



Free Flap Reconstruction of the Anterior Skull Base: A Systematic Review

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Abstract

Objectives Given the limitations in the available literature, the precise indications, techniques, and outcomes of anterior skull base free flap reconstruction remain uncertain. The objective of this study was to perform a systematic review of published literature and evaluate indications, methods, and complications for anterior skull base free flap reconstruction.

Methods A systematic review of the literature was performed using a set of search criteria to identify patients who underwent free flap reconstruction of the anterior skull base. Articles were reviewed for inclusion based on relevance, with the primary outcome being surgical complications.

Results After a comprehensive search, 406 articles were obtained and 16 articles were ultimately found to be relevant to this review—79 patients undergoing free flap reconstruction were identified. Overall complication rates were 17.7% (95% confidence interval [CI]: 16.6–33.1%) for major complications and 19.0% (95% CI: 17.8–35.5%) for minor complications.

Conclusion Microvascular reconstruction of the anterior skull base is feasible with high reliability reported in the literature.

Keywords

- ▶ systematic review
- ▶ anterior
- ▶ skull base
- ▶ free flap
- ▶ reconstruction

Introduction

Reconstruction of the anterior skull represents a challenging clinical entity in which the main goal is to provide reliable separation between the sinonasal cavities or orbit from the central nervous system. In addition, it needs to be able to support the brain and provide lining for the nasal cavity. Reconstructive options typically include grafts or local flaps, such as the pericranial flap, nasoseptal flap (NSF), or temporoparietal flap.¹ In rare situations, vascularized tissue larger than these pedicled options is needed, such as in cases

with large defects following cancer resection, significant trauma or recurrent cerebrospinal fluid (CSF) leaks, complicated infections such as in osteomyelitis, compromise of local tissue such as in osteoradionecrosis, or exhaustion of local tissue options from prior reconstruction.¹

Microvascular free flap reconstruction represents a possible option in these complicated situations. Free tissue transfer has the benefit of providing ample vascularized tissue with desired tissue type and quality. Literature on free flap reconstruction of the anterior skull base is limited to retrospective institutional case series and case reports. The

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objective of this study was to perform a systematic review of published literature and evaluate indications and methods for anterior skull base free flap reconstruction, as well as complications and reconstructive outcomes.

Materials and Methods

Search Strategy

The published literature was searched using strategies created by a medical librarian (M.D.) for surgical flaps for reconstruction of the anterior skull base. The search strategies were established using a combination of standardized terms and keywords and were implemented in Ovid Medline 1946-, Embase 1947-, Scopus 1960-, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, and Clinicaltrials.gov. All searches were completed in November 2018. Duplicates were identified and excluded. Each unique citation was then screened by abstract and title. Relevant articles then underwent full-text review. Additional articles were identified through references.

Inclusion and Exclusion Criteria

Candidate articles were independently reviewed by two authors and inclusion and exclusion criteria were uniformly applied for article selection. Articles were considered eligible if they included patients who underwent free flap reconstruction of the anterior skull base. To keep the review contemporary, only articles published in 2009 or later were included. The primary outcome was surgical complications, characterized as minor or major. Major complications included those that required a return to the operating room or that threatened the integrity of the reconstruction. Minor complications included those that were managed conservatively. Other variables included age, sex, etiology of defect, indication for reconstruction, extent of defect, pre- or postoperative radiotherapy (XRT), variety of free flap, and vessels used for anastomosis. Studies were excluded if they could not be adequately interpreted to extract relevant data regarding the included patients, reconstruction, or surgical complications.

Quality and Risk of Bias

The methodological index for nonrandomized studies (MINORS) criteria were used to assess study quality and risk of bias.²

Statistical Analysis

Meta-analysis was unable to be performed due to small sample size and heterogeneity of reported data. A pooled estimate was instead calculated for the rates of minor and major complications, respectively.

