

ONLINE FIRST

Risk Factors Associated With Repair of Orbital and Lateral Skull Defects

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Objective: To explore the complications and associated risks factors after orbital exenteration and lateral skull base defect repair.

Methods: Patients who had undergone a reconstruction of their orbital cavity and lateral skull base defects were selected from our departmental database. The outcome of interest was postoperative complications. The risks factors were defined as age, sex, history of radiation therapy, and intracranial involvement (with and without dural involvement). Information was collected on the type of reconstruction used after the orbital cavity repair. The χ^2 test and logistic regression were used to analyze associations between postoperative complications and the various risks factors.

Results: Of the 32 identified patients, 19 had intracranial involvement (9 with dural involvement). Twenty-four patients underwent reconstruction with free tissue transfer in the same setting. Reconstruction with free tissue transfer was significantly associated with fewer major postoperative complications ($P < .053$). There was a trend toward more complications with a history of radiation therapy or intracranial involvement.

Conclusions: Reconstruction of the orbital cavity and lateral skull base can be challenging, especially if there is a history of radiation therapy and intracranial involvement. Free tissue transfer is a safe and effective method for reconstruction of such defects.

Arch Facial Plast Surg. 2012;14(2):97-103.

Published online December 19, 2011.

doi:10.1001/archfacial.2011.1301

ORBITAL CAVITY AND LATERAL skull base defect repairs are devastating procedures that can leave complicated defects with many reconstructive challenges. The main goals of reconstruction are to restore the boundaries between the orbit and the surrounding structures and to create an aesthetically acceptable result. The main issues that need to be considered include addressing the dead space; isolating the orbit from the sinonasal space and brain; reconstruction of the orbital rim; the need for cancer surveillance; the impact of radiation therapy; and the possibility of prosthetic implantation.

Depending on the need to address any of these issues, the orbit can be reconstructed in a number of ways, ranging the spectrum of the reconstructive ladder.¹⁻³ The orbital and skull base defects can be left to heal by granulation, which can take 2 to 3 months, and it may be cumbersome to care for the wound until it is fully epithelialized.⁴ The use of split-thickness skin grafts could provide faster healing because the granulation period is avoided.^{5,6} These procedures are simple and safe and allow careful cancer surveillance if recurrence is of

concern. One potential disadvantage is a less desirable aesthetic result. Also, this type of reconstruction is not suitable for very large defects in which a sturdy seal is needed between the orbit and the sinuses or brain.⁷

Other viable options are the use of regional flaps,⁸⁻¹⁰ which provide more possibilities for filling up the cavity and recreating the barriers between the orbit and the surrounding structures. The temporalis muscle flap has been widely described as a flap that can give more volume to the orbit, obturate small bony defects, and provide covering for dural tears. Nevertheless, several problems have been noted. Donor site contour abnormalities are common.⁸ Also, the reach might be limited, and tumors invading beyond the orbit laterally may mandate wider fields of resection that may involve either the flap itself or its vascularity.¹¹ In this situation, even if enough muscle is viable for reconstruction, the need for postoperative radiation therapy may leave the tissue too scarred for use.¹²

Given the aforementioned issues, free tissue transfer has been preferred in certain situations in which the demands for orbital reconstruction require bulk and a seal from the sinuses or the skull base.^{13,14} Once in place, a free flap will withstand the rig-

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ors of postoperative radiation therapy,^{15,16} increase the viability of underlying bone,¹⁷ and decrease the risk of osteoradionecrosis,¹⁸ which can lead to meningitis and death.¹⁹ For these reasons, when large defects demand the use of bone grafts to restore the contours of the orbit, free flaps have the potential of providing healthy vascularized tissue to support the reconstruction in a single stage. However, the use of free tissue transfer increases the complexity of the case and can add perioperative risk.

