Free flap transfer, a safe and efficient method for reconstruction of composite skull base defects after salvage resection of advanced intra- and extracranial communicating tumors

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Abstract

Propose: Surgical treatment of advanced intra- and extracranial communicating skull base tumors is challenging, especially for the reconstruction of the large composite defect left by tumor resection. The aim of the study is to evaluate the utility of the free flap reconstruction of the defects resulting from radical resection of these tumors.

Methods: The clinical data of 17 consecutive patients who underwent free flap reconstruction for defect left by salvage resection of advanced intra- and extracranial communicating tumors from 2013 to 2019 were retrospectively collected and analyzed.

Results: There were 5 squamous cell carcinomas, 4 adenoid cystic carcinomas, 2 basal cell carcinomas, 2 meningiomas, 1 anaplastic hemangiopericytoma, 1 pleomorphic adenoma, 1 osteosarcoma and 1 chondrosarcoma. All patients had recurrent neoplasms, 2 of which had pulmonary metastasis. A modified radical cervical dissection was performed in 6 patients. The anterolateral thigh flap myocutaneous (ALT) flap and rectus abdominis myocutaneous (RAM) flap were used in 15 patients (88.2%) and 2 patients (11.8%), respectively. Complications were seen in 3 of 17 patients (17.6%) with 1 total flap loss. The median PFS duration was 31 months. The 3- and 5-year PFS rate was 0.47 and 0.24, respectively. The mean OS duration was 66 months. The 3- and 5-year OS rate was 0.85 and 0.68, respectively.

Conclusion: Free flap transfer is a safe and effective method with acceptable complications, useful for reconstruction of large composite skull base defects after salvage resection of advanced intra- and extracranial communicating tumors. The functional and cosmetic results are satisfying.

Introduction

Most of the malignancy involving the skull base are locally malignant, with lymph node metastasis rate of 3–5%, and even less distant metastasis [1]. Radical resection of these tumors, even in advanced stages, can generally achieve satisfactory effect.

Advanced intra- and extracranial communicating skull base tumors are usually huge, involving multiple anatomical areas, and even accompanied by regional lymph node metastasis.
Salvage surgical resection may result in large three-dimensional composite tissue defects with exposure of dura mater or brain, which poses a great challenge to reconstruction [2]. Failure of reconstruction may carry potentially life-threatening complications. In the past, without reliable means of reconstruction, these patients were often thought to have lost the chance of surgery.

Reconstruction of skull base should preserve residual functions, reduce morbidity and have ability to tolerate postoperative radiotherapy with acceptable cosmetic effect [3]. Non-vascularized grafts or locoregional flaps are effective in patients treated with limited resection. However, in the case of salvage surgery, composite resection, large three-dimensional defects, or other complex reconstructive problems like perioperative radiation, free flap transfer provides a more robust reconstruction and should be considered the workhorse [4, 5]. Free flap transfer has developed as a highly reliable method for repairing large head and neck defects for the past two decades [5, 6, 4, 7–9, 2, 10, 11].

Nevertheless, the number of advanced intra- and extracranial communicating skull base tumors is limited in previous reports, and thus the safety and efficiency of free flap transfer for these tumors has not been clarified. In this study, we retrospectively analyzed the cases with advanced intra- and extracranial communicating skull base tumors that were surgically treated at the Cancer Hospital, Chinese Academy of Medical Science and Peking Union Medical College from 2013 to 2019. The clinical features, surgical details, experience for reconstruction, complications as well as outcome were reported.

Materials And Methods

From 2013 to 2019, 45 patients underwent craniofacial reconstruction with free flap transfer after tumor ablation in the Department of Neurosurgery, Cancer Hospital, Chinese Academy of Medical Science and Peking Union Medical College. The inclusion criteria were as follows: advanced recurrent malignant skull base tumors; both intra- and extracranial extension; reconstruction with free flap transfer. A total of 17 patients were included in the final analysis (Table 1).

Written consent from all patients have been obtained.
All the free flap transfer reconstruction procedures were performed immediately after the tumor resection. The clinical data analyzed included demographics, surgical and reconstructive details, complications, adjuvant therapy, and outcomes.

Table 1
summary of patient clinical data, reconstructive surgical details and outcome

