAS (American Orthopaedic Foot and Ankle Society) scoring system [17].

2.3 | Statistical Analysis

The data were analyzed in accordance with the Guidelines for Statistical Reporting of Clinical Studies [18]. SPSS 22.0 software



FIGURE 1 | A 9-year-old male presented with a soft defect of the medial ankle due to traffic injury. (A) Soft tissue defect after debridement. (B) The designed ALTP flap of the donor site. (C) Free ALTP flap was harvested. (D, E) The donor and recipient regions were closed directly after the operation. (F, G) Donor area and recipient area about 2 months after surgery. (H, I) Donor area and recipient area about 5 months after surgery.

(SPSS Inc., US) was used for statistical analysis. Quantitative data were expressed as mean \pm standard deviation and analyzed using two independent sample *t*-tests. Qualitative data were expressed as numbers or percentages and compared using χ^2 test and Fisher exact test. A two-sided *p* value of < 0.05 was considered statistically significant.

3 | Results

Due to the limited area of PPF excision, it can only repair small areas of distal lower limb soft tissue defects. Therefore, this study was based on the range of PPF adaptation being less than 60 cm^2 . Ultimately, 124 patients met the inclusion criteria, of which 68 patients were in the FPF group (including 43 male and 25 female), with an average age of 36.8 ± 17.6 years, and 56 patients were in the PPF group (including 35 male and 21 female), with an average age of 37.3 ± 17.4 years. The comparison of basic data (age, BMI, comorbidities, cause of injury, ASA, defect site etc.) between the two groups showed no statistical difference, indicating that the two groups were relatively homogenous and comparable (Table 1).

After debridement, the area of soft tissue defects in the two groups (FPF group and PPF group) was compared, and no statistically significant difference was found (38.2 ± 11.2 vs.

$39.3 \pm 12.6 \text{ cm}^2$, $p = 0.58$). When PPF rotational flaps were used to repair the wound, some areas were designed for the closure of the donor site, which resulted in the need to obtain a larger flap size to repair the same defect area. Therefore, the flap size in the PPF group was larger than that in the FPF group (56.3 ± 15.5 vs. $43.2 \pm 11.7 \text{ cm}^2$, $p < 0.001$). At the same time, because FPF can design appropriate tissue flaps to fill complex wounds according to the needs of the wound, the results of this study show that the deep tissue damage in the FPF group is greater than that in the PPF group. The amount of intraoperative bleeding in the PPF group was significantly lower than that in the FPF group due to the use of tourniquets during flap cutting (81.1 ± 25.4 vs. $146.0 \pm 38.3 \text{ mL}$, $p < 0.001$). There was no significant difference in flap cutting time between the two groups, but the total surgical time in the FPF group was longer than that in the PPF group due to the need for vascular anastomosis (149.3 ± 26.0 vs. $130.7 \pm 25.6 \text{ min}$, $p < 0.001$) (Table 2).

An analysis was conducted on the incidence of complications in the donor and recipient site after surgery. The incidence of complications in the recipient site of the PPF group was significantly higher than that of the FPF group (of which two cases of complete necrosis and nine cases of partial necrosis occurred in the PPF group, while five cases of wound dehiscence occurred, four cases of complete necrosis and two cases of partial

