Indian Journal of Surgical Oncology
https://doi.org/10.1007/s13193-024-02031-8

ORIGINAL ARTICLE

Endoscopic Craniofacial Resection, an Emerging Epitome of Anterior Skull Base Tumor Resection

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Received: 2 June 2024 / Accepted: 13 July 2024

Abstract

Anterior skull base (ASB) malignancies have conventionally been treated with craniofacial resection (CFR), yet this approach is associated with significant morbidity and mortality rates. Recent advancements in endoscopic surgical techniques offer a promising alternative. This study aims to evaluate the morbidity, mortality, recurrence, metastasis, and survival rates of open CFR versus endoscopic CFR for ASB malignancies. A retrospective analysis was conducted on 24 patients who underwent surgery for sinonasal malignancies between January 2017 and July 2023. Patient demographics, tumor characteristics, surgical details, complications, and outcomes were assessed. Surgical procedures included endoscopic resection or open CFR. Statistical analyses were performed using Fisher's exact test and Wilcoxon rank sum test. Survival was estimated using the Kaplan-Meier method. Among 24 patients, 18 underwent CFR, with 13 receiving endoscopic CFR and 5 undergoing open CFR. Male predominance (mean age 40.8 years) and squamous cell carcinoma were common. Endoscopic CFR showed favorable outcomes in terms of visualization, bleeding, surgery duration, complications, and cosmesis compared to open CFR. All endoscopic patients underwent piecemeal resection, with 12 achieving negative margins. Postoperative radiotherapy was administered to all patients. Mean survival time was similar between endoscopic (709±5.5 days) and open (707±7 days) groups, with no significant difference in recurrence rates. Endoscopic CFR emerges as a feasible alternative to open CFR for ASB malignancies, offering comparable outcomes with reduced morbidity. Advancements in endoscopic techniques demonstrate promising results, highlighting the potential of endoscopic surgery in this complex anatomical region. Further studies are warranted to validate these findings and establish endoscopic CFR as a standard approach for ASB malignancies.

Keywords Craniofacial resection · Endoscopic skull base surgery · Endoscopic craniofacial resection · Open craniofacial resection

Introduction

Anterior skull base (ASB) malignancies have traditionally been managed with craniofacial resection (CFR), which combines a bifrontal craniotomy with a transfacial approach and may involve postoperative radiation and chemotherapy [1]. CFR was previously considered the gold standard for treating ASB tumors and was a significant breakthrough when first described by Ketchum in 1963 [2]. Resection of the cribriform plate dramatically reduced recurrence rates [3]. However, CFR is associated with longer recovery times and potential major complications due to edema from brain retraction and replacement of cranial bone as a free graft [4]. Numerous studies have found that after craniofacial resection (CFR), major postoperative complication rates can be as high as 40%, and postoperative mortality rates can be around 5% [4, 5]. Besides the high morbidity and mortality

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Published online: 22 July 2024

associated with CFR, other factors have affected this treatment algorithm [6]. Firstly, many experts have questioned the belief that en bloc resection is consistently achieved with CFR. In reality, in this complex anatomical region, skull base tumors removed through this approach often require piecemeal resection to obtain clear margins, which limits the en bloc resection argument as an advantage to CFR [7]. Secondly, there is no evidence to support the idea that en bloc resection provides any oncologic advantage. Recent studies strongly suggest that achieving true negative surgical margins is far more crucial than the manner in which a tumor is removed (en bloc versus piecemeal resection). The third point raised by advocates of CFR is that repairing large anterior cranial defects through endoscopy is not safe. However, current techniques have been developed to enable safe endoscopic repair of such defects in the anterior skull base. The advancements in endoscopic surgical instrumentation, intraoperative image guidance, and optical aids have led to significant improvements in endoscopic skull base surgery, making trans-nasal endoscopic resection a feasible alternative to CFR [8, 9]. Over the last decade, the field of endoscopic skull base surgery has evolved from endoscopic resection of benign sinonasal tumors to endoscopic-assisted CFR to en bloc resection of sinonasal malignancy purely endoscopically. The aim of this study is to evaluate and compare the morbidity, mortality, recurrence, metastatic, and survival rates of open CFR and endoscopic CFR for malignant tumors of the anterior skull base and determine the limitations of endoscopic CFR for anterior skull base malignancies.

