Vascularized Bone Reconstruction for Recalcitrant Clavicular Nonunion

A Systematic Review of the Literature

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Purpose: Clavicular nonunion is an uncommon complication with a significant impact on quality of life and can be difficult to manage. In recalcitrant cases, or situations unfavorable for take of nonvascularized grafts, vascularized osseous reconstruction may be utilized. Several donor sites for such flaps have been described, with each associated with unique benefits and drawbacks.

Methods: A systematic review utilizing MEDLINE and Embase databases was performed for cases of vascularized bone reconstruction for clavicle nonunion.

Results: Twenty-six papers met inclusion, comprising 67 patients. Mean age was 43.1 years, across 32 male and 35 female patients. Mean period of nonunion was 43.2 months in the fibular group, 42.0 months in the medial femoral condyle (MFC), and 12 months in the rib flap group. Patients had undergone a mean of 2.67 prior operations at the time of vascularized osseous flap; a proportion of patients had undergone prior locoregional radiotherapy (9/26) or been complicated by infection (12/22). Radiological union was achieved in 95.2% (20/21) of fibular flaps, 95.6% (25/27) of MFC flaps, and 66.7% (2/3) of rib flaps. Mean time to union was 10.6 months for the fibular group, 7.8 months for the MFCs, and 4.-0 months for the rib flaps. Complications occurred in 55.6% (20/36) of patients having fibular flaps, 26.1% (6/23) of MFC flaps, and 50% (2/4) of rib flaps.

Conclusions: All osseous flaps yielded similar and consistent rates of union when used to reconstruct defects of the clavicle. Higher complication rates, particularly donor site morbidity, were noted with fibula and rib flaps when compared to the MFC.

Key Words: clavicle, vascularized bone, flap, nonunion

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Clavicular nonunion is an uncommon complication that can be challenging to manage.[1] Symptoms include pain, limited range of motion, reduced strength and function, as well as compression of the brachial plexus or underlying vessels, and can be disabling.[2] Clavicular nonunion has been found to have a greater detrimental effect on quality of life than nonunions of the femur, tibia, and humerus.[3]

A recent Cochrane review did not reveal superiority for any surgical approach for clavicular nonunion,[4] and there is currently no consensus on the optimal characteristics of autologous bone used for reconstruction.[2] As microsurgical techniques have advanced, osseous free flaps have been increasingly utilized to bridge bony defects.[5] Osseous flaps confer osteoconductive, osteoinductive, and osteogenic properties providing the scaffolding, growth factors, and osteocytes necessary for union, and are of particular utility in settings not suited to nonvascularized bone grafting, such as recalcitrant nonunions or defects where graft take may be compromised by prior infection, scarring, or radiation injury.[6,7] Various sources of osseous flaps have been described in the literature, with donor sites including the fibula,[8–19] medial femoral condyle,[20–30] rib,[31–34] and acromion.[35]

Thus, the objective of this study was to assess and compare outcomes and complications of various osseous flaps for the reconstruction of recalcitrant clavicular nonunion by systematically reviewing the literatures.

METHODS

Search Strategy

A literature search was performed in May 2023 in accordance with the preferred reporting items for systematic reviews and meta-analysis guidelines, using MEDLINE (1946–present) and EMBASE (1974–present) databases. The terms "clavicle" or "clavicular" and "flap" or "vascularized bone" or "vascularized graft" were used as keywords, MeSH terms, or via wildcard enquiries.

Eligibility Criteria

Studies were eligible for inclusion if they were published in the English language and reported outcomes following the use of vascularized osseous flaps for clavicular nonunion in either individuals or cohorts. Articles were excluded if the indication for an osseous flap was not nonunion. After exclusion of duplicates, abstracts were screened for relevance before progressing to full-text appraisal by 2 independent assessors (J.C. and G.K.). Articles were reviewed by both authors to determine relevance and inclusion, and any disagreements were resolved via consensus. The reference lists of all included papers were manually screened to identify further potentially relevant studies.

Data Extraction

Data was extracted from the texts, tables and figures of included papers. Parameters of interest included patient and fracture characteristics, approach to reconstruction and outcomes including union rates, complications, and follow-up period. Given the heterogeneous reporting of outcomes, data was often reported for the subset of studies conveying the relevant information.