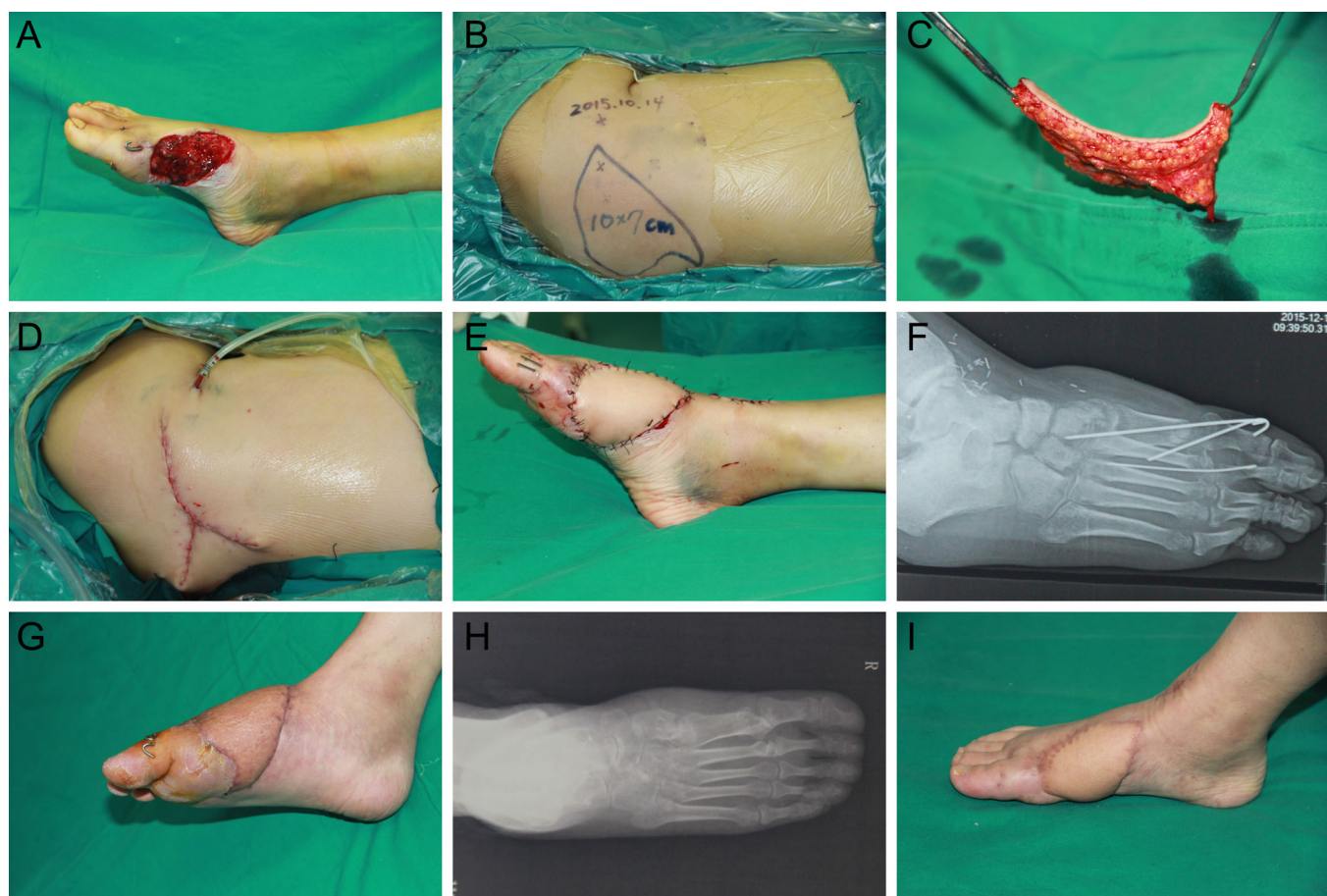


FIGURE 2 | A 28-year-old female presented with a soft defect of the 1/2 foot due to a crash injury. (A) Soft tissue defect after debridement. (B) The designed CSAP flap of the donor site. (C) A free CSAP flap was harvested. (D, E) The donor and recipient regions were closed directly after the operation. (F, G) X-ray and appearance of the recipient area about 2 months after surgery. (H, I) X-ray and appearance of the recipient area about 6 months after surgery.

