


REVIEW ARTICLE



The use of ipsilateral skin grafts or local flaps for the closure of a free radial forearm flap donor site: a systematic review

Keisuke Shimbo^a , Yukako Okuhara^a and Kazunori Yokota^b

^aDepartment of Plastic and Reconstructive Surgery, Hiroshima Prefectural Hospital, Hiroshima, Japan; ^bDepartment of Plastic and Reconstructive Surgery, Hiroshima University Hospital, Hiroshima, Japan

ABSTRACT

Skin grafts from distant sites are typically used to close free radial forearm flap (FRFF) donor sites. However, a variety of closure methods have been reported that avoid a second donor site. These are divided into four groups: separately combined full-thickness skin graft (FTSG), FTSG method based on V-Y closure, perforator flap, and non-perforator flap. We aimed to assess the differences in outcomes, including adapted FRFF size and postoperative complications, among the four groups of closure methods used for FRFF defects. Applying the Preferred Reporting Items for the PRISMA protocol systematic reviews and meta-analysis, the PubMed and MEDLINE medical databases were searched from inception to September 2020 to identify articles about closure using an ipsilateral FTSG or local flap of the FRFF donor site. Study characteristics, FRFF size, complication rates were extracted for analysis. Twenty-four studies were included for analysis. The FTSG method based on V-Y closure was the most widely used and could be adapted to the largest and more variable FRFF sizes. The short-term complications rate was lowest for the FTSG method based on V-Y closure and the highest for the perforator flap method. The FTSG method based on V-Y closure was considered to be the most convenient and reliable. However, FRFF size should be restricted to $\leq 60\text{cm}^2$, and the non-perforator flap can be a good choice if FRFF is $< 35\text{cm}^2$.

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Introduction

The free radial forearm flap (FRFF) is a well-known procedure that is widely used to reconstruct tissue defects, particularly in head and neck regions. Direct closure of the donor site is frequently not possible because the resulting flap defect is too large or skin laxity is insufficient around the distal forearm side. Therefore, skin grafts are often required for donor site defects. Several methods for repairing such defects have been reported [1], such as split-thickness skin graft (STSG) [2–4] and full-thickness skin graft (FTSG) [4–7]. However, methods that harvest skin from distant areas obviously require a new sacrifice from the second donor site. Moreover, color mismatch may remain an aesthetic problem regardless of the skin graft type harvested from distant sites. Thus, ipsilateral FTSG methods [8–20] and local flap methods [21–31] to avoid a second donor site have been reported and may be the most effective methods for not only minimally invasive procedures but also for improved aesthetic appearance. Elliot [21] first reported a V-Y perforator flap that was based on the ulnar artery perforator for the closure of an FRFF donor site, and Liang [14] subsequently reported the FTSG method based on V-Y closure. Although the FTSG method based on V-Y closure has been the most commonly used, non-perforator flap methods, such as Z-plasty [25], double-opposing rhomboid transposition flaps [26], hatchet flaps [27–29], double-opposing rotation flaps [30], and bilobed flaps [31], were described in sequence thereafter. More recently, there have been reports of several types of separately combined FTSG methods, where the FTSGs were

outlined from the proximal portion of the FRFF to the proximal forearm along the vascular pedicle, separately harvested, and subsequently transferred to the FRFF defect by combining the two [8–13]. As stated above, the ipsilateral FTSG methods are classified as a separately combined FTSG method [8–13] and an FTSG method based on V-Y closure [14–20] from a difference in the method of FTSG harvesting. The local flap methods are classified as a perforator flap method [21–24] and a non-perforator flap method [25–31] due to differences in the flap. These four groups of methods have advantages and disadvantages, and a randomized comparison is yet to be performed. Specifically, there is uncertainty about how large of an FRFF defect can be adapted to these closure methods, and which methods are safer and have the fewest complications. The applicable sizes and postoperative complications among the four groups of methods have not yet been reflected as true clinical benefits. It can be hypothesized that ipsilateral FTSG methods would be applicable to larger FRFF defects and have fewer complications than local flap methods because FTSG has a high degree of freedom for FRFF defect size and is the simplest way to close the donor site. However, it can be difficult to obtain substantial information on these closure methods because the outcomes of each closure method have only been previously analyzed as separate studies for each method, and a systematic review of this topic is not yet performed. Therefore, the aim of our study is to assess the differences in outcomes including adapted FRFF size and postoperative complications among the four group of methods used for FRFF defects.