Therefore, reconstruction of the orbital cavity and lateral skull base is complex, and choices are mostly empirically based. Previously published case series do not specifically consider the risk factors that are associated with patients undergoing orbital exenteration and how to determine when the more complex free tissue transfer reconstructions should be prioritized. In this study, we looked at patients who underwent orbital exenteration alone or in combination with lateral skull base resection. We launched an exploratory study to characterize (1) our own patient population, which had undergone orbital exenteration with and without lateral skull base resection, and (2) the complications and associated risk factors after orbital reconstruction. We describe the most

commonly used free flaps in our series and detail the rationale of choosing various options to reconstruct the orbital cavity.

METHODS

PATIENTS

We identified patients from 1995 to 2008 at the University of Washington, Seattle, and affiliated hospitals. Patients who were considered for the study underwent orbital exenteration or lateral skull base defect repair either as a result of trauma or oncologic resection and were approved by the institutional review board of the University of Washington. Information was collected regarding the cause of the orbital defect, type of defect, year of diagnosis, date of service(s), type of reconstruction, and use of postoperative radiation therapy. Postoperative complications were the outcome of interest. Because some patients underwent multiple procedures, we considered complications that arose only after the first procedure in which the orbit was exenterated as well as any complications throughout the follow-up period. In an effort to specifically capture those complications that occur during the perioperative period, we focused on the complications that arose after the first procedure in which the orbit was exenterated, as mentioned above, but before hospital discharge. For the bivariate and multivariate analyses, we named these *complications before hospital discharge*. We assessed the following risk factors: (1) defects involving the intracranial cavity (with and without dural involvement), (2) preoperative radiation therapy, (3) type of reconstruction (free flap vs other), (4) age at time of orbital reconstruction, and (5) sex.

Table 1. Patient Demographics

Variable	No. (%)
Age at operation, y	
≤42	8 (25)
43-67	17 (53)
≥68	7 (22)
Sex	
Male	20 (62)
Female	12 (38)
Reason for repair	
Oncologic	28 (88)
Trauma	3 (9)
Arteriovenous malformation	1 (3)
History of radiation therapy	
Yes	10 (31)
No	22 (69)
Intracranial involvement	
Yes	12 (38)
No	20 (62)
Dural involvement	
Yes	11 (34)
No	21 (66)

Table 3. Overview of Complications

Type of Complication	Any Complication	Complication After Reconstruction Only
Intracranial	8	6
Cerebrospinal fluid leak	3	2
Meningitis	1	0
Epidural hematoma	1	1
Pneumocephalus	3	3
Flap compromise	3	3
Wound infection	4	3
Hematoma	1	1
Wound dehiscence	1	1
Osteomyelitis	1	0

Table 2. Primary Reconstruction of the 32 Patients

Free Tissue Transfer (n=27)	No. (%)	Artery	Vein
Rectus abdominis	12 (38)	7 STs, 3 FAs, 1 AP, 1 LA	6 EJs, 3 FVs, 2 IJs, 1 STV
Radial forearm	11 (34)	7 STs, 4 FAs, 1 ST	10 EJs, 1 FV
Megaflap	1 (3)	1 ST	1 FV
Scapula	1 (3)	1 FA	1 FV
Anterolateral thigh	2 (6)	2 FAs	1 EJ, 1 FV
Other (n=5)			
Pericranial + STSG	2 (6)	NA	NA
STSG	1 (3)	NA	NA
Granulate	2 (6)	NA	NA

Abbreviations: AP, ascending pharyngeal artery; EJ, external jugular vein; FA, facial artery; FV, facial vein; IJ, internal jugular vein; LA, lingual artery; NA, not applicable; ST, superior thyroid artery; STSG, split-thickness skin graft; STV, superficial temporal vein.

STATISTICAL ANALYSIS

Statistical analyses were performed using Stata version 10.0 (Stata Corp). χ^2 Tests were used to determine the associations between our outcome variable(s) (complications) and the various risks factors outlined above. In multivariate analysis, dummy variables were created for intracranial involvement (with and without dural involvement), history of radiation therapy, use of free tissue transfer, sex, and age at exenteration (divided in tertiles). The date of service was used as the continuous variable.