patient	Age/Sex	Previous treatments	Comorbidities	Histology	Tumor invasion	Flap type	Recipient vessels	Neck dissection	Complications
1	50/M	OP	Diabetes	SCC	ACF; MS; ES; SS; NC; Orbit	ALT	Superficial temporal A, V	No	Local dehiscence of incision
2	61/F	OP + RT	No	Anaplastic meningioma	ACF; MCF; MS; ES; Maxilla; Mandible; Facial skin	ALT	External carotid A; Internal jugular V	No	No
3	61/F	OP	Skin ulceration and infection	Pleomorphic adenoma	MCF; PCF; Parotid gland; Petrous bone; Periotic skin	ALT	External carotid A; Internal jugular V	Yes	No
4	49/M	OP + RT + CT	Skin ulceration and infection; Hemiplegia	Anaplastic hemangiopericytoma	MCF; PCF; Inner ear; Periotic skin	ALT	External carotid A; Internal jugular V	No	Septic shock
5	54/F	OP + RT	Skin ulceration and infection; DVT	Atypical meningioma	MCF; PCF; ES; Orbit; Petrous bone; Periotic skin	ALT	External carotid A; Internal jugular V	No	Total flap loss; Ipsilateral cerebral infarction
6	39/F	OP + RT	Skin ulceration and infection; Pulmonary metastasis	Osteosarcoma	ACF; MCF; MS; Orbit; Facial skin	ALT	External carotid A; External jugular V	No	No
7	49/M	OP + RT + CT	No	ACC	MCF; ES; Orbit	RAM	Superior thyroid A; Internal jugular V	No	No
8	53/M	OP + RT	Diabetes	Chondrosarcoma	ACF; ITF; Orbit; Facial skin	ALT	Facial A; External jugular V	No	No
9	55/M	OP	Hypertension	ACC	MCF; PCF; Petrous bone; Parotid gland; Ear	ALT	External carotid A; Internal jugular V	No	No
10	55/F	OP + RT	CSF otorrhea; Pulmonary metastasis	ACC	MCF; ITF; Petrous bone; Temporomandibular joint	ALT	External carotid A; Internal jugular V	Yes	No
11	63/F	OP	Diabetes; Hypertension	BCC	MCF; Petrous bone; temporalis	ALT	Facial A, V	No	No
12	56/F	OP + RT + CT	No	SCC	ACF; FS; SS; Orbit; Facial skin	ALT	Superficial temporal A, V	No	No
13	63/M	OP + RT	No	ACC	MCF; Middle ear; Periotic skin	ALT	Superior thyroid A; Facial V	Yes	No
14	68/F	OP	Diabetes; Hypertension	SCC	MCF; PCF; Ear; Parotid gland	ALT	External carotid A; Internal jugular V	Yes	No
15	62/M	OP + RT + CT	No	BCC	ACF; MCF; Orbit; ES; NC; Maxilla; Facial skin	RAM	Superficial temporal A, V	No	No
16	63/M	OP + RT + CT	No	SCC	ACF; Orbit; Facial skin	ALT	Facial A, V	Yes	No

M, male; F, female; OP, operation; RT, radiotherapy; CT, chemotherapy; DVT, deep venous thrombosis; CSF, cerebrospinal fluid; SCC, squamous cell carcinoma; I
carcinoma; ACF, anterior cranial fossa; MCF, middle cranial fossa; PCF, Posterior cranial fossa; FS, Frontal Sinus; MS, maxillary sinus; ES, ethmoid sinus; SS, s
infratemporal fossa; RAM, Rectus abdominis flap; ALT, anterolateral thigh flap; A, artery; V, vein; H, hour; Mo, months

patient	Age/Sex	Previous treatments	Comorbidities	Histology	Tumor invasion	Flap type	Recipient vessels	Neck dissection	Complications
17	69/M	OP	No	SCC	MCF; PCF; Petrous bone; Ear	ALT	Facial A; Internal jugular V	Yes	No

M, male; F, female; OP, operation; RT, radiotherapy; CT, chemotherapy; DVT, deep venous thrombosis; CSF, cerebrospinal fluid; SCC, squamous cell carcinoma; I carcinoma; ACF, anterior cranial fossa; MCF, middle cranial fossa; PCF, Posterior cranial fossa; FS, Frontal Sinus; MS, maxillary sinus; ES, ethmoid sinus; SS, s infratemporal fossa; RAM, Rectus abdominis flap; ALT, anterolateral thigh flap; A, artery; V, vein; H, hour; Mo, months

The surgical decision was made by joint consultation of a dedicated multidisciplinary team which included neurosurgery department, head and neck department, oncology department and radiotherapy department. We adopted a two-team approach. The first surgical team was responsible for resection of the tumor and preparing the recipient vessels. The second team was responsible for harvesting the free flap and vascular anastomosis. Before operation, we performed an ultrasound Doppler to identify the perforators. The extent of resection included the neoplasm and the surrounding structures involved. The “En Bloc” resection was attempted whenever possible. The ultimate goal of operation was the radical resection of tumor and to ensure negative margins confirmed by intraoperative frozen sections. Following resection, the dural defect was reconstructed in a standard fashion using fascia lata graft, reinforced with overlying fat strips and fibrin glue (harvested from the same donor site as free flap) (Fig. 1d). A concomitant modified radical cervical dissection was performed in patients with positive neck lymph node detected on the preoperative clinical or radiological assessments (Fig. 1d). The size and the elements of the flap were finally determined when the tumor resection was done (Fig. 1e).