Materials and methods

This systematic review was performed in accordance with the Preferred Reporting Items for the PRISMA protocol systematic reviews and meta-analysis and structured around existing recommended guidelines [32].

Search methods

A systematic electronic search of the literature was performed by using PubMed and MEDLINE to identify relevant articles that were published from inception through September 2020. The following search terms were used: 'radial forearm flap donor site' or 'free flap donor site' with 'local' or 'ipsilateral' or 'closure'. The retrieved articles were also manually searched for any additional articles identified through references not identified in the primary search. This search was performed by two separate authors independently (K.S. and Y.O.).

Inclusion and exclusion criteria

Articles were included in this systematic review if they complied with the following criteria, except for the article type of exclusion criteria: (1) articles reported on closure of an FRFF donor site using the ipsilateral FTSG or local flap and (2) articles described the FRFF defect size and/or complications of the donor site. Conversely, the following articles were excluded: (1) non-English articles, duplicate titles, cadaveric studies, abstracts and conference presentations, review articles, commentaries, editorials, and opinions; (2) articles reported the closure method of forearm defect that had no part in the FRFF; (3) articles described using an ipsilateral meshed FTSG, ipsilateral STSG and tissue expansion because these three methods were expected to adapt to a larger FRFF defect and show difficulty in evaluating complications.

Data collection and quality assessment

The following variables were extracted by two independent authors (K.S. and Y.O.) from the included studies: publication year, number of patients, type of closure methods (e.g. separately

combined FTSG, FTSG method based on V-Y closure, perforator flap, and non-perforator flap), FRFF size, complications (e.g. partial necrosis and dehiscence) and follow-up in months. Two independent authors (K.S. and Y.O.) evaluated the study design and the level of evidence of each article using the Oxford Center for Evidence-Based Medicine. To assess the methodological quality, the Newcastle-Ottawa Scale (NOS) was used for the retrospective cohort studies and National Institute of Health (NIH) Quality Assessment Tool for Case Series Studies was used for the case series studies. Disagreements were resolved by a third independent author (K.Y.).

Statistical analysis

A meta-analysis of patients whose FRFF defect was repaired with ipsilateral forearm site was conducted separately for the following four groups: separately combined FTSG method, V-Y flap method, local perforator flap method, and local non-perforator flap method. FRFF size within each group was calculated by translating the representation of multiplication to a multiplicative value for convenience. The pooled complication rates and confidence intervals were calculated based on the random-effects model. Heterogeneity was evaluated using the Cochran Q and I^2 tests. I^2 values <25% were considered low heterogeneity and p -values <0.05 were considered statistically significant. The analyses were performed using the metafor package for R version 3.6.2.

Results

Study selection and characteristics

A total of 1340 articles were identified in our search using the selected terms and inclusion criteria. After duplicate removal, 37 titles were identified, and a further manual search of other sources and references of relevant articles revealed two more articles. Thirty-nine abstracts were reviewed, and 11 articles were excluded. The full texts of the 28 articles were reviewed, and 4 articles were excluded. Finally, 24 articles encompassing 850 cases were identified for analysis in our study (Figure 1). The included