Results

Study Selection

Results were exported to endnote for a total of 406 results. Of these, 200 duplicates were assumed to be accurately identified and removed for a total of 206 unique citations. After screening by abstract and title, 146 articles were excluded,

with 60 articles remaining. After review of the full text, 33 of these articles were excluded, with 27 articles remaining. Of these, 11 articles published prior to 2009 were excluded, with 16 meeting criteria following systematic review (►Fig. 1). The articles are summarized in ►Table 1.

Patient Demographics

Among the included studies, 79 patients were identified as having undergone free flap reconstruction of the anterior skull base. The minimum reported patient age was 11 years old and the maximum was 73. There were 21 reported males (61.8 valid % [valid percentage being defined as the value when missing data are excluded]) and 13 reported females (38.2 valid %). Twenty-one patients underwent preoperative XRT (26.6%). There were 17 reported cases of postoperative XRT (►Table 2).

Flaps and Indications

Patients who underwent free flap reconstruction had a preoperative diagnosis of neoplasm (52 patients, 65.8%), trauma (19, 24.1%), or osteomyelitis, osteoradionecrosis, osteitis, or infection (8, 10.1%). Neoplasm histology included squamous cell carcinoma, melanoma, adenocarcinoma, meningioma, esthesioneuroblastoma, salivary gland malignancies, sarcoma, and chordoma. Forty-eight patients (60.8%) had an isolated anterior skull base defect, and 28 patients (35.4%) had an anterior skull base defect with orbital exenteration. Fifty-eight patients (73.4%) underwent reconstruction due to the size of the defect and 19 (24.1%) did so due to prior local or regional flap failure. Thirty-four patients (42.5%) underwent reconstruction with a radial forearm free flap, and 18 underwent reconstruction with latissimus dorsi (22.5%) (►Table 3).

Complications

Major complications included 12 cases (15.2%) requiring a return to the operating room. Of these, seven cases (8.9%) were due to CSF leak, two cases (2.5%) were due to major wound infections, two cases (2.5%) for exposed mesh (with 1 such case requiring a 2nd free flap), one case (1.3%) for hematoma, one case (1.3%) for free flap failure, and one (1.3%) for partial flap loss. Furthermore, there were two cases (2.5%) of exposed mesh from the reconstruction that did not require a return to the operating room. Minor complications included eight cases (10.1%) of donor site morbidity, three (3.8%) CSF leaks managed conservatively, two (2.5%) minor wound infections treated with antibiotics, one (1.3%) recipient site wound dehiscence, and one case (1.3%) of meningitis.

Overall complication rates are thus 17.7% (95% confidence interval [CI]: 16.6–33.1%) for major complications and 19.0% (95% CI: 17.8–35.5%) for minor complications (►Table 4).

Outcomes

Seven studies out of 16 (43.8%) report follow-up, ranging from 2 to 156 months with a median of 16.5 months. However, only four of these studies (25.0%) comment on disease-free or disease-specific survival, and only six (37.5%) studies describe overall survival. These data were reported too heterogeneously for meaningful analysis.