On the first day after operation, the patients were usually transferred to the intensive care unit for observation.
The flaps were clinically monitored by capillary refilling time and observing the flap color and temperature. For highly suspected cases, further monitoring systems were adopted such as the Doppler evaluation and pinpricking of the flap to observe the bleeding.

Progression free survival (PFS) was determined from the date of surgery to the date of documented progression. Overall survival (OS) was determined from the date of surgery to the last follow-up or death. Statistical analyses were performed using SPSS statistics software (version 21.0; IBM Corp).

Results

Clinical and histological data

Over the 7-year period, 17 consecutive patients (9 male, 8 female) underwent free flap transfer for reconstruction of composite skull base defects after resection of advanced intra- and extracranial communicating tumors. The average patient age was 57.1 ± 7.53 years (range, 39–69 years). All patients had recurrent neoplasms, of which 6 were previously treated with surgery, 6 were surgery and radiotherapy, and 5 were surgery, radiotherapy and chemotherapy. Ten patients had comorbidities before operation such as diabetes, hypertension, pulmonary metastases, skin ulcers and infections caused by tumor invasion. The pathological entities included 5 squamous

cell carcinomas, 4 adenoid cystic carcinomas, 2 basal cell carcinomas, 2 meningiomas, 1 pleomorphic adenoma, 1 anaplastic hemangiopericytoma, 1 osteosarcoma and 1 chondrosarcoma. The average hospitalization time was 23.3 days (range, 15–52 days).

Reconstructive surgical technique

The anterolateral thigh flap myocutaneous (ALT) flap and rectus abdominis myocutaneous (RAM) flap were used in 15 patients (88.2%) and 2 patients (11.8%), respectively. Neck vessels were the preferred recipient vessels in the majority of patients (64.7%). The recipient arteries were the external carotid artery (n = 8), facial artery (n = 4), superficial temporal artery (n = 3), superior thyroid artery (n = 2). The recipient veins were the internal jugular vein (n = 9), superficial temporal vein (n = 3), facial vein (n = 3), external jugular vein (n = 2). No vein grafts were required. All arterial pedicles were anastomosed in an end-to-end manner. End-to-end venous anastomoses were performed in 8 patients and end-to-side to the internal jugular vein in 9 patients (Fig. 1f). A modified radical cervical dissection was performed in 6 patients. In all cases, the donor-site defect was closed primarily. The duration of operation from induction of anesthesia to leaving the operating room averaged 7 hours (range, 4.5–11 hours).

Complications

Complications were seen in 3 of 17 patients (17.6%). One total flap loss occurred in a 54-year-old obese female (#5) who had received prior surgery and radiotherapy and was diagnosed with DVT preoperatively. The patient developed flap crisis and ipsilateral cerebral infarction on the third postoperative day. After surgical exploration, arterial thrombosis was found and the flap lost after vascular reanastomosis. The flap was removed and the defect was reconstructed with ipsilateral pedicled pectoralis major myocutaneous flap. One patient (#4), who was diagnosed with skin ulceration and infection caused by tumor invasion preoperatively, developed septic shock and severe hemodynamic disturbance on the second postoperative day, and eventually died.

Local incision dehiscence occurred in one patient (#1) two days after suture removal and gradually improved after conservative treatment.
All the other flaps survived without any partial or total necrosis. There was no donor site complication, and no other complications such as cerebrospinal fluid leaks, meningitis, abdominal wall hernia and dysfunction of lower limb movement were observed.

Outcomes

The mean follow-up time was 31.7 months (range, 1–82 months). The median PFS duration was 31 months (Fig. 2a). The 3- and 5-year PFS rate was 0.47 and 0.24, respectively. The mean OS duration was 66 months (Fig. 2b). The 3- and 5-year OS rate was 0.85 and 0.68, respectively. All patients except for one who died perioperatively were generally satisfied with the cosmetic outcome (Fig. 1h). Nine patients received postoperative adjuvant therapy, of which 4 received radiotherapy, 4 received chemotherapy, and 1 received both radiotherapy and chemotherapy.

Among 17 patients, six patients died during the follow-up period, of which 3 patients died for local tumor progression within 12 to 36 months and 3 patients died of unrelated diseases.
Seven patients are alive with tumor, while 3 patients are currently alive without evidence of disease.

Case 1

A 54-year-old female (Fig. 3) presented with a recurrent atypical meningioma in middle and posterior cranial fossa involving the right ethmoid, orbit and ear with periotic skin ulceration (Fig. 3a-d). A radical resection of the tumor was performed, leaving a large composite defect in the middle and posterior cranial fossa and ear (Fig. 3f). A fascia lata graft harvested from thigh was used for repair of dural defect. An ALT flap (13*8 cm^2) was used for the large three-dimensional defect reconstruction (Fig. 3i, j). The patient died of other unrelated diseases without evidence of tumor one year after the operation.