Materials and Methods

Study Design

A retrospective chart analysis was conducted to identify patients who underwent resection of malignant tumors of the anterior skull base between January 2017 and July 2023. Records were evaluated for patient age, sex, diagnosis, tumor staging, histopathologic findings, operative procedure, operative time, estimated blood loss, complications, hospital stay, intensive care unit (ICU) stay, postoperative course, follow-up, recurrence rates, metastasis, and mortality. All the carcinomas were staged according to the AJCC 8th edition, and olfactory neuroblastomas were staged according to the Kadish staging system. Staging was based on preoperative examination, computed tomography (CT), magnetic resonance imaging (MRI), and surgical and pathologic reports. All patients included in this study underwent CFR either by open/endoscopic for curative intent. Exclusion criteria for this were patients with tumors deemed unresectable, who underwent palliative resection or debulking procedure. Skull base resections not including resection of the cribriform plate were also excluded. The protocol for this study was reviewed and approved by the institutional review board.

Radiology

Preoperative Imaging Prior to surgery, all patients underwent a comprehensive radiological evaluation. This included high-resolution computed tomography (CT) scans and magnetic resonance imaging (MRI) of the skull base region. CT scans provided detailed anatomical information regarding bony structures, while MRI scans offered superior soft tissue resolution, aiding in tumor localization and delineation.

Tumor Localization and Extension Radiological images were meticulously reviewed to determine the precise location and extent of the anterior skull base tumor. This assessment involved identifying the involvement of critical structures such as the cribriform plate, ethmoid sinuses, frontal sinus, and anterior cranial fossa meninges and brain (Fig. 1).

Assessment of Tumor Vascularity Contrast-enhanced imaging studies, including CT angiography or MR angiography, were utilized to evaluate the vascularity of the tumor and its relationship with surrounding blood vessels. This

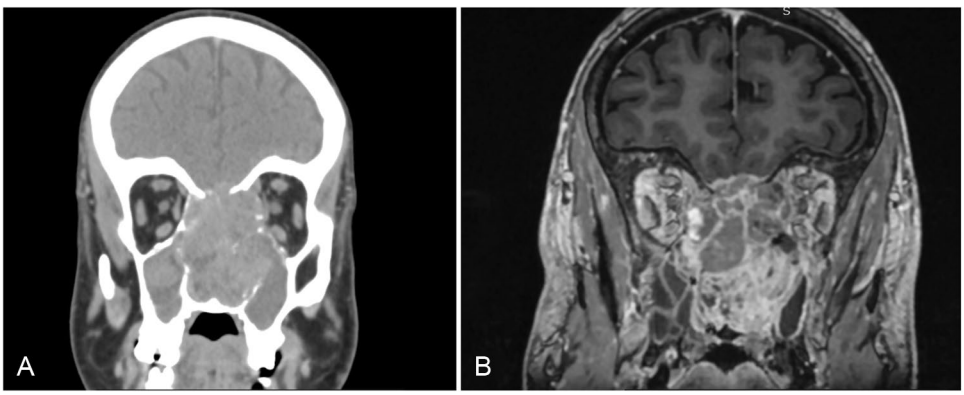

Fig. 1 **A** Contrast-enhanced computed tomography of nose and paranasal sinuses showing locally advanced sinonasal malignancy. **B** T2W MR image showing the lesion abutting the anterior skull base

information was crucial for surgical planning, particularly in cases where vascular encasement or invasion was suspected.

Surgical Procedure

All tumors in the TER group were resected with an endoscopic approach alone, without external incisions, as described previously by Casiano et al. [10].

Decongestion and Exposure

Basic ergonomics of the surgery is similar to that of any endoscopic sinus surgery. The patient is kept in a supine position with a 30° head up. Decongestion is done with 1:80,000 adrenaline solution for 10 min. The exposure is decided mainly based on the radiological and endoscopic findings (see Table 1).