RESULTS

PATIENT CHARACTERISTICS

We identified 32 patients who underwent orbital exenteration or lateral skull base defect repair during 1995 to 2008 at the University of Washington and affiliated hospitals. Their demographics are listed in **Table 1**. The mean age was 59 years (age range, 15-86 years), and the mean follow-up time was 26.48 months. Twenty patients were male and 12 were female. Nineteen patients underwent fronto-orbital craniotomies (12 with dural involvement), and 9 underwent preoperative radiation therapy.

Table 2 details the types of reconstructive methods that were used in this study. Twenty-seven patients ultimately required free tissue transfer. Among these free tissue transfers, rectus abdominis free flaps were the most commonly used, followed by radial forearm free flaps. The most common arteries and veins that were harvested to revascularize the free flaps were the superior thyroid artery and the external jugular vein, followed by the facial artery and the facial vein. There were 18 total complications that occurred in 13 patients.

The complications observed throughout the follow-up period are detailed in **Table 3**. Of the complications that occurred after orbital exenteration, 3 were defined as major (1 cerebrospinal fluid leaks, 1 tension pneumocephalus, and 1 epidural hematoma; the latter 2 occurred in the same patient). Two free flaps were compromised, requiring take-back revision surgery. Two patients developed

hematomas, and 1 patient developed wound dehiscence/breakdown.

The other complications occurred in the 4 patients who did not undergo reconstruction with free flaps. Of these complications, 4 were defined as major (2 cerebrospinal fluid leaks and 2 tension pneumocephali). The latter 2 complications were infections, 1 of which was localized to the wound and 1 of which was osteomyelitis.

BIVARIATE ANALYSIS

For the statistical analyses, we removed 2 patients who did not have orbital exenteration in the primary setting. The results of our bivariate analysis are illustrated in **Table 4**. The complications that occurred after orbital exenteration were further limited to those that occurred before hospital discharge. There were no significant associations between intracranial involvement, history of radiation therapy, sex, age, and presence of any postoperative complications. In contrast, there was a significant association between complications before hospital discharge and the method of reconstruction, such that reconstruction with free tissue transfer appeared protective ($P < .053$). Subgroup analysis revealed that this association was specific to patients with defects that included intracranial involvement ($P < .008$).

MULTIVARIATE ANALYSIS

Results from our multivariate analyses using *any complication* and *complication before hospital discharge* as the outcome variables are summarized in **Table 5**. There was a trend toward the presence of any complication in patients with a history of radiation therapy, older age (≥ 68 years), intracranial involvement, and being male. Among these, the strongest association was noted for patients with a history of radiation therapy, although it was not statistically significant ($P < .06$). Dural involvement did not seem to increase the odds of having either any complication or a major complication before discharge. Also, the protective effect of reconstruction of the orbital cav-

Table 4. Bivariate Analysis of Complications After Reconstruction

Covariates	Any Complication		Complication Before Hospital Discharge	
	χ^2	P Value	χ^2	P Value
Intracranial involvement				
None	1 [Reference]	NA	1 [Reference]	NA
Yes	0.01	.91	1.86	.17
Age, y				
≤ 42	1 [Reference]	NA	1 [Reference]	NA
43-67	2.77	.10	0.35	.56
≥ 68	1.73	.42	3.73	.44
Free flap				
Any	0.14	.71	0	> .99
For primary reconstruction	1.66	.20	3.75	< .053
Prior radiation therapy	0.78	.38	0	> .99
Sex				
Female	1 [Reference]	NA	1 [Reference]	NA
Male	1.82	.18	0.06	.97

Abbreviation: NA, not applicable.