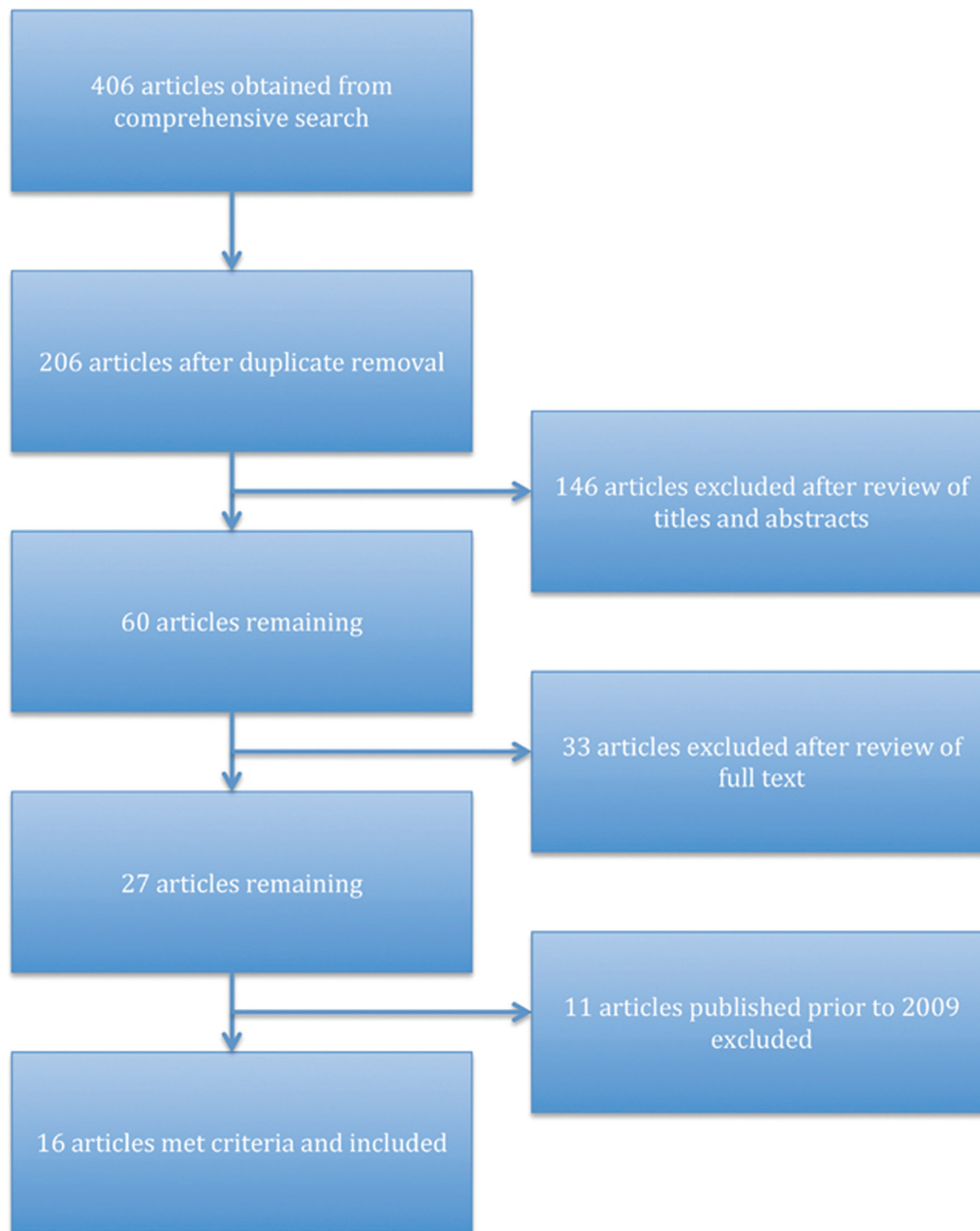


Fig. 1 Flow diagram for selection of studies.

Quality and Heterogeneity

Study quality as assessed by the MINORS criteria is shown in ►Table 5. The median score was 8 out of a possible 16 points. The minimum score was 4 and the maximum score was 12. Included studies included case reports, case series, and retrospective chart reviews.

Discussion

This systematic review summarizes the existing literature on microvascular free flap reconstruction of the anterior skull base.

Surgical Complications

The most common major complication was development of a CSF leak requiring return to the operating room, of which

seven cases (8.9%) were reported, followed by exposed mesh during reconstruction. However, all reported cases of exposed mesh were reported in a single study.³ There was only one reported instance of free flap failure and one partial flap loss out of 80 free flaps, implying a 97.5% flap success rate. These data imply that free flap reconstruction is a safe option for anterior skull base defects.