Tumor Resection

Tumor resection can be performed either with cold steel or coblation. In most of the cases in this study, coblation-assisted resection is performed. A meticulous peritumor resection is performed with at least a 1-cm margin. Tumor is delivered either in toto or piecemeal fashion (Fig. 2A, B). Intraoperative frozen section was sent to confirm the adequacy of margin clearance in all cases. Orbit was managed as per the Iannetti et al. recommendation. That is, involvement of the medial rectus, orbital apex, or extensive orbital adnexal is considered an indication of orbital exenteration. In all remaining scenarios, endoscopic removal of lamina papyracea followed by resection of periorbita was done at least. Margins were sent separately after the resection of the tumor (Fig. 2A–D).

Table 1 Algorithm of surgical exposure

Disease extent	Corridors
Limited to nasal cavity and ethmoids without sphenoidal extension	Bilateral nostrils
Limited to nasal cavity with sphenoidal extension	Bilateral nostrils + posterior septectomy
Involvement of the maxillary sinus	Bilateral nostrils + removal of ipsilateral-anteromedial wall of maxillary sinus
Frontal recess/floor of frontal sinus	Bilateral nostrils + superior septectomy

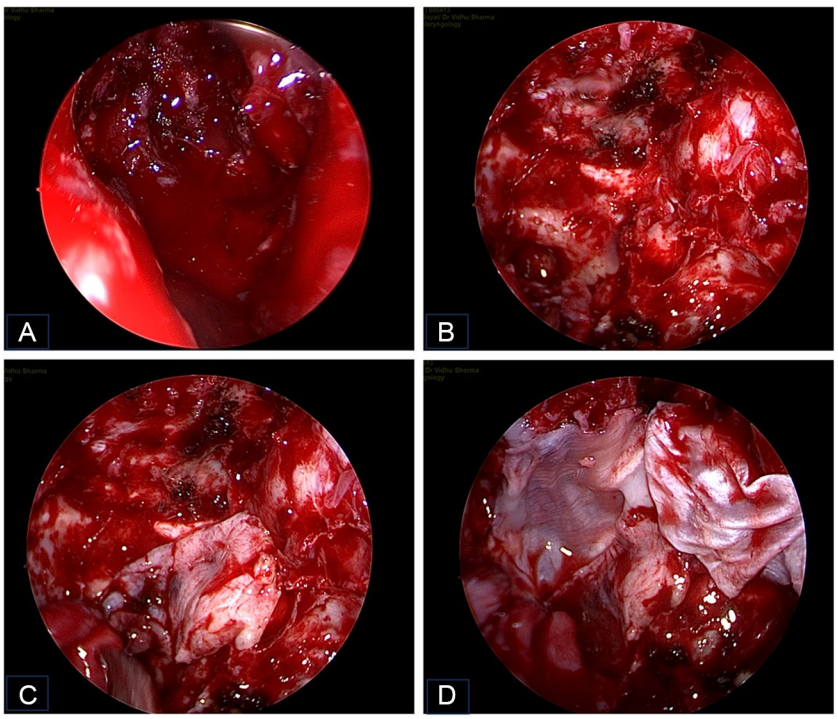

Fig. 2 Intraoperative endoscopic images: **A** tumor, **B** complete resection tumor showing the anterior skull base, **C** Hadad-Bassagasteguy flap, **D** final reconstruction of the skull base using fascia lata

Skull Base Reconstruction

Depending on the extent of the disease, skull base reconstruction is decided. If the tumor is not invading the septum grossly or lower 2/3rd of the septum does not come in margin clearance, then the Hadad-Bassagasteguy flap is considered for reconstruction. In all other scenarios, fascia lata and fat are considered. In case of a dura breach, fascia or Duragen is considered (Figs. 2 and 3). Postoperative CT scan was done to ensure the complete resection as well as to evaluate the intracranium (Fig. 4).