Table 5. Multivariate Analysis of Complication After Reconstruction

Covariates	Any Complication		Complication Before Hospital Discharge	
	OR (95% CI)	P Value	OR (95% CI)	P Value
Intracranial involvement				
None	1 [Reference]	NA	1 [Reference]	NA
Yes	4.9 (0.63-38.14)	.13	6.15 (0.67-56.81)	.11
Age, y				
≤42	1 [Reference]	NA	1 [Reference]	NA
43-67	0.39 (0.04-3.87)	.42	0.27 (0.19-3.91)	.34
≥68	2.11 (0.14-31.52)	.59	4.58 (0.21-100.10)	.33
Free flap	0.17 (0.01-2.85)	.22	0.07 (0.003-1.80)	.11
Date of service	1.15 (0.73-1.84)	.54	0.89 (0.61-1.29)	.53
Prior radiation therapy	12.25 (0.86-174.30)	.06	10.7 (0.53-219.20)	.12
Sex				
Female	1 [Reference]	NA	1 [Reference]	NA
Male	4.87 (0.57-41.63)	.15	3.61 (0.38-34.71)	.27

Abbreviations: CI, confidence interval; NA, not applicable; OR, odds ratio.

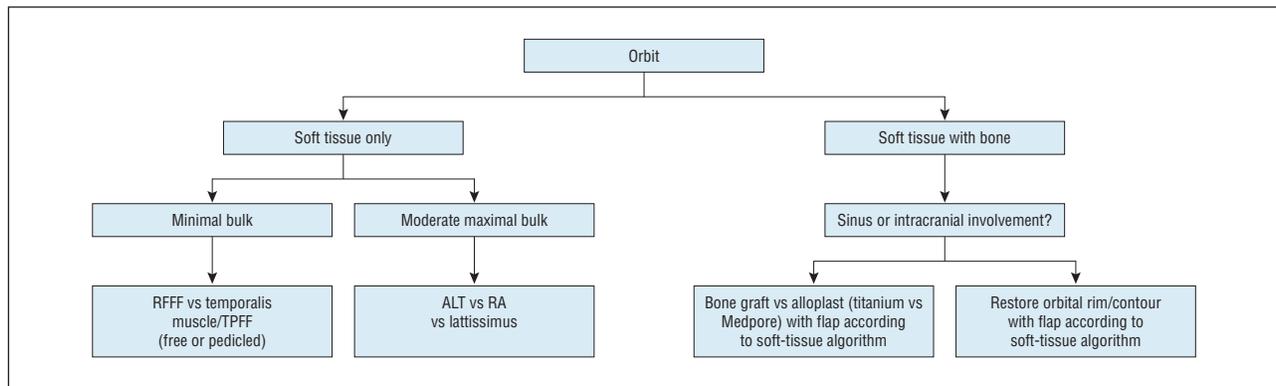


Figure 1. Algorithm used for approach of orbital and lateral skull base defects. First, categorization occurs to determine whether the defect contains soft tissue only or soft tissue with bone. Defects containing soft tissue only can be repaired with a temporalis muscle flap vs a thin, pliable free flap. If there is a history of radiation therapy or if radiation therapy is expected in the field of the temporalis muscle, we recommend using the radial forearm free flap (RFFF). When moderate to maximal bulk is desired, bulky flaps with a relatively long pedicle length, such as the anterolateral thigh (ALT) and the rectus abdominis (RA) free flaps, are almost always the better choice. When defects involve bone, consideration must be given to whether the orbit needs to be sealed from either the intracranial or the sinus cavities. If the defect involves the sinuses or the brain, then bone grafts or alloplast is used for bony contouring followed by a soft-tissue free flap. If there is no sinus or intracranial involvement, then the orbital rim contour is restored followed by either a pedicle or a free flap. Medpore is manufactured by Porex Surgical Inc. TPF indicates temporoparietal fascia flap.