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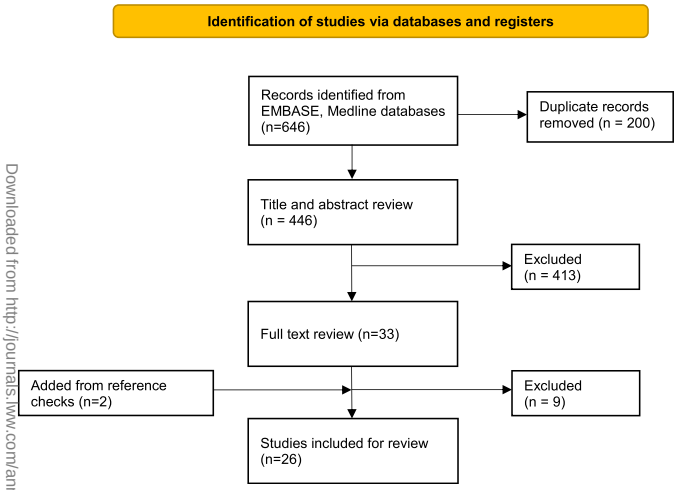

FIGURE 1. The preferred reporting items for systematic reviews and meta-analysis flow diagram or new systematic reviews, which included searches of databases and registers only.

Statistical Analysis

Categorical variables were presented as frequency and percentage. Continuous variables were presented as means with standard deviations.[36]

RESULTS

Study Selection

The electronic literature search yielded 646—after removal of duplicates, 446 remained for screening of titles and abstracts. Thirty-three underwent full-text review, with 2 further articles found during screening of reference lists. Twenty-six papers met the inclusion criteria (refer Fig. 1).

Patient Characteristics

The 26 included studies yielded a total cohort of 67 patients (32 males and 35 females) with a mean age of 43.1 years (Table 1). The mean age for patients undergoing fibular flaps was 44.2 ± 14.7 years (n = 36); medial femoral condyle flaps was 41.2 years (n = 27); and rib flaps was 45.5 years ±10.3 (n = 4).

Smoking status was reported in 2 studies assessing fibular flaps, with all 3 patients (100%) being smokers, and 3 studies reporting on medial femoral condyle flaps, with 5 of 16 (31.3%) being smokers. Diabetic status was reported in 2 case reports involving free fibular flaps, with both patients (100%) being diabetic, and 2 series assessing MFCs with all 11 cases (100%) being diabetic. Body mass index was reported as greater than 30 for all patients receiving fibular flaps (1 study; 3 patients) and 42.9% of patients where a MFC was utilized (1 study; 3 of 7 patients).

Pain was the most common preoperative symptom reported, noted in 39 of 47 patients (82.98%), followed by decreased range of motion (16 of 47 patients; 34.0%) and functional limitation (12 of 47 patients; 25.5%).

TABLE 1. Patient Characteristics

	Fibula		MFC		Rib	
Parameters	n and/or %	Patients (Studies) Reported	n and/or %	Patients (Studies) Reported	n and/or %	Patients (Studies) Reported
Age	44.22 ± 14.67	36 (11)	41.2	27 (11)	45.50 ± 10.28	4 (4)
Gender		36 (11)		27 (11)		4 (4)
Male	19 (52.78%)		10 (37.04%)		3 (75%)	
Female	17 (47.22%)		17 (62.96%)		1 (25%)	
Smoker		3 (2)		16 (3)		0 (0)
Yes	3 (100%)		5 (31.25%)		-	
No	0 (0%)		11 (68.75%)		-	
Diabetes		2 (2)		11 (2)		0 (0)
Yes	2 (100%)		0 (0%)		-	
No	0 (0%)		11 (100%)		-	
Hypertension		2 (1)		0 (0)		0 (0)
Yes	2 (100%)		-		-	
No	0 (0%)		-		-	
BMI		3 (1)		7 (1)		0 (0)
BMI >30	3 (100%)		3 (42.86%)		-	
BMI <30	0 (0%)		4 (57.14%)		-	
Symptoms		27 (10)		16 (5)		4 (4)
Pain	19 (70.37%)		16 (100%)		4 (100%)	
Functional limitation	4 (14.81%)		5 (31.25%)		3 (75%)	
Deformity	2 (7.41%)		-		-	
Impaired motor function	13 (48.41%)		-		3 (75%)	
Impaired sensation	9 (33.33%)		-		3 (75%)	
Decreased range of motion	4 (14.81%)		9 (56.25%)		3 (75%)	
Swelling/ congestion	-		-		2 (50%)	

BMI, body mass index.