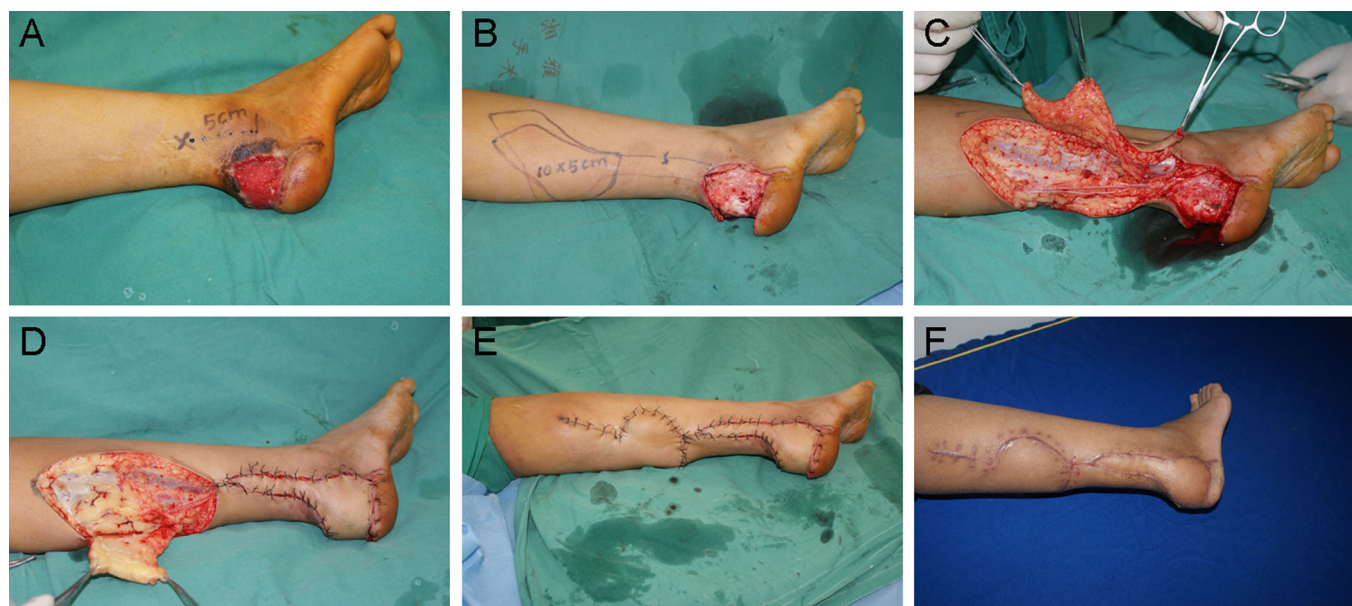


FIGURE 3 | A 34-year-old female presented with a soft tissue defect in the heel of foot due to traffic injury. (A) Soft tissue defect after debridement. (B) The designed PAP flap of the donor site. (C) PAP flap was harvested. (D, E) To close the donor area and the recipient area directly, local flap transposition was performed in the donor area. (F) Donor area and recipient area about 3 months after surgery.