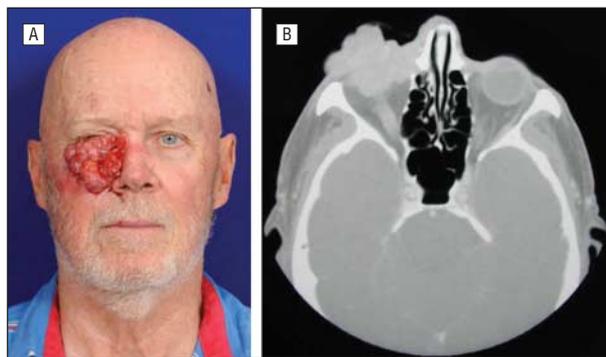


Figure 2. Basal cell carcinoma involving the right orbit, cheek, and nasal wall. A, A 72-year-old man with a 10-year history of a basal cell carcinoma involving the right orbit and extending to the cheek, inferiorly, and to the right nasal wall and ala, medially. B, Axial view of a computed tomogram showing invasion into the right orbit and nasal wall.

ity with free tissue transfer remained largely unchanged (although slightly less significant) after adjustment for intracranial involvement, age, sex, and history of radiation therapy (Table 4).

COMMENT

Orbital exenterated cavity and lateral skull base defects pose many unique challenges for reconstruction. Restoring the boundaries with surrounding spaces such as the sinuses and the brain, recreating the contour of the orbital rim, the need for cancer surveillance, and the possibility of prosthetic implantation are all issues that must be considered before undertaking reconstruction of the exenterated cavity. In this case series, we showed that having a history of radiation therapy and a defect with intracranial involvement might be associated with postoperative complications and that free tissue transfer might be protective in such instances.

Having a history of radiation therapy has been previously noted to be associated with postoperative complications in patients who undergo free flap reconstruction. Halle et al²⁰ found that radiation therapy before the free flap operation was related to an increase in risk of free flap necrosis, increased flap loss infections, and delayed wound healing. Although there appears to be a posi-

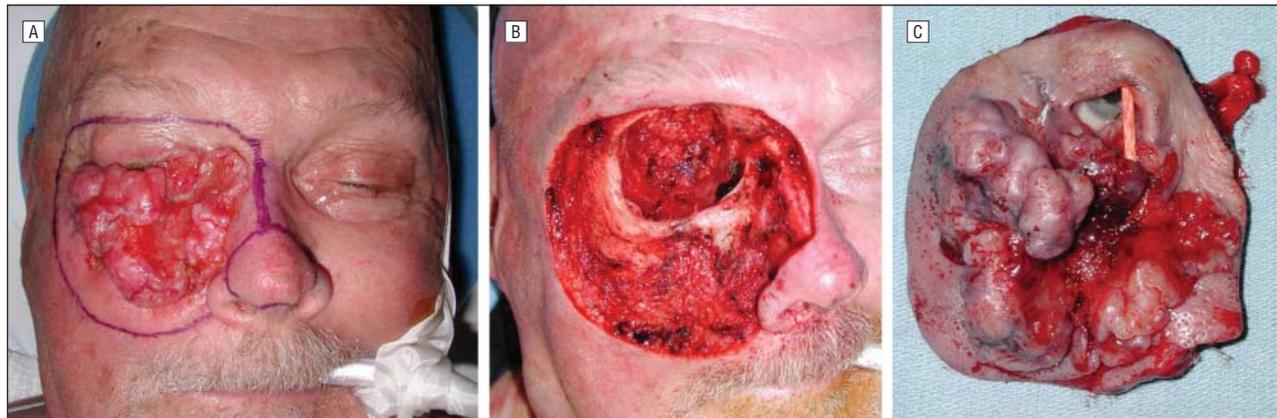


Figure 3. Intraoperative planning of tumor resection. A, The nasal tip subunit is marked for reconstruction purposes. B, Intraoperative view of orbit, cheek, and nasal defect. C, Resected tumor specimen involving orbital exenteration.