Nonunion Characteristics

88.1% of patients were reported to have a nonunion following trauma (21 studies; 37 of 42 patients) (Table 2). 12.5% of initial injuries were noted to be open fractures, and the remainder closed (7 studies, 16 patients). Only 2 studies reported on initial fracture comminution, with 33.3% of patients (2 of 6) demonstrating a multifragmentary injury. 77.3% of initial injuries were noted to be displaced (7 studies, 17 of 22 patients).

Nonunion type was reported in nine studies with a cohort of 32 patients—the most frequently encountered type of nonunion was atrophic (9 patients; 28.1%). Nine patients (28.1%) had gone on to develop a pseudarthrosis as a consequence of the nonunion.

Previous radiation therapy to the site was reported in 34.6% of patients (10 studies; 9 of 26 patients). 54.6% of nonunions were documented to have been previously infected (12 studies, 12 of 22 patients).

The mean period of nonunion was 41.5 months across all groups, with a mean of 43.2 ± 28.1 in patients receiving fibular flaps (n = 14),

TABLE 2. Nonunion Characteristics

	Fibula		MFC		Rib	
Parameters	**n and/or %**	**Patients (Studies) Reported**	**n and/or %**	**Patients (Studies) Reported**	**n and/or %**	**Patients (Studies) Reported**
Traumatic		21 (10)		17 (7)		4 (4)
Yes	19 (90.48%)		15 (88.24%)		3 (75%)	
No	2 (9.52%)		2 (11.76%)		1 (25%)	
Open/closed		7 (3)		8 (3)		1 (1)
Open	0 (0%)		1 (12.50%)		1 (100%)	
Closed	7 (100%)		7 (87.50%)		-	
Comminuted		0 (0)		6 (2)		0 (0)
Yes	-		2 (33.33%)		-	
No	-		4 (66.67%)		-	
Displaced		15 (4)		6 (2)		1 (1)
Yes	14 (93.33%)		2 (33.33%)		1 (100%)	
No	1 (6.67%)		4 (66.67%)		-	
Nonunion		28 (11)		27 (11)		4 (4)
Yes	24 (85.71%)		27 (100%)		4 (100%)	
No	4 (14.29%)		0 (0%)		0 (0%)	
Type		12 (4)		9 (4)		1 (1)
Pseudoarthrosis	9 (75%)				-	
Atrophic	1 (8.33%)		7 (77.78%)		1 (100%)	
Malunion	1 (8.33%)		0 (0%)		-	
Bone loss	1 (8.33%)		0 (0%)		-	
Fibrous	0 (0%)		1 (11.11%)		-	
Hypertrophic	0 (0%)		1 (11.11%)		-	
Period of nonunion (months)	43.21 ± 28.07	14 (7)	42	24 (8)	12	1 (1)
Radiation		14 (5)		10 (3)		2 (2)
Yes	4 (28.57%)		4 (40%)		1 (50%)	
No	10 (71.43%)		6 (60%)		1 (50%)	
Infection		6 (6)		15 (5)		1 (1)
Yes	4 (66.67%)		7 (46.67%)		1 (100%)	
No	2 (33.33%)		8 (53.33%)		-	
No. previous operations	3.04 ± 1.89	23 (9)	2.45	20 (8)	1.33 ± 1.53	3 (3)
Previous operations		23 (10)		23 (9)		3 (3)
Yes	23 (100%)		20 (86.96%)		2 (66.67%)	
No	0 (0%)		3 (13.14%)		1 (33.33%)	
Total operations	70		49		4	
Previous operations (type)		23 (10)		23 (9)		4 (3)
ORIF	13 (56.52%)		5 (10.20%)		1 (25.00%)	
ORIF + bone graft	17 (73.91%)		13 (26.53%)		2 (50.00%)	
Removal of hardware	10 (43.48%)		2 (4.08%)		1 (25.00%)	
Debridement	4 (17.39%)		2 (4.08%)		0 (0%)	
Percutaneous fixation	1 (4.35%)		1 (2.04%)		0 (0%)	
Not stated	4 (17.39%)		26 (53.06%)		1 (25.00%)	
Defect size	6.11 ± 1.25	24 (9)	2.94 ± 2.01	10 (6)	7	1 (1)