Case 2

A 62-year-old male (Fig. 4) presented with a recurrent basal cell carcinoma involving the ACF, MCF, orbit, nasal cavity, maxilla and facial skin (Fig. 4a-e). The patient underwent a maxilla resection and orbital exenteration for the removal of the recurrent tumor. The “En Bloc” resection was performed (Fig. 4g, h). A RAM flap was used for the reconstruction of the craniofacial defect (Fig. 4i, j). The flap was completely survival without any complications. The patient received adjuvant radiotherapy and was disease-free until 72 months after surgery with an acceptable appearance.

Discussion

Endonasal endoscopic approach has been increasingly used in the operation of skull base tumors during the last decades. However, in some complex situations, such as advanced intra- and extracranial communicating tumors, open approaches are preferable or even mandatory [7]. In these cases, radical resection of tumors frequently results in complex composite defects involving the dura, brain, and surrounding areas such as the orbit, ear, maxilla, hard palate, and skin. Reliable methods of reconstruction are therefore required to achieve the following goals: (1) separation of the CNS from the external environment and the upper aerodigestive tract; (2) supporting the brain and orbit; (3) obliteration of dead space; (4) replacement of lost skin coverage; (5) restoration of the three-dimensional appearance of bony and soft tissues [8, 6, 12].

The use of local flaps such as temporalis and galeal-pericranial flaps is limited by their inadequate tissue, frequent unavailability and restricted arcs of rotation[10]. Regional pedicled flaps, such as the submental and pectoralis major flaps, have the disadvantage that the distal tip of the flap, and thus the most unreliable, is usually the part of the flap that reaches the intracranial defect [6].

In patients previously operated and/or irradiated and those planned for postoperative radiotherapy, both local and regional flaps are usually unreliable or unavailable.
Radiotherapy have been reported to result in partial or total local flap loss in up to 7–20% of patients [13]. Therefore, when large three-dimensional composite defects are encountered, microvascular free tissue transfer may be more suitable. Free flap transfer in these cases provides adequate, well-vascularized and robust tissue coverage of the defects, with consequent lower complication rates. It has been reported that the wound related complication of locoregional flaps is much higher than that of free flaps (36% vs. 10%) [12]. Free flaps do not have the attachment of a pedicle and have flexibility in design. Besides, free flaps have good tolerance to irradiation, and can be harvested according to the types of defect tissue, such as fasciocutaneous or myocutaneous flap [14]. Resto et al. [15] suggested pectoralis major flap can be an important alternative to free flap reconstruction of composite lateral skull base defect in selected cases. One patient (#5) in our cohort had a pedicled pectoralis major flap as replacement of necrotic free flap caused of arterial thrombosis.

An ideal free flap for skull base reconstruction should meet the following criteria: adequate tissue volume, availability of diverse tissue types on one pedicle with consistent anatomy, versatility in design, minimal donor-site morbidity, and feasibility of a two-team approach [9]. A variety of free flaps including anterolateral thigh flap (ALT), rectus abdominis flap (RAM), radial forearm flap, latissimus dorsi flap and fibula flap for craniofacial reconstruction have been reported [16, 9, 11, 17–21]. In earlier reviews, the RAM was the workhorse for microvascular flap reconstruction of skull base due to the large volume of soft tissue that it provides, allowing for better obliteration of complex dead space [16]. The advantages of the RAM also include excellent vascularity with long vascular pedicle of up to 15 cm, versatility to be used with or without skin paddle, primary closure of the donor site and simultaneous harvesting in a two team setting [10, 16]. Disadvantages of this flap include large abdominal scar, bulkiness sometimes and susceptibility of patients to postoperative hernia formation [18]. Currently at our center, the use of the RAM has largely been replaced by the ALT as it has many of the benefits of the RAM without the donor site morbidity. In the present series, the ALT flap was used in all but 2 of the cases to reconstruct composite skull base defects. The ALT flap has been described more frequently in the last decades’ publications [3]. The ALT flap, based on the descending branch of the lateral circumflex femoral artery, has many advantages of RAM flap such as reliability, long vascular pedicles, versatility in the components and two team approach. The thigh donor site can be closed primarily and does not violate functional motor unit and thus leads to minimal morbidity [17]. The thigh scar can be more cosmetically acceptable to patients. The use of this flap also avoids a separate donor site for harvesting of fat strips and fascia grafts. The main disadvantage to this flap is the anatomic variability of the perforating vessels. This has become less problematic with more experience of the flap harvest gained.