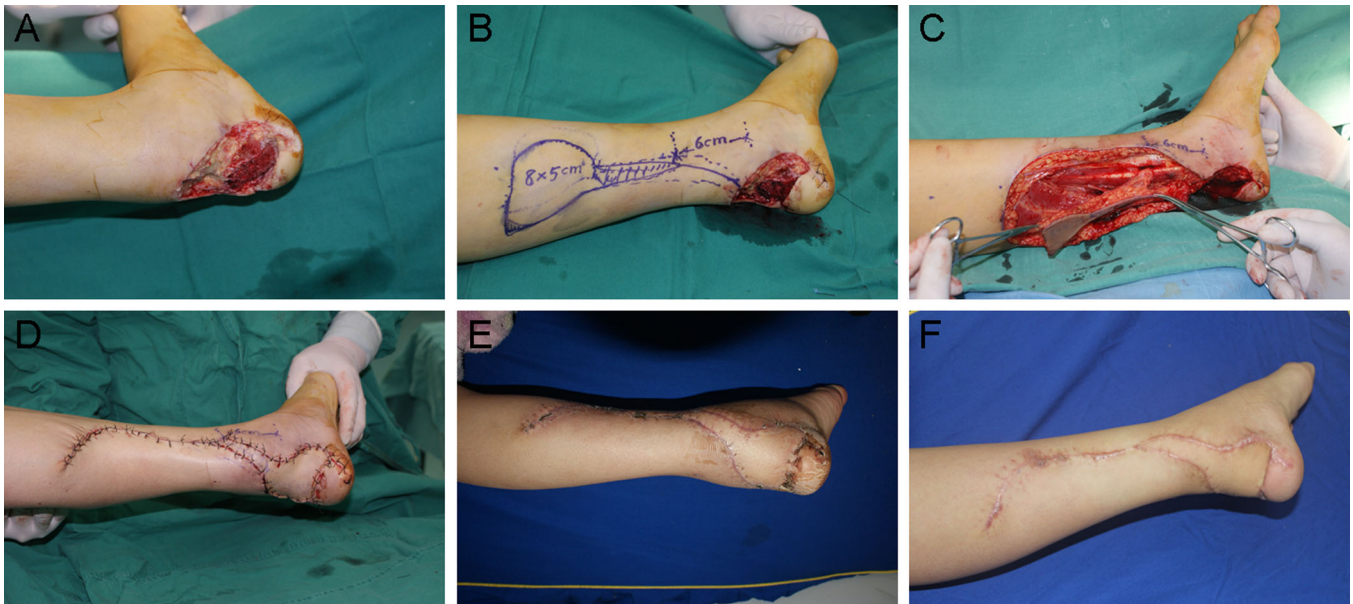


FIGURE 4 | A 20-year-old male presented with a soft tissue defect in the heel of foot due to traffic injury. (A) Soft tissue defect after debridement. (B) The designed PTAP flap of donor site. (C) PTAP flap was harvested. (D) The donor and recipient regions were closed directly after the operation. (E) Donor area and recipient area about 1 month after surgery. (F) Donor area and recipient area about 3 months after surgery.

necrosis occurred in the FPF group). In the FPF group, the main reason for flap necrosis was six cases of vascular crisis (of which two survived after emergency vascular exploration, and the other four required subsequent secondary FPF repair), while in the PPF group, the main reason for flap necrosis was two cases of vascular crisis and nine cases of distal blood supply insufficiency (of which eight required FPF repair). Wound dehiscence patients were treated with suture therapy, while a few patients with partial necrosis and local infection or hematoma were treated with wound dressing changes. In the FPF group, the donor site could be directly closed, while 18 cases of skin grafting were required to repair the donor site in the PPF group, resulting in delayed healing of the donor site (Table 2).

At the end of 12 months, the affected limb's esthetics and function were evaluated. Among the results, the subjective evaluation of overall esthetics showed that the appearance of the donor and recipient sites in the FPF group was significantly better than that in the PPF group (excellent and good rate: 89.7% vs. 64.3%, $p = 0.001$), and the objective evaluation results were also consistent. The results of the ankle joint function evaluation showed that the ankle joint function recovery of the PPF group was better than that of the FPF group (excellent and good rate: 69.1% vs. 85.7%, $p = 0.03$). Considering that the injury severity of the FPF group was greater than that of the PPF group, which affected the ankle joint function (Table 3).

To exclude the influence of wound severity on the clinical efficacy of flap repair, 15 cases of chimeric-ALTP were removed from the free flap group and then compared with the pedicled flap group again. Other results showed the same trend as before, and only the ankle joint function evaluation trend changed. The results showed that there was no significant difference between the two groups (excellent and good rate: 88.7% vs. 85.7%, $p = 0.78$) (Supporting Information S1: Tables 1–3).

4 | Discussion

Previous studies have shown that the reliability of the results of perforator flap surgery is reduced by inconsistent factors such as surgical techniques, injury site, and size of the soft tissue defect [19]. Assessing the effectiveness of PPF and FPF in treating distal lower limb soft tissue defects (traumatic) remains a challenge. This study aimed to increase the reliability of the results by strictly controlling the inclusion criteria to ensure that the basic conditions of the soft tissue defects in both groups were consistent.

With the advancement of perforator flap technology, various body area flaps have been progressively explored, including the ALTP flap, latissimus dorsi musculocutaneous (LD) flap, CSAP flap, and deep inferior epigastric perforator (DIEP) flap among others [8, 9, 20, 21]. Within this research center, a comparative analysis between DIEP and ALTP flaps for soft tissue defect repair in pediatric foot cases demonstrated superior clinical outcomes with ALTP flaps in terms of short-term and long-term complications, scar formation, as well as morphological and functional results [8]. Similarly, when comparing DIEP and CSAP flaps for soft tissue defect reconstruction in children's feet, CSAP flap exhibited advantages such as reduced operation time and harvest duration along with lower fat hyperplasia rate and improved long-term cosmetic effects compared to DIEP flap [9]. Therefore, it can be concluded that ALTP and CSAP are currently the most suitable donor sites for repairing distal soft tissue defects in the lower limb.