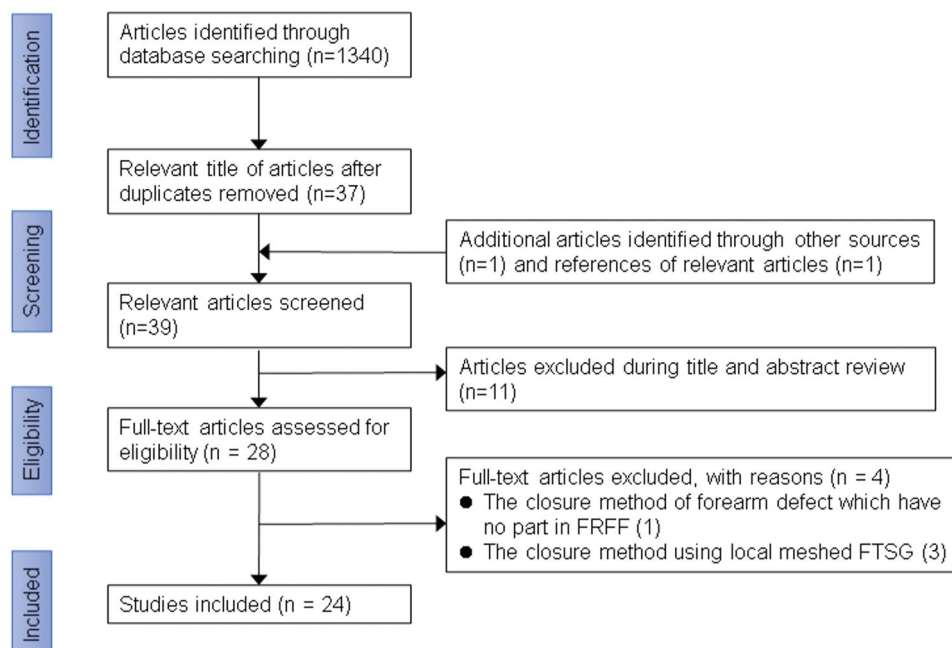


Figure 1. Systematic review article selection process shown by a PRISMA flow diagram.

Table 1. Summary of included studies and study design characteristics.

Study	Study design	Number of patients	Classification of closure characteristics (no.)	Follow-up in months, mean (range)	Level of evidence	Quality assessment score*
Gonzalez-Garcia et al., 2009 [8]	Case series	4	Separately combined FTSG (4)	3	4	5/9
Riecke et al., 2015 [9]	Case series	30	Separately combined FTSG (30)	3	4	5/9
Kim et al., 2016 [10]	Case report	10	Separately combined FTSG (10)	6	5	–
Moreno-Sanchez et al., 2016 [11]	Case series	100	Separately combined FTSG (100)	36 (6–78)	4	7/9
Shimbo et al., 2019 [12]	Case series	5	Separately combined FTSG (5)	NR	4	4/9
Krane et al., 2020 [13]	Case series	68	Separately combined FTSG (68)	6.6	4	8/9
Liang et al., 1994 [14]	Case series	15	V–Y closure of FTSG (15)	NR	4	4/9
van der Lei et al., 1999 [15]	Case series	7	V–Y closure of FTSG (7)	NR	4	4/9
Shiba et al., 2003 [16]	Case series	15	V–Y closure of FTSG (15)	NR	4	4/9
Shuidam et al., 2005 [17]	Retrospective cohort	34	V–Y closure of FTSG (19)	26.1 (11.3–35.9)	3	7/9
Squadrelli-Saraceno et al., 2010 [18]	Case series	132	V–Y closure of FTSG (132)	18 (4–72)	4	5/9
Krishnan et al., 2017 [19]	Case series	209	V–Y closure of FTSG (209)	NR	4	4/9
Pirlich et al., 2018 [20]	Retrospective cohort	39	V–Y closure of FTSG (21)	NR	3	5/9
Elliot et al., 1988 [21]	Case series	55	Perforator flap (55)	NR	4	3/9
Hsieh et al., 2004 [22]	Case series	10	Perforator flap (10)	NR	4	4/9
Shoaib et al., 2009 [23]	Case series	5	Perforator flap (5)	NR	4	4/9
Potet P et al., 2020 [24]	Retrospective cohort	101	Perforator flap (36)	12	3	7/9
Hui et al., 1999 [25]	Case report	2	Non-perforator flap (2)	NR	5	–
Akyurek et al., 2002 [26]	Case report	1	Non-perforator flap (1)	12	5	–
Bashir et al., 2010 [27]	Case series	9	Non-perforator flap (9)	NR	4	4/9
Jaquet et al., 2012 [28]	Retrospective cohort	44	Non-perforator flap (22)	27 (7–82)	3	7/9
Lane et al., 2013 [29]	Case series	45	Non-perforator flap (45)	43.7 (6–100)**	4	7/9
Hamahata et al., 2016 [30]	Retrospective cohort	17	Non-perforator flap (11)/ perforator flap (6)	1 week	3	6/9
Mashrah et al., 2019 [31]	Case series	13	Non-perforator flap (13)	7	4	7/9

FTSG, full-thickness skin graft; NR, not recorded.