tive association between intracranial involvement and the presence of a major postoperative complication after orbital exenteration and/or lateral skull base defect repair, it is not possible to determine from our study why this is the case. Even though we did not see a significant association between free tissue transfer reconstruction and postoperative complications, there was a trend toward this association in bivariate analysis among patients with intracranial involvement. In fact, of all the patients with intracranial involvement, those who did not receive free tissue transfer after their orbital exenteration had a complication. Interestingly, despite the possibility that violation of the dura would seem to make the defect more complex, our study did not show an association between dural involvement and the presence of postoperative complications in our multivariate analysis. Subgrouping into only those patients with intracranial involvement still did not show a significant association (data not shown). It is possible that the limited number of patients, coupled with the fact that most patients ultimately underwent reconstruction with a free flap, obscured a true association between dural involvement and postoperative complications. However, it is also possible that reconstruction with well-vascularized tissue, as happened in all but 1 patient with dural involvement, helped minimize complications in these patients. Finally, it should be stated that given our limited sample size, testing multiple covariates for the association with postoperative complications in multivariate models can result in data overfitting. Therefore, studies of larger size will be needed to fully address these issues.

Reconstruction with free tissue transfer was not significantly associated with the presence of a postoperative complication. However, this result needs to be interpreted with caution for a number of reasons. First, more of our patients underwent free tissue transfer as the first attempt to reconstruct the orbit or lateral skull base. For this reason, there are not enough patients who underwent reconstruction with other methods to adequately compare the complication rate between those who underwent reconstruction with free flaps and those who underwent reconstruction with other methods such as pedicled myocutaneous flaps. Second, most of our patients ultimately underwent free flap reconstruction, which

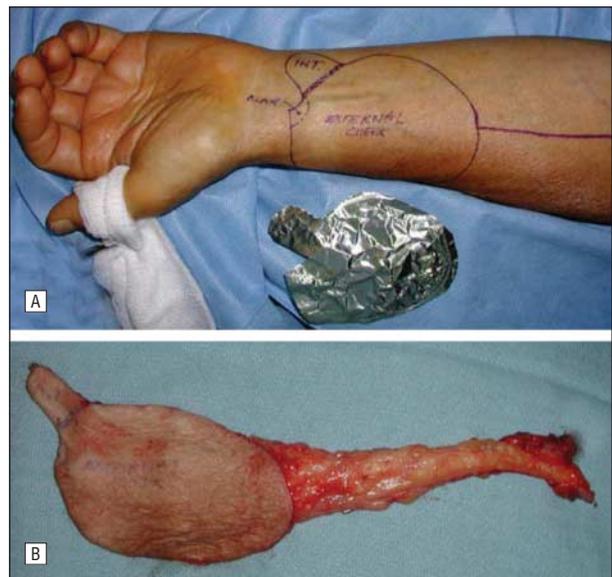


Figure 4. Intraoperative planning of reconstruction. A, Reconstruction with a radial forearm free tissue transfer. A foil template is used to outline the orbital/cheek defect with respect to the nasal subunits. A portion of the distal ulnar skin is initially outlined to provide internal nasal lining; then, an adjacent segment corresponding to the alar component is outlined. B, Harvested radial forearm flap with pedicle.

might reflect the bias of our own institution's patient population or surgeons' preferences in addressing these defects. Therefore, there is a significant selection bias in this cohort, such that those patients who underwent reconstruction with other methods successfully and did not need a free flap are not as well represented in our series.