Due to the peculiarity of the ankle joint and surrounding tissue, pedicled flaps are also commonly used in the repair of this site, including PAP flap and PTAP flap [10]. In 2006, Hallock reported the first combination of perforator flap and propeller flap technology and proposed the concept of perforator propeller flap, which greatly improved the flexibility of flap transfer [22].

TABLE 1 | Patient's physical condition and wound injury.

Variable	FPF group (N = 68)	PPF group (N = 56)	p value ^c
Age (year)	36.8 ± 17.6	37.3 ± 17.4	0.87
Gender			> 0.99
Male	43	35	
Female	25	21	
Smoking history			0.86
No	37	29	
Yes	31	27	
Alcohol history			0.59
No	40	30	
Yes	28	26	
BMI			0.98
< 25 kg/m ²	35	28	
≥ 25–29.9 kg/m ²	22	19	
≥ 30 kg/m ²	11	9	
Comorbidities ^a			0.14
No	45	29	
Yes	23	27	
Cause of injury			0.82
Traffic accident	28	25	
Crash injury	23	16	
Other cases	17	15	
ASA			0.42
I	37	24	
II	26	26	
III	5	6	
Wound location			0.85
Distal tibia 1/3	25	19	
Ankle and 1/2 foot	43	37	
Open-wound periods (days)	16.4 ± 8.9	17.7 ± 9.1	0.44
Frequency of debridement	2.4 ± 0.8	2.3 ± 0.6	0.23
Wound condition			< 0.001
Soft tissue defect	14	27	
Combined tendon defect	26	23	
Combined injury ^b	28	6	
Soft tissue defect size (cm ²)	38.2 ± 11.2	39.3 ± 12.6	0.58

Abbreviations: ASA, American Society of Anesthesiologists; BMI, body mass index; FPF, free perforator flap; PPF, pedicled perforator flap.

^aDiabetes mellitus, peripheral vascular disease, hypertension, hemodialysis.

^bTendon defect and fracture or bone defect.

^cTwo-sided Fisher's exact test or Student's *t*-test.

Our team's previous studies showed that the peroneal perforator flap, without sacrificing the sural nerve and small saphenous vein, can still have reliable blood flow in the flap, reduce the damage of the donor area, improve the appearance of the flap pedicle, and is one of the ideal methods for repairing foot and ankle wounds. However, attention should be paid to removing all the tough fascial fiber bundles around the perforating

vessels, leaving only a little loose connective tissue [23]. In 1986, Amarante et al. reported for the first time a distally based fasciocutaneous flap based on the perforating branch of the posterior tibial artery, which was also widely used in the reconstruction of soft tissue defects in the foot [24]. These two pedicled flaps can be used to solve most defects in the distal lower extremities, ankles, and feet [25–28].

TABLE 2 | Intraoperative and postoperative results of the flap.

Variable	FPF group (N = 68)	PPF group (N = 56)	p value ^b
Soft tissue repair			—
ALTP	43	—	
CSAP	25	—	
PTAP	—	24	
PAP	—	32	
Flap size (cm ²)	43.2 ± 11.7	56.3 ± 15.5	< 0.001
Operative blood loss (mL)	146.0 ± 38.3	81.1 ± 25.4	< 0.001
Operation time (min)	149.3 ± 26.0	130.7 ± 25.6	< 0.001
Flap harvested time (min)	45.4 ± 7.7	47.2 ± 7.6	0.20
Vascular anastomosis time (min)	29.4 ± 4.6	—	—
Recipient complications	62/6	40/16	0.005
Total flap necrosis	4	2	
Partial flap necrosis	2	9	
Wound dehiscence	0	5	
Causes of complications			—
Venous congestion	6	2	
Distal ischemic necrosis	0	9	
Infection or hematoma	2	2	
High tension	0	5	
Donor site			< 0.001
Closure	68	38	
Skin graft ^a	0	18	
Additional treatment until wound healing			—
Suture the wound	0	5	
Dressing change	2	5	
Secondary flap	4	8	

Abbreviations: ALTP, anterolateral thigh perforator flap; CSAP, circumflex scapular artery perforator flap; PPF, free perforator flap; PAP, peroneal artery perforator flap; PPF, pedicled perforator flap; PTAP, posterior tibial artery perforator flap.