In the last decade, the radial forearm flap, latissimus dorsi flap and fibula flap were rarely used. The radial forearm flap is harvested as a fasciocutaneous flap making it pliable and thin. This makes it criticized for inadequate tissue volume to repair a large three-dimensional defect. The donor site requires reconstruction with split thickness skin grafting, and patients may experience functional deficits in the forearm [10]. However, it has been reported that the radial forearm flap could be reliable when used in a double-layer fashion in large skull base defect [22]. Although the latissimus dorsi flap has large amount of skin and potential muscle volume for microvascular transfer, it is not practical that the patient needs to reposition twice intraoperatively [16]. The fibula flap has become the primary flap for bony reconstruction of the head and neck since 1986, especially when postoperative radiation is expected [16, 4]. However, osseous defects left by resection of skull base tumors rarely require hard support [23]. Considering that most patients in our cohort need postoperative adjuvant radiotherapy or have received radiotherapy previously, we believe that soft tissue reconstruction is far more important than osseous reconstruction. A new classification concept of skull base defects has been raised by Yano et al. [24], and they supposed that defects of class Ib, IIb or defects of the skin or orbital contents and combined defects should be reconstructed with a free flap. Rosenthal et al. [25] proposed a classification of periauricular defects that class I should be reconstructed with regional rotation flap or radial forearm flap, class II with ALT or radial forearm flap and class III with ALT or RAM flap.

Many publications have reported postoperative complications of free flap for skull base reconstruction and its risk factors. The overall complication rate of a variety of the free flaps is 10–32%, and partial or complete flap failure occurs in 2–9% [3, 25, 26, 12, 7, 27]. The overall incidence of complications in this series was 17.6% and the rate of flap loss was 5.9%, which compared well with the literature. The use of free flaps has significantly decreased postoperative nervous complications, and reduced the incidence of CSF leaks from 25 to 6.5% [7].

However, no CSF leaks occurred in our cohort, which may be due to our careful closure of the dural defects (fascia lata graft, fat strips and vascularized flap). It has been reported that history of radiation therapy, medical comorbidities and the extent of intracranial tumor extension were independent predictors of complication rate [26]. Thompson et al. [28] supposed that there was a higher wound complication rate in those with a history of smoking and diabetes. Postoperative facial fistula and recipient-site infection occurred mainly in low-BMI patients, reported by Heo et al. [29]. Flap crisis included infection, arterial and venous thrombosis, and vascular thrombosis remains the primary reason of flap failure [30]. In the series, one patient (#5) developed both ipsilateral cerebral infarction and flap crisis with clinical manifestations in skin temperature, color and capillary refill on the third postoperative day. After surgical exploration followed by a second flap transfer and anticoagulant therapy, hemiplegia was improved and the incision healed at the time of discharge. Yang et al. [30] noted that free flap loss was 6.2-times more likely to develop in patients undergoing surgical exploration after 72 hours. So, the most important thing is to identify signs of flap crisis as early as possible, and then explore without hesitation. Llorente et al. [7] supposed that all patients should receive prophylaxis with anticoagulant therapy.

In the past, in cases of advanced skull base tumors, the indication for radical surgery is limited since an adequate reconstruction is usually hard to perform. At present, free flaps transfer for skull base reconstruction allow much wider and radical tumor resections, early radiotherapy and effective chemotherapy [19]. Llorente et al. [7] reported that the 5-year local disease control rate was 43%, and the 5-year disease-specific survival rate was 36%. In this series, the median PFS was 31 months and the mean OS was 66 months. As salvage surgeries for advanced skull base tumors, the outcomes are acceptable and satisfying. Besides, the removal of the tumor reduced the patient's pain (both physical and mental) and resulted in a better quality of life over the patients' lifetime.

Conclusions

The free flap transfer proved to be efficient for covering large composite three-dimensional skull base defects resulting from the salvage removal of advanced intra- and extracranial communicating tumors even with regional lymph node metastasis or distant metastasis. The complications at both donor and recipient sites are rare and acceptable. The surgical procedures are safe and the outcomes are satisfying.

Declarations

Funding: No funding was received for conducting this study.

Data availability: De-identified raw data available upon request.

Code availability: Available upon request.

Author contributions: J-H W, D-Z L and H-J L conceived the idea. H-J L and D-Z L collected the data. H-J L analyzed the data and drafted the manuscript. All authors participated in the surgical procedure.

Compliance with ethical standards

Conflict of interest: All authors declare that they have no conflict of interest.

Ethics statement: The study was approved by the Cancer Hospital, Chinese Academy of Medical Science and Peking Union Medical College Research Ethics Committee. Written consent from patients that are identifiable from the images have been obtained.