Most Common Indications and Surgical Techniques

Most patients underwent reconstruction due to a defect from resection of a neoplasm. The most commonly reported indication for free flap reconstruction was the sheer size of the defect. Although this term was inconsistently and not uniformly used, we identified a few common themes that were included in this indication. (1) Combination with

Table 1 Summary of included articles

Study	Study design	Number of patients	Flaps described	Pathology	Indication for free flap	Extent of defect
Kang et al 2018 ⁶	Retrospective chart review	4	ALT	Neoplasm	Prior locoregional flap failure	SB
Vargo et al 2018 ⁷	Retrospective chart review	10	Radial forearm (n = 7), fibula (n = 1), latissimus dorsi (n = 1), temporoparietal fascia with bone graft (n = 1)	Neoplasm (n = 5), trauma (n = 3), osteomyelitis (n = 2)	Size of defect (n = 2), prior locoregional flap failure (n = 8)	SB
Costantino et al 2017 ⁸	Retrospective chart review	7	Omentum	Neoplasm (n = 5), osteoradionecrosis (n = 2)	Size of defect	SB (n = 5), SB with OE (n = 2)
Betz et al 2016 ⁹	Case report	1	Radial forearm	Osteomyelitis	Size of defect	SB
Yano et al. 2016 ¹⁰	Case series	2	ALT	Neoplasm	Size of defect	SB with frontal and nasal bone involvement
Duchateau et al. 2014 ¹¹	Case report	1	Radial forearm	Neoplasm	Prior treatment depriving patient of other options	SB
Thakker and Fernandes 2014 ³	Retrospective chart review	12 ^a	Radial forearm (n = 6), thoracodorsal artery perforator (n = 4), ALT (n = 3)	Neoplasm (n = 11), Osteoradionecrosis (n = 1)	Size of defect	SB (n = 4), SB with OE (n = 8)
Yeo et al 2014 ¹²	Case report	1	Radial forearm	Neoplasm	Prior XRT	SB
Manjila et al 2013 ¹³	Case report	1	ALT	Neoplasm	Size of defect	SB
Biron et al 2012 ¹⁴	Case series	3	Radial forearm	Trauma (n = 2), osteoradionecrosis (n = 1)	Size of defect	SB
Girod et al 2012 ¹⁵	Retrospective chart review	17	Latissimus dorsi	Neoplasm (n = 16), osteitis (n = 1)	Size of defect	SB with OE
Inman and Ducic 2012 ¹⁶	Retrospective chart review	11	Radial forearm (n = 8), Rectus (n = 3)	Trauma	Size of defect	SB
Sinha et al 2012 ⁵	Case series	5	Radial forearm	Neoplasm (n = 4), trauma (n = 1)	Prior locoregional flap failure	SB
Biglioli et al 2011 ¹⁷	Retrospective chart review	2	Radial forearm	Neoplasm	Prior locoregional flap failure	SB
Guthikonda et al 2009 ¹⁸	Case report	1	ALT	Neoplasm	Size of defect	SB with OE
Zhang et al 2009 ¹⁹	Retrospective chart review	1	DIEP	Neoplasm	Size of defect	SB, craniofacial involvement with skin

Abbreviations: ALT, anterolateral thigh; DIEP, deep inferior epigastric perforator; OE, orbital exenteration; SB, anterior skull base; XRT, external beam radiation therapy.
^aExposed mesh following reconstruction for first patient necessitated 2nd free flap.

Table 2 Patient demographics

Total patients	79	
Age (y)	Minimum	11
	Maximum	73
Gender	Male	21 (61.8 valid %)
	Female	13 (38.2 valid %)
XRT	Preoperative	21
	Postoperative	17

Abbreviation: XRT, external beam radiation therapy.

orbital exenteration. The sheer volume of the orbital contents removed, in addition to the skull base defect, precludes repair with local options. A pericranial flap in this setting likely could serve as a dural repair and separation between

nasal contents and the cranium, but the volume is frequently insufficient. Likewise, the temporalis muscle flap is a good option for orbital reconstruction, but the lack of arc of rotation and length makes it unable to reach the anterior cranial fossa. In addition, the removal of orbital contents allows free transferred tissue to have a relatively short pedicle, allowing for safe delivery of pedicle vessels to both the facial notch and the superior temporal vessels. (2) Anterior defects involving the anterior frontal table or the nasal bone, effectively precluding the use of either a NSF or pericranial flap. (3) Resection of dura with few local or regional options to cover the area. (4) Local tissue compromise from previous infection and/or radiation. (5) Compromise of local reconstructive options due to prior trauma. Altogether, we plead future researchers to more uniformly define or categorize indications for free tissue transfer to the anterior skull base.