*The Newcastle–Ottawa Scale (NOS) was used for the retrospective cohort studies and National Institute of Health (NIH) Quality Assessment Tool for Case Series Studies was used for the case series. **Follow-up of 33 patients.

studies comprised of 5 retrospective cohort studies (Level 3), 16 case series (Level 4), and 3 case reports (Level 5). Of the 5 retrospective cohort studies, 3 were considered to be of higher methodological quality (NOS score ≥ 7 points) and 2 were considered to be of moderate quality (NOS score 4–6 points). Of the 16 case series studies, 4 were considered to be of good quality (NIH score ≥ 7 points), 11 were of moderate quality (NIH score 4–6 points), and one was of poor quality (NIH score ≤ 3 points) (Table 1). GRADE assessments were low for selected studies in this systematic review because of the study design. The ipsilateral FTSG method was used in a large portion (75%) of all cases, with the most common method being the FTSG method based on V–Y closure (49%). Conversely, the local flap method was rarely used (25%) (Figure 2). The non-perforator flap method included five different methods, and a hatchet flap was used in a relatively high proportion of those (74%) (Table 2).

FRFF size

The mean FRFF sizes were $39.5 \pm 20.1 \text{ cm}^2$ for the separately combined FTSG method, $41.8 \pm 16.6 \text{ cm}^2$ for the FTSG method based on V–Y closure, $31.4 \pm 10.0 \text{ cm}^2$ for the perforator flap method, and $31.1 \pm 6.9 \text{ cm}^2$ for the non-perforator flap method (Table 3). The mean FRFF size was similar in both ipsilateral FTSG methods and the same held for both local flap methods. The ipsilateral FTSG method was used for larger FRFF and had a greater variety of sizes than the local flap method. The non-perforator flap methods had the least variation in size.

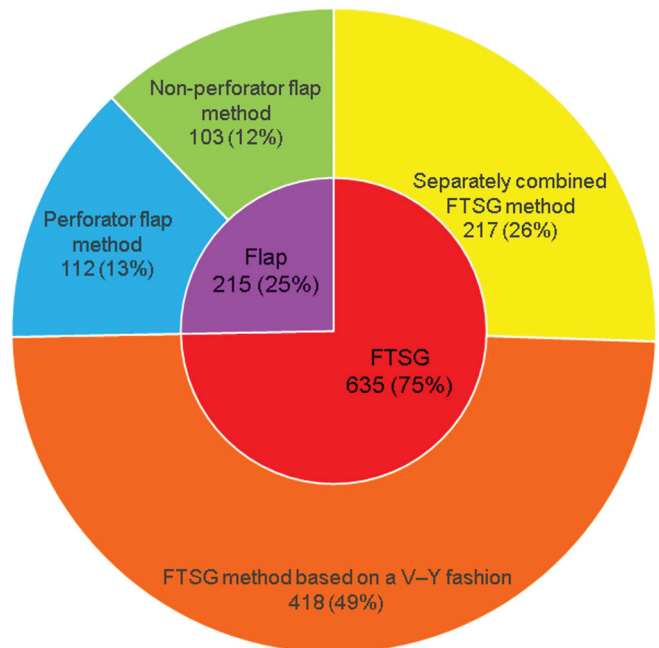


Figure 2. Information about the classified local closure method (used in 24 studies and 850 cases).

Complications

The follow-up times varied or were not recorded, and long-term complications, such as hypertrophic scars, were not evaluated in most of the studies; hence, we extracted only short-term

Table 2. Summary of the included studies characteristics.