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Figures

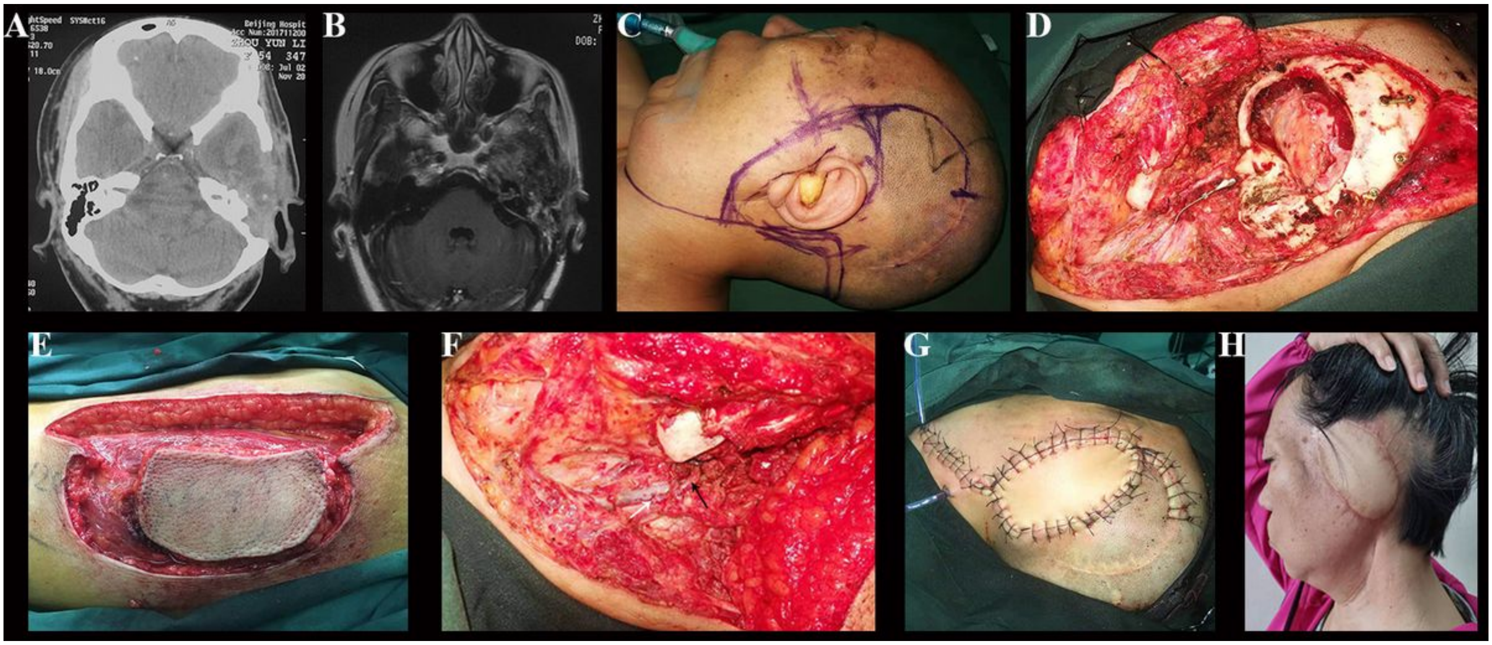

Figure 1

(a-c) A 55-year-old female with recurrent adenoid cystic carcinoma of left middle cranial fossa and ear. (d) The dural defect was reconstructed with fascia lata graft and fat strips (arrow) and a modified radical cervical dissection was performed. (e) The ALT flap used for reconstruction of skull base defect. (f) Arrow (white): venous anastomoses; arrow (black): arterial anastomoses. (g, h) Intraoperative and 18-month postoperative view of the ALT flap reconstruction