42.0 months in those where an MFC was utilized (n = 24), and 24.0 months in cases where a rib flap was inset (n = 2). Two series reporting on rib flaps did not comment on period of nonunion. Patients had undergone a mean of 2.67 prior operation across all groups (n = 46), with 38.0% having received previous open reduction internal fixation (ORIF) alone, and 64.0% having failed a previous ORIF with additional bone grafting.

Where reported, the average defect size reconstructed with fibular flaps was 6.1 ± 1.3 cm (n = 24), 2.9 ± 2.0 cm in those receiving an MFC (n = 10), and 7 cm where a rib flap was utilized (n = 1).

Management

88.2% of MFCS were raised on the descending geniculate artery (n = 15) and the remainder on the superomedial genicular artery (n = 2; 6 studies) (Table 3). All 4 rib flaps were raised on the thoracodorsal pedicle.

The recipient artery used was reported in 18 studies (53 patients)—the most common recipient was the thoracoacromial artery (31 patients; 58.5%), followed by the transverse cervical artery (19 patients; 35.8%). The recipient vein was noted in 15 studies (37 patients)—the thoracoacromial vein was most commonly used (15 patients; 40.5%), followed by the external jugular vein (13 patients; 35.1%).

Two of 6 patients (33.33%; 4 studies) received augmentation with nonvascularized bony autograft in addition to the fibular flap, compared to 8 of 8 (100%; 4 studies) patients in the MFC cohort. Eight of 12 patients receiving a fibular flap (66.67%; 4 studies) underwent additional synthetic bone grafting—synthetic graft was also utilized in a single patient receiving an MFC.

Outcomes

Radiological union was achieved in 47 of 51 total flaps (92.2%; 23 studies)—20 of 21 (95.2%) of fibular flaps; 25 of 27 (95.6%) MFC flaps, and 2 of 3 (66.7%) rib flaps (Table 4). Clinical union with resolution of symptoms was also reported in another patient receiving a rib flap—however, this was not assessed radiologically. Mean time to union was 10.6 ± 7.5 (n = 20), 7.8 (n = 25), and 4.0 ± 1.7 (n = 3) months for the above flaps, respectively.

The majority of patients reported improvement in pain, including 14 of 19 (73.7%) patients receiving fibular flaps and all patients where MFC (n = 7) and rib (n = 4) flaps were utilized. Similarly, most patients reported improvement in power, including 11 of 14 (78.6%) fibular flaps and all MFC (n = 7) and rib (n = 1) flaps. Postoperatively, all MFC flaps had no restriction in range of motion, compared to 7 of 11 (63.64%) fibular flaps and 2 of 4 (50%) rib flaps.

The complication rate was 44.4% (28 of 62; 22 studies) across all flaps. Twenty of 36 (55.6%) patients receiving fibular flaps, 6 of 23 (26.1%) MFC flaps, and 2 of 4 (50.0%) rib flaps sustained a complication, with the most common being hardware failure requiring removal or revision (20.0%; 8 of 40); however, radiological union was still