The use of free flaps has previously been described as safe and effective. Of note, Olsen et al²¹ declared that immediate reconstruction of extensive sino-orbital defects using free tissue transfer was "extremely successful" compared with the alternatives. In fact, the flaps in their case series had 100% survival, and they did not believe that free flap reconstruction could create problems because of masking of recurrent disease. Another case series, performed by Urken et al,²² demonstrated successful free tissue transfer for skull base defects in 23 of 26 patients. The other 3 patients had flap failure but underwent successful reconstruction with a second free flap. Urken and

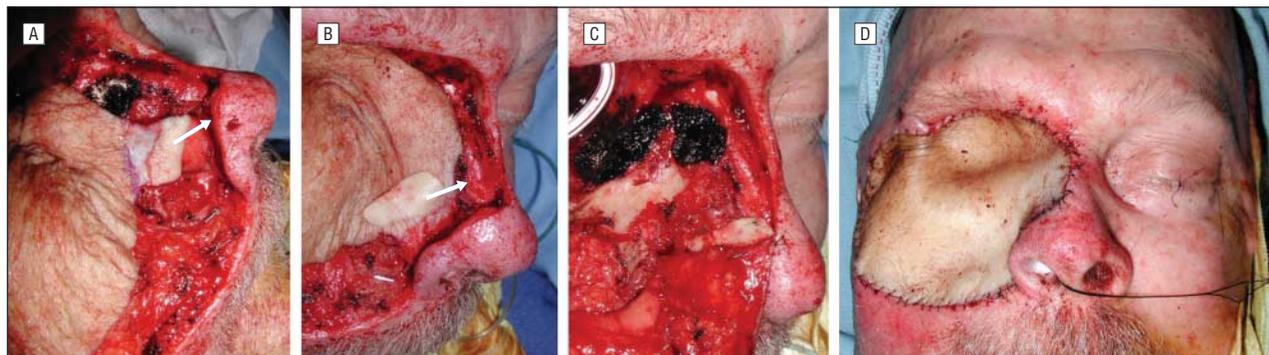


Figure 5. Four-part series showing the radial forearm flap inset. A, The distal-most tip of the ulnar portion of the radial forearm flap is used for the internal lining, and an adjacent area of deepithelialized flap is buried under the native alar/vestibular skin. The arrow reveals the distal-most portion of the ulnar skin getting tucked to provide the nasal lining. B, A conchal ear cartilage graft is used to shape the right nasal ala and to buttress the nasal sidewall and valve. C, The ear cartilage graft is illustrated in situ. D, Intraoperative inset.

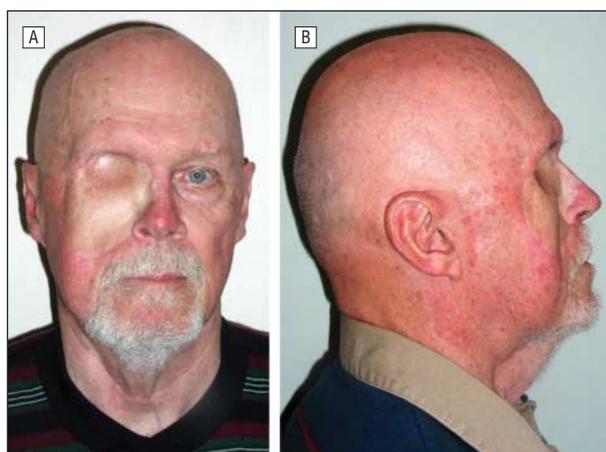


Figure 6. Three-year postoperative results. A, Front view. B, Lateral view.

colleagues stated that the complexity of the reconstruction problem was directly related to the violation of normal boundaries between contiguous fluid-secreting cavities, with one being sterile and the others possessing threatening bacterial flora. Their solution was to provide a watertight seal of each cavity to protect not only the dura but also the nutrient pedicle to the flap. According to flap choice, their preference for the rectus abdominis for many of the defects in their series was based on its reliable vascular territory, the length and size of the vascular pedicle, and the convenience of harvest in the supine position. Neligan et al²³ found that free flap reconstruction exhibited a significantly higher incidence of uncomplicated primary wound healing (95.0% vs 79.5% for local flaps and 64.8% for pedicle flaps) and a much lower incidence of flap loss (0%), cerebrospinal fluid leak (5.0% vs 14.8% and 11.8%), meningitis (0% vs 3.7% and 5.9%), and abscess (0% vs 9.3% and 17.6%) when compared with defects reconstructed with local flaps and pedicled myocutaneous flaps. The pericranial flap was found to provide a reliable dural seal. They determined that free flap reconstruction should be the preferred method of reconstruction because of the high incidence of primary wound healing in the free flap group. Also, the use of the free flap is the most cost-effective, as reflected in shorter hospitalizations. Finally, in a case series by Funk et al,²⁴ 21 patients with cranio-orbito-facial