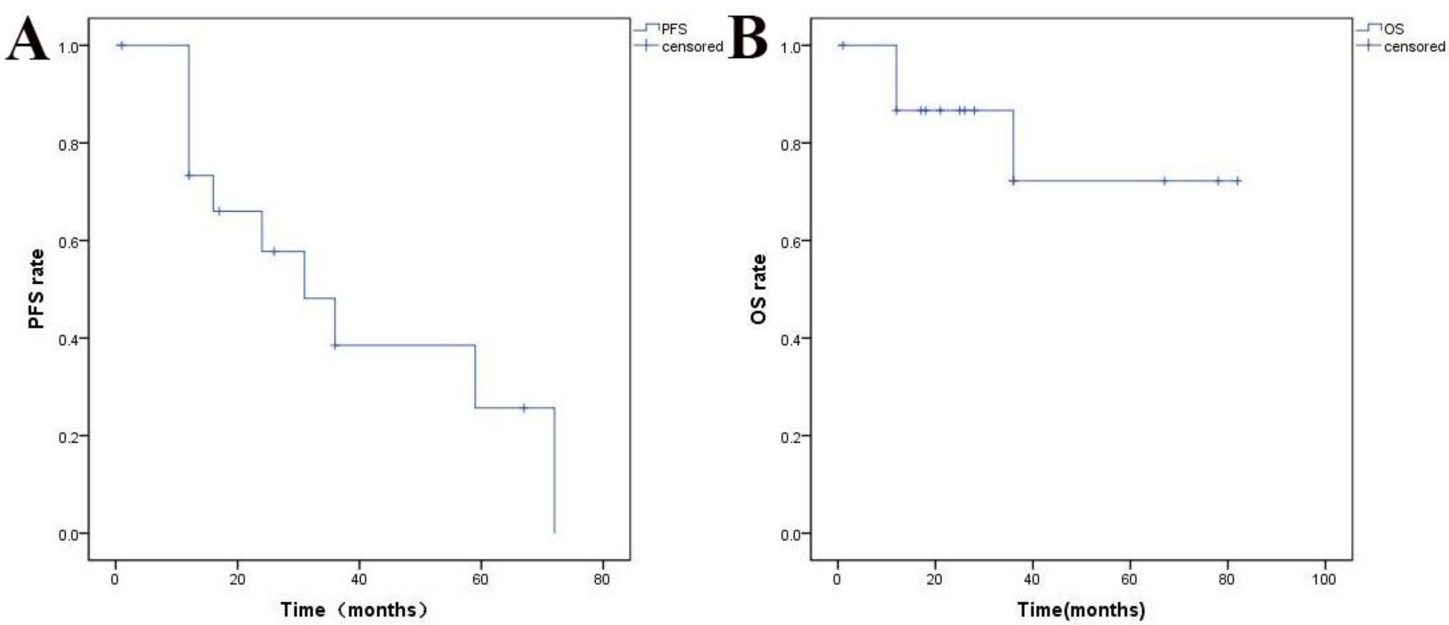

Figure 2

Kaplan-Meier survival curves. (a) PFS. (b) OS

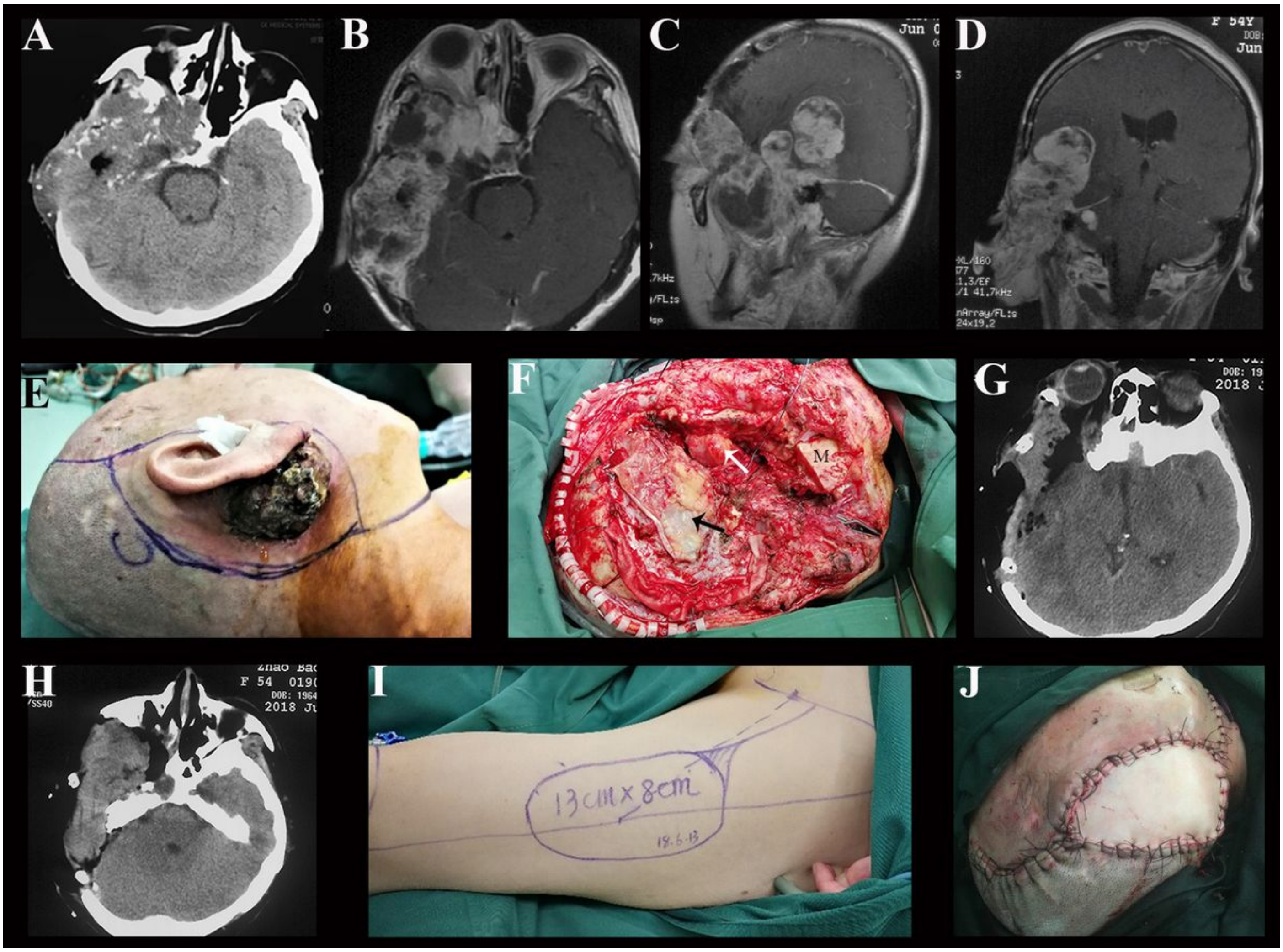

Figure 3

(a-d) Preoperative CT and T1-weighted contrast-enhanced MRI demonstrated an irregularly shaped tumor with heterogeneous enhancement invading MCF, PCF, orbit, ethmoid sinus and the right ear with skin ulceration. (e) The incision surrounding the lesion. (f) Radical resection of the tumor with negative margins. M, mandible; arrow (white): periorbital fat; arrow (black): the dural defect was reconstructed with fascia lata graft and fat strips. (g, h) Postoperative CT indicated satisfactory tumor resection and skull base reconstruction. (i, j) The ALT free flap used to repair the defect