In the case of open CFR, two highly skilled head and neck surgeons, sometimes in collaboration with a neurosurgeon, successfully conducted open anterior skull base resections using the standard CFR approach. In certain cases where additional access was required, they employed transfacial methods. The CFR approach ensured that no facial incisions were made, thereby avoiding any damage to the skin or soft tissues through the use of coronal incisions with a facial degloving approach. For reconstruction purposes, the team utilized either a peri-cranial flap, microvascular free tissue transfer, or a combination of both techniques.

Statistical Methods

Statistical comparison between the endoscopic CFR and open CFR groups was performed using Fisher's exact test for categorical variables and Wilcoxon rank sum test for continuous variables. Survival was estimated using the Kaplan-Meier method. Wilcoxon-Mann-Whitney test *U* test was applied to see the difference in survival time. Outcomes were estimated using overall survival, disease-free survival, local control, regional control, and progression-free survival. All tests were two-tailed and the significance level was set at $P < .05$. All analyses were performed using SPSS software version 26.0 (SPSS Inc., Chicago, IL).

Results

Demography and Clinical Features

From 2018 till 2023, a total of 24 patients underwent surgery for sinonasal malignancy. Eighteen patients required craniofacial resection; the rest of the six patients underwent trans-nasal endoscopic resection of the tumor. Out of

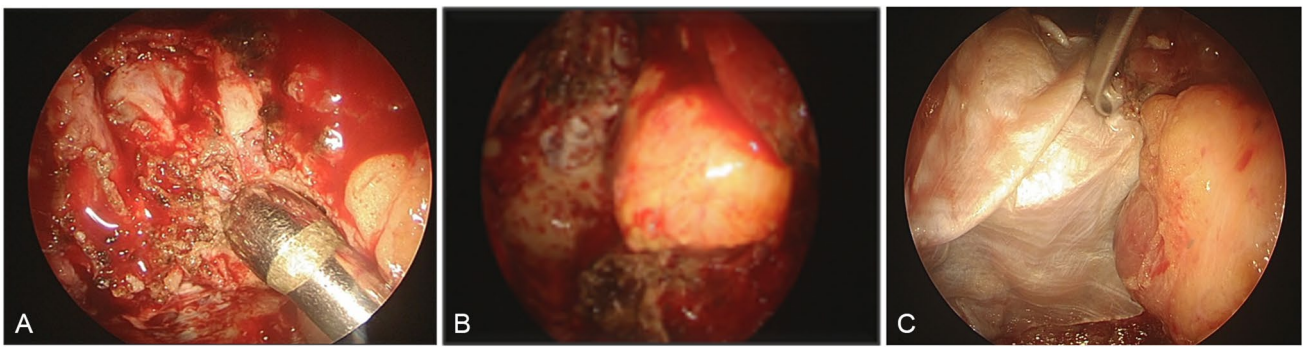

Fig. 3 Management of orbit: **A** tumor abutting the periorbita, **B** resected periorbita with extraconal fat, **C** fascia lata used to reconstruct the periorbita