TABLE 3. Management

	Fibula		MFC		Rib	
Parameters	n and/or %	Patients (Studies) Reported	n and/or %	Patients (Studies) Reported	n and/or %	Patients (Studies) Reported
Recipient artery		35 (11)		18 (7)		0 (0)
Thyrocervical	5 (28.57%)		0 (0%)		-	
Transverse cervical	16 (45.71%)		3 (16.67%)		-	
Thoracoacromial	16 (45.71%)		15 (83.33%)		-	
Axillary	1 (2.86%)		0 (0%)		-	
Superior thyroid	4 (11.43%)		0 (0%)		-	
Recipient vein		19 (9)		18 (6)		0 (0)
External jugular	10 (52.63%)		3 (16.67%)		-	
Transverse cervical	3 (15.79%)		1 (5.56%)		-	
Internal jugular	1 (5.26%)		0 (0%)		-	
Axillary	1 (5.26%)		0 (0%)		-	
Thyrocervical	1 (5.26%)		0 (0%)		-	
Cephalic	2 (10.53%)		3 (16.67%)		-	
Thoracoacromial	5 (26.32%)		10 (55.56%)		-	
Subclavian	0 (0%)		1 (5.56%)		-	
Type of fixation		32 (11)		20 (8)		4 (4)
Screws alone	2 (6.25%)		0 (0%)		0 (0%)	
Compression plate	28 (87.50%)		18 (90.00%)		2 (50%)	
Intramedullary pin + tension band	1 (3.13%)		0 (0%)		0 (0%)	
Ligament reconstruction	1 (3.13%)		0 (0%)		0 (0%)	
Hook plate	0 (0%)		1 (5.00%)		0 (0%)	
External fixator + lag screws	0 (0%)		0 (0%)		1 (25%)	
K wire alone	0 (0%)		1 (5.00%)		1 (25%)	
Plus autogenous bone graft		6 (4)		8 (4)		1 (1)
Yes	2 (33.33%)		8 (100%)		-	
No	4 (66.67%)		0 (0%)		1 (100%)	
Plus synthetic bone graft		12 (4)		1 (1)		1 (1)
Yes	8 (66.67%)		1 (100%)		-	
No	4 (33.33%)		0 (0%)		1 (100%)	

achieved at final follow-up in all of these cases. Flap hematomas were reported in 7.5% of cases (3 of 40; 14 studies), all of which occurred in the fibular group.

Final follow occurred at a mean of 22.4 months (range 6–54).

DISCUSSION

In cases of failed operative fixation resulting in recalcitrant nonunion, there is likely benefit in the use of free bony flaps for reconstruction. The transfer of bone graft with an independent vascular supply augments the normal processes that take place during fracture healing, with expedited delivery of osteoinductive proteins (such as BMP-2, BMP-7, FGF, IGF, and pDGF), mesenchymal stem cells, osteoprogenitor, and osteogenic cells.[37] Bony flaps may provide robust structural support at an earlier stage, particularly when corticoperiosteal bone is utilized,[38] and can withstand mechanical loading sooner with lower rates of stress fracture due to their enhanced ability to remodel.[39] The literature has described successful reconstruction of clavicular nonunion using flaps harvested from the medial femoral condyle, fibula, and rib.

This study assessed 27 studies detailing the use of vascularized osseous flaps for reconstruction of clavicular nonunion. We identified that a significant proportion of the patients had undergone prior locoregional radiotherapy (9/26) or previous operations (mean 2.66 per patient), or had been complicated by previous infection (12/22, where reported). All of these factors are likely to increase risk of further nonunion.

It is especially notable that of 47 patients who had undergone previous operations, 34 had received nonvascularized bone graft during prior fixation. This highlights the importance of vascularized modalities being part of the treating surgeon's armamentarium and renders the high rates of union observed in this review impressive.

Our study demonstrates that fibular and rib flaps tended to be utilized to bridge larger osseous defects (mean defect size of 6.11 ± 1.25 cm and 7 cm, respectively), compared to medial femoral condyle and acromial flaps, which were used when smaller lengths of bone were required (mean defect diameter of 2.94 ± 2.01 and 2.5 cm, respectively). Union rates were comparable between fibular and medial femoral condyle flaps (95.24% and 95.59% respectively), while 2 of 3 rib flaps and the single acromial flap also went on to unite.