Study	Classification of closure characteristics (no.)	Detailed characteristics	FRFF size (cm ²)		Short-term complications	
			Mean	Range	Partial necrosis (%)	Other (%)
Gonzalez-Garcia et al., 2009 [8]	Separately combined FTSG (4)	Two or four triangular FTSGs	20	15–30	0	NR
Riecke et al., 2015 [9]	Separately combined FTSG (30)	Two spindle-shaped FTSGs	25	NR	0	Seroma (3.3)
Kim et al., 2016 [10]	Separately combined FTSG (10)	Two curved FTSGs	NR	NR	0	NR
Moreno-Sanchez et al., 2016 [11]	Separately combined FTSG (100)	Two or four triangular FTSGs	24.5	15–70	7.0	Tendon exposure (2.0), Hematoma (15.0), Dehiscence (5.0)
Shimbo et al., 2019 [12]	Separately combined FTSG (5)	Two semi-elliptical FTSGs	5.1 × 7.3	NR	20.0	NR
Krane et al., 2020 [13]	Separately combined FTSG (68)	Two crescent-shaped FTSGs	69.2	12–144	33.8	Tendon exposure (8.8), Infection (14.7), Hematoma/seroma (1.5),
Liang et al., 1994 [14]	V–Y closure of FTSG (15)	–	9 × 6	5 × 7–11 × 7	0	NR
van der Lei et al., 1999 [15]	V–Y closure of FTSG (7)	–	NR	4 × 6–5 × 9	0	NR
Shiba et al., 2003 [16]	V–Y closure of FTSG (15)	–	NR	3 × 8–5 × 13	26.7	Dehiscence (6.7)
Zuidam et al., 2005 [17]	V–Y closure of FTSG (19)	–	26.2	20–40	0	NR
Squadrelli-Saraceno et al., 2010 [18]	V–Y closure of FTSG (132)	–	NR	NR	11.4	Tendon exposure (1.5)
Krishnan et al., 2017 [19]	V–Y closure of FTSG (209)	–	NR	NR	1.0	NR
Pirlich et al., 2018 [20]	V–Y closure of FTSG (21)	–	55.73*	NR	23.8	NR
Elliot et al., 1988 [21]	Perforator flap (55)	V–Y flap	NR	Up to 8 × 4	NR	NR
Hsieh et al., 2004 [22]	Perforator flap (10)	Bilobed flap	5.8 × 8.1	5 × 6–8 × 8	10.0	NR
Shoaib et al., 2009 [23]	Perforator flap (5)	V–Y flap	6.4 × 4.4	6 × 4–7 × 5	0	NR
Potet P et al., 2020 [24]	Perforator flap (36)	Keystone flap	28.7	NR	0	Dehiscence (16.7), Tendon exposure (2.8), Hematoma (2.8), Infection (8.3), Epidermolysis (11.1)
Hui et al., 1999 [25]	Non-perforator flap (2)	Z-plasty	4 × 5.8	4 × 5.5–4 × 6	0	NR
Akyurek et al., 2002 [26]	Non-perforator flap (1)	Double-opposing rhomboid transposition flaps	6 × 4	6 × 4	0	NR
Bashir et al., 2010 [27]	Non-perforator flap (9)	Hatchet flap	NR	NR	0	Dehiscence (11.1)
Jaquet et al., 2012 [28]	Non-perforator flap (22)	Hatchet flap	19.8	NR	9.0	NR
Lane et al., 2013 [29]	Non-perforator flap (45)	Hatchet flap	37.7	19.3–60.5	4.4	Epidermolysis (24.4), Dehiscence (11.1)
Hamahata et al., 2016 [30]	Non-perforator flap (11)	Double-opposing rotation flaps	7.1 × 4	5.5 × 3.5–8 × 4.5	27.3	NR
Mashrah et al., 2019 [31]	perforator flap (6)	V–Y flap	6.1 × 4.0	5.5 × 4–7 × 4	100	NR
	Non-perforator flap (13)	Bilobed flap	31.6	4 × 6–5 × 8	7.7	NR

FTSG: full-thickness skin graft; FRFF: free radial forearm flap; NR: not recorded. *Mean of 8 cases.

complications data. The total complications rate was highest for the perforator flap method (31.6%), but lowest for the FTSG method based on V–Y closure method (6.9%). The partial necrosis rate of the separately combined FTSG method (14.3%) and the perforator flap method (12.3%) was higher than those of the other closure methods. Three group methods of these values except for the perforator flap demonstrated low heterogeneity with Cochran's Q test and had I^2 values < 25%. The dehiscence rate of the local flap method was higher than those of the ipsilateral FTSG methods (Table 4).

Discussion

Among all the cases, the ipsilateral FTSG method comprises the largest portion (75%); we reasoned that this is because it is fool-proof and easier than the local flap methods. Among the methods of the four classified groups, the FTSG method based on V–Y closure is the most commonly used (49%), probably because V–Y closure by FTSG is the simplest way to close the donor site for reconstruction because of its comprehensible design. The local flap methods are the least commonly used method (25%). The

Table 3. FRFF size stratified by closure method.

Method	Number of available articles	Number of available patients	Mean \pm SD (cm ²)
Separately combined FTSG method	5	207	39.5 \pm 20.1
FTSG method based on V–Y fashion	3	42	41.8 \pm 16.6
Perforator flap method	4	57	31.4 \pm 10.0
Non-perforator flap method	6	94	31.1 \pm 6.9

FRFF: free radial forearm flap; FTSG: full-thickness skin graft.