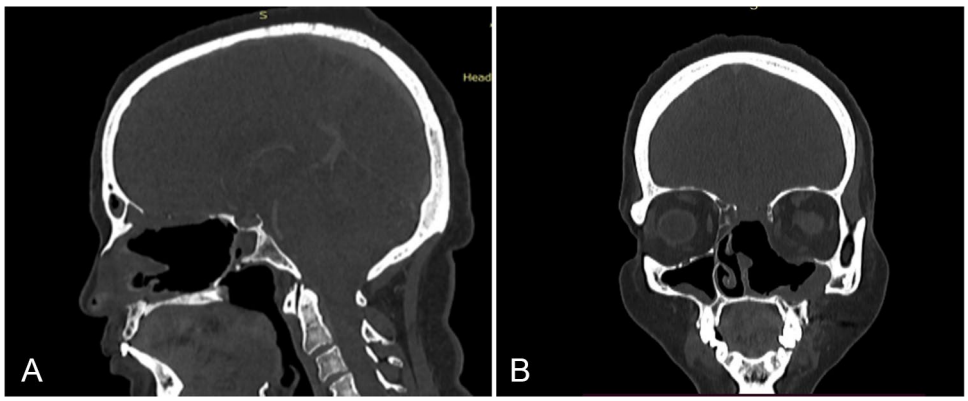

Fig. 4 Postoperative CT scans showing the complete resection of tumor

18 patients who underwent CFR, 13 patients were transnasal endoscopic CFR and 5 underwent open CFR. Male patients were predominant in the sample with a mean age of 40.8 ± 2.1 years. The most common histopathology was squamous cell carcinoma. Among two patients classified as stage I, all were squamous cell carcinoma (SCC). Among four patients classified as stage II, two were SCC and two were adenocarcinoma. Among five patients classified as stage III, three were squamous cell carcinoma (SCC), one was adenocarcinoma, and one was adenoid cystic carcinoma. Finally, among 11 patients classified as stage IVa, 5 were SCC, 2 were adenocarcinoma, 4 were adenoid cystic carcinoma, and 1 was myoepithelial carcinoma. A total of eight patients of SCC, three patients of adenocarcinoma, four patients of adenoid cystic carcinoma, one patient of myoepithelial carcinoma, and two patients of olfactory neuroblastoma underwent CFR. The rest of the features are described in Table 2.

Table 2 Demography and clinical features

Parameters	Frequency	Percentage
Age (mean)	40.8±2.1	
Gender		
Male	19	81%
Female	5	19%
Stage		
TNM		
I	2	9.09%
II	4	18.18%
III	5	22.73%
IVA	11	50%
IVB	0	
Kadish C	1	
Kadish D	1	
Modality of treatment		
Endoscopic resection	6	25%
Open CFR	5	20.83%
Endoscopic CFR	13	54.17%
Histopathology		
Squamous cell carcinoma	12	48%
Adenocarcinoma	6	24%
Adenoid cystic carcinoma	4	16%
Olfactory neuroblastoma	2	8%
Myoepithelial carcinoma	1	4%
Radiotherapy		
Adjuvant RT	17	90%
Re-irradiation	1	9%
Chemotherapy		
NACT	1	20%
Concurrent	8	80%

Comparison of Open vs Endoscopic CFR

Overall operative parameters were favorable in the endoscopic approach in terms of visualization, bleeding, duration of surgery, and cosmesis. The mean blood loss was 500 ml (35) in the endoscopic group. One complication in each modality was observed, which was unilateral impairment of vision in endoscopic CFR and CSF leak in open CFR. The patient with vision impairment recovered after conservative management, and in the CSF leak patient, repair was done immediately. In eight patients, the skull base was reconstructed with fascia lata and fat; in five patients, both Duragen, fat, and fascia lata were used; in two patients, osteoplastic flap was used; and in three patients, the Hadad-Bassagasteguy flap was harvested for reconstruction purpose. The rest of the statistical comparison is given in Table 3.

Outcomes and Follow-up

All the patients in the endoscopic group underwent piecemeal resection. In the final histopathology, 12 patients achieved negative margins, whereas one patient had one margin positive. All the 18 patients received postoperative radiotherapy by volumetric modulated arc therapy (VMAT). The mean dose received was 62.54±3.5 Gy with a mean dose per fraction of 2.12 Gy. Fourteen patients received simultaneous integrated boost (SIB) and four received sequential boost type of fractionation. All the 18 patients completed a median follow-up of 20 months (range, 18–22), and the mean survival time was 709±5.5 days in the endoscopic group and 707±7 days in the open group (Mann-Whitney U-30, $p > 0.05$). All the 18 patients are alive at the end of the study. One patient had recurrence at 1-year follow-up which was adenocarcinoma of intestinal variant. For this, the patient underwent open revision CFR with anterior skull base reconstruction.