^aSplit or full-thickness skin graft.

^bTwo-sided Fisher's exact test or Student's *t*-test.

Bekara et al. conducted a systematic review of the repair of lower limb soft tissue defects with free and pedicled flaps and showed that the failure rate and total complication rate of pedicled flaps were comparable to that of free flaps [29]. Although partial necrosis of pedicled flaps was significantly higher than that of free flaps, the success of actual coverage appeared to be similar [30]. Koh et al. multicenter study compared the results and showed that the overall success rate of FPFs was 90.1%, and the overall success rate of pedicled flaps was 92.3%. There was no significant difference between the two groups. They also believed that peripheral vascular disease was the only significant comorbidity risk factor for failure of free and pedicled flaps [31]. Unlike soft tissue defects resulting from tumor resection, soft tissue defects caused by lower limb trauma often involve injury to the surrounding tissue. Therefore, flaps based on tissue around the defect are considered to have a higher risk of necrosis than free flaps obtained from healthy tissue [32]. In lower limb soft tissue repair, compared to free flaps, pedicled flaps are considered to have a higher risk of partial flap necrosis, but the overall

complication rate is similar [33]. Bekara et al. compared the partial necrosis rates of free and pedicled flaps for repairing lower limb soft tissue defects, and the results showed that the complication rate of the pedicled flap group was 6.88%, while the complication rate of the free flap group was 2.70%, with a significant difference [29]. The results of this study show that the overall incidence of complications in the PPF group is significantly higher than that in the FPF group under the same defect area. Among them, nine cases of PPF had distal necrosis of the flap, mainly due to the twisting and deformation of the blood vessels after flap rotation and compression of the pedicle, leading to a distal ischemic condition in the flap tissue. Therefore, there are certain requirements for PPF surgery, such as designing the flap without exceeding the maximum supply range of the perforator vessel, keeping the pedicle and subcutaneous tunnel as loose as possible, and carrying a certain number of perforator vessels.

In the reconstruction of soft tissue defects caused by trauma, most cases of pedicled flaps can be treated with conservative

TABLE 3 | Evaluation of esthetic and functional outcomes at 12 months follow-up.

Variable	FPF group (N = 68)	PPF group (N = 56)	p value ^c
Cosmetic evaluation			
Subjectively ^a	61/7	36/20	0.001
Excellent	34	12	
Good	27	24	
Moderate	6	13	
Poor	1	7	
Objectively ^b	60/8	36/20	0.002
Excellent	33	11	
Good	27	25	
Moderate	7	12	
Poor	1	8	
Functional results	47/21	48/8	0.03
Excellent	28	27	
Good	19	21	
Fair	14	5	
Poor	7	3	

Abbreviations: FPF, free perforator flap; PPF, pedicled perforator flap.

^aGuardians of the patients.

^bBlinded third-party observer.

^cTwo-sided Fisher's exact test or Student's *t*-test.

measures or minor procedures such as skin grafts, but partial necrosis may result in exposure of implants/fractures, requiring secondary flap reconstruction in some cases [29, 34]. In this study, six cases of partial necrosis and two cases of complete necrosis required a second FPF repair in the PPF group, while four cases of complete necrosis required a second FPF repair in the FPF group. Guiller et al. reported that in 10 cases (48%) of patients who underwent flap repair for lower limb soft tissue defects caused by trauma, partial necrosis, or wound dehiscence occurred, with three patients requiring a secondary FPF repair [35]. The study by Ota et al. showed that in seven cases (29%) of patients with partial necrosis of flaps due to implant exposure or fracture sites, FPF reconstruction was required. Post-traumatic osteomyelitis at the distal lower extremity is considered a serious complication that requires complex long-term treatment [19]. In this study, no cases of osteomyelitis complications occurred because all patients were subjected to thorough debridement, and chimeric flap grafts (muscle or bone flap) were used for reconstruction in patients with deep dead space to help control infection. Therefore, it is important to choose a reasonable method of repairing the wound.