Table 4. Complications stratified by closure method.

Method	Number of available articles	Number of available patients	Total short-term complications (%)	Partial necrosis		Heterogeneity		Other (%)
				Number	Rate (95% CI)	<i>p</i>	<i>I</i> ²	
Separately combined FTSG method	6	217	22.1	31	14.3% (1.2–28.2)	0.54	0.0	Dehiscence (2.3), Tendon exposure (3.7), Hematoma/Seroma (7.8)
FTSG method based on V–Y fashion	7	418	6.9	26	6.2% (–3.7 to 15.9)	0.90	0.0	Dehiscence (0.2), Tendon exposure (0.5)
Perforator flap method	4	57	31.6	7	12.3% (*)	*	*	Dehiscence (10.5), Tendon exposure (1.8), Hematoma (1.8), Infection (5.3), Epidermolysis (7.0)
Non-perforator flap method	7	103	24.3	8	7.7% (–13.4 to 28.2)	0.98	0.0	Dehiscence (5.8), Epidermolysis (10.7)

FTSG: full-thickness skin graft; NR, not recorded. *Unmeasurable.

reason for the use of an unfamiliar method is thought to be because of the need for a particularly challenging procedure and limited size in contrast to the use of the ipsilateral FTSG method. In the non-perforator flap methods, the hatchet flap has been commonly used (74%). The hatchet flap is thought to be widely used in the non-perforator flap methods because the hatchet flap design is simple and prevents obstruction of FRFF pedicle elevation.

FRFF size

Our review found that both ipsilateral FTSG methods were adopted for similar FRFF size; particularly, used for larger FRFF and had the greater variety of sizes than the local flap method. Krane [13] reported the use of a maximum flap size of 144 cm², and Zuidam [17] reported a minimum flap size of 20 cm². Our results indicated that the ipsilateral FTSG method is easy to use because it allows a high degree of freedom for FRFF defect size. In the non-perforator flap methods, it may be easy to design a plan tailored to the FRFF size because that method shows the least variation in size (31.1 \pm 6.9 cm²). This means that an FRFF size that is >25 to 35 cm² should be suitable for non-perforator flap methods. Our analysis revealed that any local closure method can be adapted for an FRFF <25 cm². If the FRFF is 25–35 cm², the ipsilateral FTSG method, bilobed perforator flap [22], keystone flap [24], hatchet flap [27–29], double-opposing rotation flaps [30], and bilobed flap [31] are recommended. Furthermore, the ipsilateral FTSG method, bilobed perforator flap [22], and hatchet flap [27–29] have the potential to adapt to an FRFF >35 cm², but our analysis suggested that these methods should be safe for defects \leq 60 cm². Contrarily, if the FRFF is too large (>60 cm²), a FTSG from a distant site, ipsilateral meshed FTSG, ipsilateral STSG and tissue expansion are recommended. However, in this regard, it should be taken into consideration that each method adapting a larger FRFF has the following drawback: the FTSG from a distant site makes a new sacrifice in the second donor site. In terms of aesthetics, the ipsilateral meshed FTSG has no advantage over the

other methods. Ipsilateral STSG is a simple procedure because STSG area is approximately correlated with that of the FRFF; however, it may be controversial to transfer the de-epithelialized FRFF to the reconstructive site [3]. Although the tissue expansion method may have a better cosmetic outcome, it has the drawback of an additional procedure being required before raising the FRFF [33].

Complications

Our review demonstrated that perforator flap method had a higher risk of short-term complications than the other methods (31.6%). Particularly, the partial necrosis rate (12.3%) was higher for the perforator flap method and was as high as 100%, as reported by Hamahata [30]. This result suggests that the perforator flap method is more challenging than the other closure methods and should be used with caution. The dehiscence rate of the local flap method was higher than that of the ipsilateral FTSG method. Potet [24] reported a highest dehiscence rate of 16.7%, which was explained by the excessive tension in the direction of the circumference due to the feature of keystone flap. Lane [29] reported a dehiscence rate of 11.1% and used a hatchet flap for a relatively large FRFF defect (mean, 37.7 cm²; range, 19.3–60.5 cm²). Excessive tension might be produced as the FRFF size increases. Therefore, we think that the local flap methods should be used for up to a medium FRFF size of \leq 35 cm². Although the partial necrosis rate was different between ipsilateral FTSG methods, it is unclear why the partial necrosis rate of the separately combined FTSG method (14.3%) was higher than that of the FTSG method based on V–Y closure (6.2%). The separately combined FTSG method has a higher total complications rate (22.1%) than that of the FTSG method based on V–Y closure method (6.9%). The reason for the higher total complications rate for the separately combined FTSG method is thought to be caused by direct closure for the FTSG donor site, which might result in other complications such as dehiscence, hematoma, and seroma. The rate of delayed wound healing in the FRFF donor