Table 3 Flaps and indications

Preoperative diagnosis	Neoplasm	52 (65.8%)
	Trauma	19 (24.1%)
	Osteomyelitis, osteoradionecrosis, osteitis, or infection	8 (10.1%)
Defect	Isolated anterior skull base	48 (60.8%)
	With orbital exenteration	28 (35.4%)
	With involvement of frontal and nasal bones	2 (2.5%)
	With craniofacial and skin involvement	1 (1.3%)
Indication	Size of defect	58 (73.4%)
	Prior locoregional flap failure	19 (24.1%)
	Prior treatment depriving patient of other options	1 (1.3%)
	Prior XRT	1 (1.3%)
Flap used	Forearm	34 (42.5%)
	Latissimus dorsi	18 (22.5%)
	ALT	11 (13.8%)
	Omentum	7 (8.8%)
	Thoracodorsal artery perforator	4 (5.0%)
	Rectus	3 (3.8%)
	Fibula	1 (1.3%)
	DIEP	1 (1.3%)
	Temporoparietal fascia with bone graft	1 (1.3%)
Recipient arteries	Superficial temporal	19 (37.3 valid %)
	Unspecified branches of external carotid	17 (33.3 valid %)
	Lingual or facial	14 (27.5 valid %)
	Unspecified cervical vasculature	1 (2.0 valid %)
Recipient veins	Lingual or facial	16 (33.3 valid %)
	Internal jugular	13 (27.1 valid %)
	Superficial temporal	11 (22.9 valid %)
	Retromandibular	7 (14.6 valid %)
	Unspecified cervical vasculature	1 (2.1 valid %)
Vein grafts	2	

Abbreviations: ALT, anterolateral thigh; DIEP, deep inferior epigastric perforator; XRT, external beam radiation therapy.

Table 4 Reported complications

Major complications	17.7% (95% CI: 16.6–33.1%)		
	Exposed mesh from reconstruction without return to OR		2 (2.5%)
	Return to OR	12 (15.2%)	
		CSF leak	7 (8.9%)
		Major wound infection	2 (2.5%)
		For exposed mesh	2 (2.5%)
		Requiring 2 nd free flap	1 (1.3%)
		Partial flap loss	1 (1.3%)
		Free flap failure	1 (1.3%)
	Hematoma	1 (1.3%)	
Minor complications	19.0% (95% CI: 17.8–35.5%)		
		Donor site morbidity	8 (10.1%)
		CSF leak managed conservatively	3 (3.8%)
		Minor wound infection treated with antibiotics	2 (2.5%)
		Recipient site wound dehiscence	1 (1.3%)
		Meningitis	1 (1.3%)

Abbreviations: CI, confidence interval; CSF, cerebrospinal fluid; OR, operating room.

Table 5 Quality and risk of bias of included articles using MINORS criteria

Study	Clearly stated aim	Inclusion of consecutive patients	Prospective data collection	Appropriate end points	Unbiased assessment of end point	Follow-up appropriate length	Loss to follow-up less than 5%	Prospective calculation of study size	Total score
Kang et al 2018 ⁶	2	2	0	2	2	1	1	0	10
Vargo et al 2018 ⁷	2	2	0	2	2	0	0	0	8
Costantino et al 2017 ⁸	1	2	0	1	2	1	0	0	7
Betz et al 2016 ⁹	2	0	0	2	2	0	0	0	6
Yano et al 2016 ¹⁰	2	2	0	2	2	2	2	0	12
Duchateau et al 2014 ¹¹	1	0	0	1	2	1	2	0	7
Thakker and Fernandes 2014 ³	2	1	0	1	2	1	0	0	7
Yeo et al 2014 ¹²	2	0	0	1	2	2	2	0	9
Manjila et al 2013 ¹³	2	0	0	2	0	2	2	0	8
Biron et al 2012 ¹⁴	1	1	0	1	2	1	1	0	7
Girod et al 2012 ¹⁵	2	1	0	2	2	2	2	0	11
Inman and Ducic 2012 ¹⁶	1	1	0	1	1	1	0	0	5
Sinha et al 2012 ⁵	2	1	0	2	1	2	2	0	10
Biglioli et al 2011 ¹⁷	1	1	0	1	2	2	2	0	9
Guthikonda et al 2009 ¹⁸	2	0	0	1	1	0	0	0	4
Zhang et al 2009 ¹⁹	2	2	0	2	2	0	0	0	8