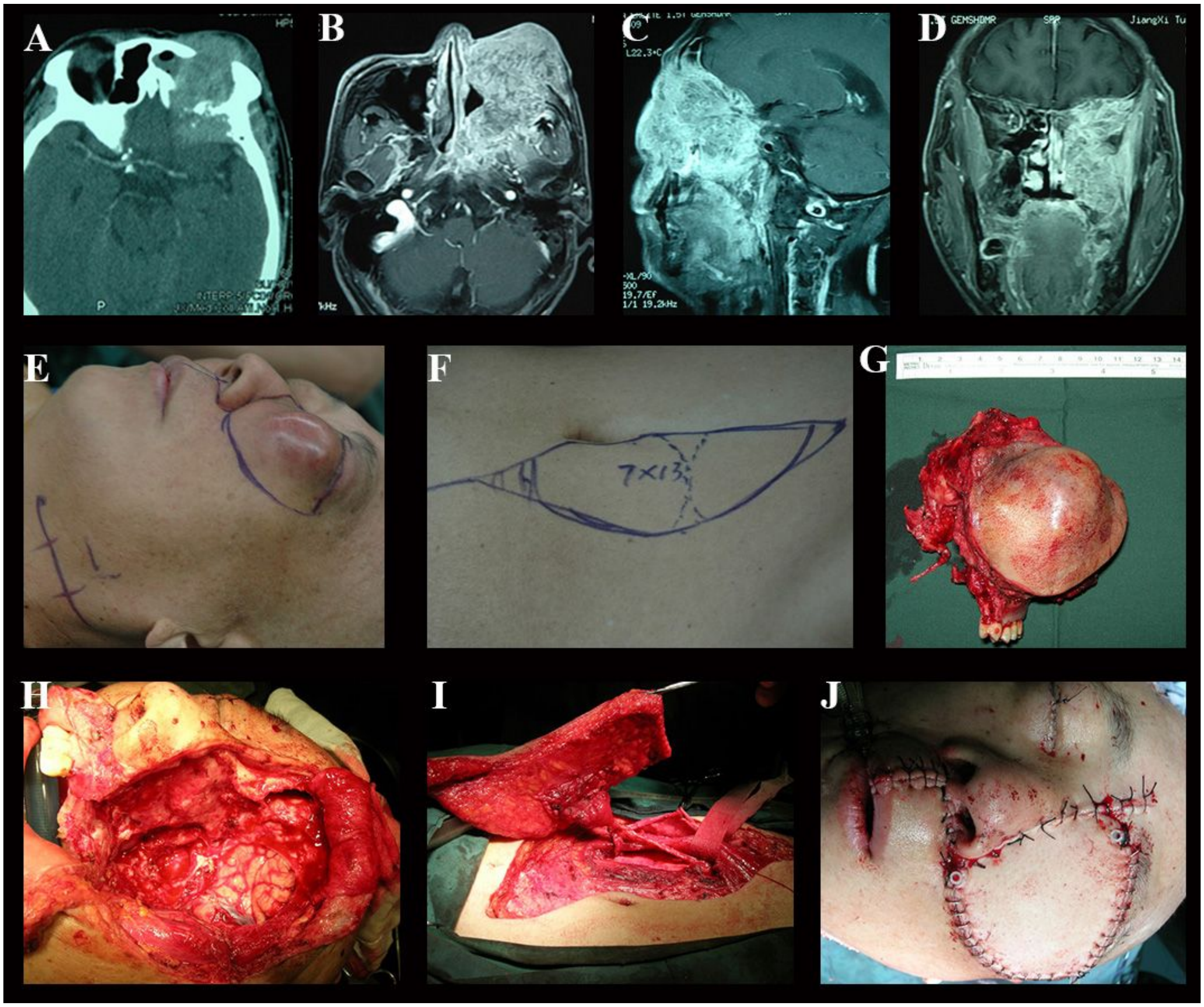

Figure 4

(a-d) Preoperative CT and T1-weighted contrast-enhanced MRI demonstrated an irregularly shaped tumor with heterogeneous enhancement invading ACF, MCF, orbit, ES and nasal cavity. (e) Facial skin was invaded by the tumor. (f, i, j) The RAM free flap used to repair the composite defect. (g, h) The “En Bloc” resection with negative margins was achieved