site that was reconstructed by STSG or FTSG harvested from a distant site has been shown to be 6% [34] and is rarely different in the FTSG method based on V-Y closure method. The FTSG method based on V-Y closure method can be most recommended in terms of the complications.

Strengths and limitations

This is the first systematic review to investigate local closure methods for FRFF. Although this review maintained an adequate number of cases ($n=850$) for an objective analysis, there were several limitations to this review. First, quality of studies included in this analysis was variable, with the majority being case series and case reports (79%). Additionally, there were a variety of closure methods that could impact FRFF size as well as complications among the included studies. Thus, we categorized the selected studies into four groups; however, there was some degree of inconsistency across the closure methods in each group (for example, the non-perforator flap group included five different methods). Thus, these factors could impact the validity of our conclusions. Second, there was inconsistency in reporting the FRFF size data among included studies (written by width \times length or by area), which complicated data interpretation. The FRFF size within each group was calculated by translating the representation of multiplication to a multiplicative value. However this might not only cloud the applicable FRFF size (width \times length) but also impact our conclusions. There was also inconsistency in the reporting of complications data among the included studies, which limited our ability to conduct a meta-analysis. Most of the studies focused on the surgical technique used; thus, data extraction was not possible from some studies. Specifically, other factors, such as the term of wrist fixation and the range of hand movements, could have affected the complication rates, but were rarely commented on in all studies. Additionally, the follow-up times varied or were not recorded, and long-term complications, such as hypertrophic scars, were not evaluated in the majority of studies, so we extracted only short-term complications data. Regarding the aesthetic results, most patients expressed satisfaction with the cosmetic appearance in all studies. However, it was difficult to demonstrate which local closure method was best unless the methods were performed on the same patient (obviously not possible). Nevertheless, this review provided significant information about the characteristics of each local closure method.

Conclusions

The results of this review show that the FTSG method based on V-Y closure is a convenient and suitable choice, as shown by it being the most widely used method; that it could be adapted to the largest flap sizes; that it could accommodate the wider range of FRFF sizes; and that it had the lowest short-term complications. In this regard, however FRFF size should be $\leq 60\text{ cm}^2$ depending on an individual's figure and skin laxity, and the FTSG requires that the length of the FRFF not exceed one-third of the length from the distal end of the FRFF to the elbow crease (e.g. under $7 \times 9\text{ cm}$). Although the ipsilateral FTSG method is generally simple and reliable, the local flap method may be superior in terms of long-term donor site morbidity, including aesthetic results. Non-perforator flaps, especially hatchet flaps and bilobed flaps, are thought to be a good choice if the FRFF is $< 35\text{ cm}^2$ (e.g. up to $7 \times 5\text{ cm}$) (Figure 3). The local closure method choice depends on the preference of the surgeon; however, it is important to use

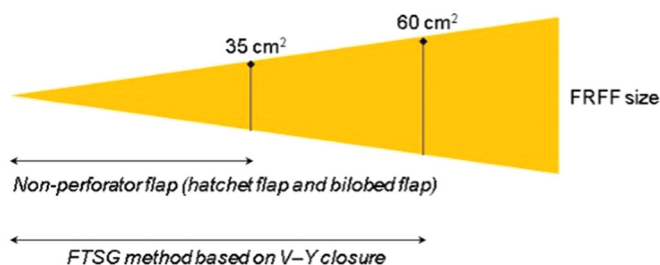


Figure 3. Recommended local closure method of FRFF donor site.

the local closure method with knowledge of each characteristic in any case. It should be taken into consideration that these conclusions are based on low-quality evidence for the aforementioned reasons. Further investigations are necessary to provide standardized outcomes and draw more reliable conclusions.

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Disclosure statement

No potential conflict of interest was reported by the author(s).

ORCID

Keisuke Shimbo  <http://orcid.org/0000-0003-0761-4147>

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