Abbreviation: MINORS, methodological index for nonrandomized studies.

Flap Choice

Flap choice for the microvascular surgeon involves multiple factors, including defect size, nature of the tissue to be reconstructed, availability of recipient vessels, patient body habitus, patient level of activity and acceptance of donor site morbidity, and ultimately the surgeon's prefer-

ence and familiarity with various flaps. In papers from the early 2000s, rectus flaps were the predominant flap used.⁴ Within our contemporary systematic review, rectus flaps were relatively rare, with forearms being the predominant flap, followed by latissimus and anterolateral thigh (ALT). The majority of flaps was used as onlay flaps, covering dura or its

replacement. Whether different tissue types such as fascia/muscle/fat have better ability to heal is a very interesting question, but was beyond the scope of this review. Instead, we speculate that the shift in flap choice is driven by the decreased risk of donor site morbidity and the exceptionally long pedicle that can be obtained with these flaps. In addition, the evolution of flap choice is affected by an increase in defects requiring free tissue transfer after endoscopic endonasal resections.^{5,6}

In terms of distribution of flaps, our review noted a predominant use of latissimus for orbital exenteration (17/28). For isolated anterior skull base reconstruction, forearms and ALT were the most widely used flaps (37/48). We caution against making conclusions regarding the superiority of one flap versus another. The rate of complications appeared similar across flaps, and multiple other factors may have played a role in flap choice.

Most microvascular reconstruction was performed with a radial forearm. The popularity of this flap is likely due to its pliability and lack of bulk, in addition to ability to harvest with a long vascular pedicle, as well as familiarity among most microsurgical surgeons, all of which can be desirable in reconstructing the anterior skull base.

Study Limitations

The major limitation of this study is limited and heterogeneous outcome reporting. Many studies had very limited follow-up, and among those that did, the minimum length of follow-up was as low as 2 months. Few studies provided data regarding survival or functional outcomes, and again this reporting was too heterogeneous for any analysis.

Another significant limitation of this study is reporting bias. This systematic review of the existing literature reflects high success rates and low complication rates. Many papers only included only a few patients; thus, the focus in these papers was more related to surgical technique or curiosity of a rare use of free flaps. It is likely that many anterior skull base free flap reconstructions with worse outcomes, including free flap failures, have not been reported.

The MINORS scores for these studies were also low, with a median score of 8 points. Prospective data was limited, with studies being limited to case reports and retrospective case series. Furthermore, there was a wide variety in defects, flaps used, indications, and data reporting on the whole. Consequently, meta-analysis was unable to be performed.

Future Directions

Larger scale studies are needed to better assess outcomes and complications in free flap reconstruction of the anterior skull base. While these studies likely will need to be retrospective, more controlled and homogeneously reported data with long-term follow-up will allow for meta-analysis and more robust conclusions.

Conclusion

Microvascular reconstruction of the anterior skull base is a feasible option for reconstruction for large defects, prior

local or regional flap failure, or compromised local tissue from infection or radiation in the setting of resection of a neoplasm, trauma, or infection. High success rates were reported in the literature, with low rates of CSF leak and free flap failure. The most common option for reconstruction was a radial forearm free flap. Larger and more controlled studies are necessary for meta-analysis and more robust conclusions regarding anterior skull base free flap reconstruction.

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Conflict of Interest

None declared.

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