defects underwent free flap reconstruction. The intracranial contents (6 cases) or the carotid artery (4 cases) was protected from sinonasal or oropharyngeal contamination by the reconstructive flap in all cases in which it was required, and no vascular flap failures occurred in that series. Therefore, they concluded that the use of free tissue transfer flaps is safe and effective for repairing large midfacial and cranio-orbito-facial defects resulting from ablative oncologic surgery or trauma.²⁴

Based on our own experience, we developed a simple algorithm to approach defects of the exenterated orbital cavity and lateral skull base (**Figure 1**). We first categorize the defect on the basis of whether it involves soft tissue only or soft tissue with bone. For those soft-tissue-only defects for which there is no significant need to obliterate dead space (eg, in expectation of a prosthesis), either a temporalis muscle flap or a thin, pliable free flap could be used. An example of the use of a radial forearm free flap to reconstruct an extensive right orbital defect involving the cheek inferiorly and the nasal sidewall medially is shown in **Figures 2, 3, 4, 5, and 6**. Given our results, if there is a history of radiation therapy or radiation therapy is expected in the field of the temporalis muscle, we recommend using the radial forearm free flap to reconstruct the orbital cavity. The pliability of the flap is ideal to contour the cavity, and its long pedicle allows the anastomosis to occur outside the field of radiation. In eyelid-sparing exenterations, we prefer to deepithelialize the radial forearm to include only skin in the midportion of the flap, thereby mimicking the area of scleral show. This method serves to seal the suture line along the conjunctiva and provides a monitor skin paddle after surgery. In some patients, fat atrophy could occur over time, however, resulting in some orbital hollowing. When moderate to maximal bulk is desired, the use of free tissue transfer is almost always the better choice. Bulky flaps with a relatively long pedicle length include the anterolateral thigh and the rectus abdominis free flaps.

With defects that involve bone, we should consider whether the orbit needs to be sealed from either the intracranial or the sinus cavities. As noted in our study, defects that involve the intracranial cavity might be associated with major complications in the immediate

postoperative period. Although we did not see any significant association with free tissue transfer and postoperative complications, our study cannot answer whether the increase of complications among patients with intracranial involvement is attributable to that or to the reconstruction that our patients underwent. Nonetheless, we still recommend using free tissue transfer in these cases because it allows the surgeon to contour a free flap to seal the orbital cavity, from either the sinuses or the brain, without significant limitations on pedicle length or kinking. If the defect involves the sinuses or the brain, then bone grafts rather than alloplast are used for bony contouring followed by a soft-tissue free flap according to the soft-tissue bulk requirements. If there is no sinus or intracranial involvement, then the orbital rim contour is restored followed by either a pedicle or a free flap according to soft-tissue bulk needs.

In conclusion, using bivariate and multivariate regression analyses, we identified 2 potential risk factors that are significantly associated with major postoperative complications after orbital cavity and lateral skull base defect repair: a history of radiation therapy and intracranial involvement. Further studies are required to explore these associations and to further dissect in more detail what aspects of intracranial involvement, for example, are more prone to complications during these reconstructions. Free tissue transfer appears to be a safe and reliable method to address the different reconstructive challenges when there is a need to reconstruct the lateral skull base and to seal the orbital cavity from the sinuses or the brain.

Accepted for Publication: November 3, 2011.

Published Online: December 19, 2011. doi:10.1001/archfacial.2011.1301

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Financial Disclosure: None reported.

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