Although there is no consensus on the indications for vascularized bone grafting at this time, it has traditionally been recommended for defects greater than 6 cm in length, without any supporting

TABLE 4. Outcomes, Complications, Follow-up

	Fibula		MFC		Rib	
Parameters	n and/or %	Patients (Studies) Reported	n and/or %	Patients (Studies) Reported	n and/or %	Patients (Studies) Reported
Limited range of motion		11 (7)		9 (6)		4 (4)
Yes	4 (36.36%)		0 (0%)		2 (50%)	
No	7 (63.64%)		9 (100%)		2 (50%)	
Limited power		14 (5)		7 (4)		1 (1)
Yes	3 (21.43%)		0 (0%)		0 (0%)	
No	11 (78.57%)		7 (100%)		1 (100%)	
Pain		19 (8)		7 (5)		4 (4)
Yes	5 (26.32%)		0 (0%)		0 (0%)	
No	14 (73.68%)		7 (100%)		4 (100%)	
Union		21 (9)		27 (11)		3 (3)
Yes	20 (95.24%)		25 (95.59%)		2 (66.67%)	
No	1 (4.76%)		2 (7.41%)		1 (33.33%)	
Time to union (months)	10.61 ± 7.47	20 (8)	7.78	25 (11)	4.00 ± 1.73	3 (3)
Complications		36 (10)		23 (8)		4 (4)
Yes	20 (55.56%)		6 (26.09%)		2 (50%)	
No	16 (44.44%)		17 (73.91%)		2 (50%)	
Complications (type)		16 (5)		22 (7)		2 (2)
Hardware failure requiring removal	3		2		2	
Hardware removal for aesthetic reasons	1					
Neuroma			1			
Restless leg syndrome			1			
Femoral #			1			
Donor hematoma			1			
Stress fracture between flap and clavicle	1					
Ulnar nerve dysesthesia	1					
Hematoma from flap requiring evacuation	3					
Prolonged pain at donor site	4					
Wound dehiscence (flap site)	1					
Soft tissue conflict with plate	1					
Infection with partial donor site skin graft loss	1					
Venous kinking	1					
Follow-up	23.50 ± 10.44	18 (9)	20.75	20 (8)	26.33 ± 12.66	3 (3)

evidence.[38] Our study suggests that the choice of osseous flap should be based on both donor and recipient considerations, rather than purely on defect size.

Fibular flaps can be harvested to a maximum length of 15 cm[40] and should be considered when reconstructing larger defects. It is a popular choice in maxillofacial surgery[41] and has also been described in the reconstruction of humeral,[42] forearm,[43] and wrist[44] defects. However, these flaps may be associated with significant donor site morbidity, with Attia reporting complications at a rate of 53%,[45] including delayed healing, paraesthesia, ongoing pain, and hallux deformities.

Vascularized rib can provide bone up to a maximum length of 8 cm.[46] However, they are rarely performed due to concerns regarding donor site morbidity, with potentially devastating complications ranging from pneumothorax, chronic pain and scapular winging.

Medial femoral condyle flaps are generally restricted to smaller osseous defects, providing a maximum bone length of 6 cm and ample cancellous bone that can be integrated into the fixation.[47] The main advantages of MFC utilization lies in its ease of dissection and minimal donor site morbidity, with the most common complication being saphenous nerve paraesthesia[48] (although iatrogenic femoral fracture has been reported).[27] For the most part, patella alignment and knee stability is preserved, with no osteochondral pathology present on postoperative imaging.[49]

There were a number of limitations with our study. There was significant heterogeneity in fixation method, surgical experience, and patient factors. For example, there were wide variations in patient and nonunion characteristics that would likely affect the primary outcome of bone union. In addition, recalcitrant clavicular nonunion is uncommon, with limited literature describing its reconstruction technique. There were only 3 reported cases of rib flaps, making it difficult to draw reliable conclusions based on this data. The majority of studies included were case series and case reports and thus prone to publication bias. A prospective randomized controlled trial comparing different vascularized bone flaps for clavicular nonunion, or a comparison of complications and union rates following reconstruction for other indications would be useful but likely not be feasible.

Although osseous flaps are less commonly performed than nonvascularized grafting, vascularized bone should be considered not only for large defects, but also in situations where nonvascularized grafting is less likely to be successful. These include cases with hostile environments for healing, such as those complicated by radiotherapy, prior infection and scarring from multiple previous operations.

CONCLUSIONS

Our study suggests that different osseous flaps provide comparable and reliable rates of union when used to reconstruct clavicular defects. Although union rates were similar, fibular and rib flaps were associated with higher complication rates when compared to the MFC flap. The MFC free flap may be the most optimal donor site for reconstruction of defects less than 6 cm.

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