In this study, 18 patients in the PPF group needed skin grafting to repair the donor site due to excessive tension. Related studies also show that due to the limited skin tissue in the lower leg area, only small localized soft tissue defects can be repaired, and most patients require skin grafting to repair the donor site. After wound healing, there will be obvious scars, poor appearance

recovery, and impact on physical and psychological health, affecting their daily life and increasing their economic burden [36, 37]. The results of lower limb esthetic assessment in this study show that the excellent and good rates in the PPF group are significantly lower than those in the FPF group, consistent with the above results. Distal limb soft tissue defects often affect ankle function, and the functional recovery effect of the PPF group in this study was significantly better than that of the FPF group. The main reason for this is that the FPF group in this study included patients with more severe wound injuries, often with deep dead spaces, which affected ankle function. PPF (PAP or PTAP) has many advantages in the repair of foot wounds. For example, these flaps are repaired by adjacent tissues, similar in color to the skin around foot wounds, and have good appearance recovery. Most of the perforating vessels are relatively constant, and the incision is relatively convenient, without anastomosis of blood vessels, and the survival rate of the flap is high [11, 12].

Therefore, this study believes that with the improvement and popularization of microsurgical techniques, compared with PPF, FPF has the following advantages: (1) The donor area of the ALTP or CSAP flap is larger, which can meet the repair needs of irregular, large-area and deep dead cavities; (2) the perforator vessels are stable, and the flap is easy to harvest; and (3) the donor area can be directly sutured, and some skin nerves can be carried, restoring the protective sensation of the patient's foot [13, 38–40]. FPF technique is a learning curve process. For the primary medical institutions with relatively backward microsurgical technology, it should strive to choose relatively safe PPF technology for repair.

Limitations of this study include: (1) As a retrospective analysis, information bias may occur in the data of included patients, which may affect the reliability of the results; (2) there are types of flaps suitable for foot and ankle repair, and no multi-group comparison has been made. The next research can include a variety of flaps for a large sample of completely randomized controlled studies to explore which flap results are better.

5 | Conclusions

This study suggests that for patients with small distal limb defects (less than 60 cm²), FPF has the advantages of smaller donor site morbidity, lower complications of flaps, and better appearance compared to PPF. However, due to the more severe wound condition in the FPF group, the ankle joint function of FPF is inferior to that of PPF. In patients with light wound severity and small defect areas, PPF should be the first choice in areas with relatively low microsurgical techniques. If the wound severity is severe (deep dead space) and the defect area is large, FPF can be the first choice.

Author Contributions

Zhe-Ming Cao: conceptualization, data curation, formal analysis, investigation, methodology, project administration, writing—original draft, writing—review and editing. **Yan Yang:** conceptualization, data curation, formal analysis, investigation, methodology, project

administration, writing—original draft, writing—review and editing. **Li-Ming Qing:** funding acquisition, project administration, supervision, writing—review and editing. **Pan-Feng Wu:** funding acquisition, investigation, methodology, supervision, writing—review and editing. **Ju-Yu Tang:** funding acquisition, investigation, methodology, supervision, writing—review and editing. All authors have read and approved the final version of the manuscript.

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Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The original contributions presented in the study are included in the article/Supporting Information; further inquiries can be directed to the corresponding author. Pan-Feng Wu and Ju-Yu Tang had full access to all of the data in this study and take complete responsibility for the integrity of the data and the accuracy of the data analysis.

Transparency Statement

The lead author, Pan-Feng Wu, Ju-Yu Tang, affirms that this manuscript is an honest, accurate, and transparent account of the study being reported, that no important aspects of the study have been omitted, and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section.