Table 3 Comparison of various perioperative parameters

Variable	Open CFR (mean (SD))	Endoscopic CFR (mean (SD))	p value
Blood loss (ml)	750 (50)	500 (35)	<0.001
Duration of surgery (hours)	6.4 (1.2)	4 (1.1)	0.02
ICU stay (hours)	23.5 (2.4)	38.3 (2.6)	0.01
Complications	1	1	0.76
Margin negative	5/5	12/13	0.197

Discussion

Craniofacial resection has been the traditional management for malignancy involving the anterior skull base [1]. The most common malignancy involving the ASB is the locally advanced sinonasal malignancy [6, 7, 9]. Squamous cell carcinoma is the most common sinonasal malignancy described in the literature [11]. The traditional CFR is described as open procedure which involves a bi-coronal incision with bifrontal craniectomy to make an access to the anterior cranial fossa, which may be combined transfacial access either through midfacial degloving or Weber-Fergusson's incision [12]. This surgery has been backbone for the better outcome in locally advanced sinonasal malignancy specifically involving the ASB, which may be combined with adjuvant RT or chemoradiation [13]. As we described the advantages of open CFR, it is important to note it is accompanied by notable perioperative risks, including morbidity, mortality, and complications.

These limitations have prompted great surgeons ahead of us for the search of more efficacious and safer approaches to the ASB. Hence came the sole endoscopic approach to the ASB tumors. In the initial period of the past decade, many endoscopic skull base surgeons have adopted endoscopic CFR for benign sinonasal tumors, and have found this approach to be safe and efficient when compared to open CFR [14]. The tremendous improvement in visualization and close accessibility noted with this approach led to the many trials of endoscopic-assisted CFR for malignant sinonasal tumors until 2001. It was Casiano, who described a purely endoscopic anterior skull base resection for olfactory neuroblastoma in 2001 [10].

Due to the novelty of this entity and the learning curve for endoscopic surgery, it is still controversial to choose as a first choice of technique for many surgeons. In a retrospective study by Eloy et al., 66 patients underwent CFR, of which 18 patients were treated with endoscopic CFR and the rest of the 48 patients under CFR by open approach [9]. The mean age of their sample was 61.2 years (range, 39–81 years) for patients in the endoscopic group and 62.7 years (range, 35–87 years) in the open group. This was similar to our study. Also, there was male predominance in their study like the present study.

According to the principles of oncology, the histopathology and stage of a tumor are crucial determinants in determining the appropriate treatment for any malignancy. In the case of sinonasal tract malignancies, squamous cell carcinoma (SCC) originating from this region is commonly observed [11]. However, a study conducted by Nicolai et al. on the endoscopic management of sinonasal tract malignancies contradicts this notion, revealing adenocarcinoma as the most prevalent pathological type; however, this finding is omitted considering a statistical fallacy [15]. In our present study, moderately differentiated SCCs were found to be the most common. Similarly, Nicolai et al.'s research demonstrated that T4 stage carcinomas were the most frequently encountered, aligning with our findings. This has significant implications for treatment decisions, as advanced T stages directly impact the extent of resection and indirectly influence the reconstruction process. Furthermore, various histological variants of malignancies exhibit distinct prognoses. For instance, the intestinal variant of adenocarcinoma generally carries a more favorable prognosis compared to the non-intestinal variant. Therefore, considering the histopathology of the disease, meticulous attention must be paid to the resection process, particularly in such a complex anatomical area.

Open CFR holds as morbidity as any other open craniectomy procedure. Kim et al. in their retrospective study compared hospital stay, ICU stay, bleeding amount, and operation time between open and endoscopic groups [12]. They found statistically significant differences between both groups, similar to our study. External incision and the requirement of more amount of tissue manipulation and cosmetic morbidity are a few limitations of the open approach as per the literature.

Despite these advantages, concerns have been raised regarding the safety and efficiency of endoscopic techniques. Two important issues are the feasibility of en bloc resection through this route and some considered repairing a large anterior skull base defect endonasally to be inadequate. Let us see these two problems one by one. The oncological safety of piecemeal vs en bloc resection is significantly questioned in literature in the context of endoscopic CFR. In a systematic review by König et al., there was no statistically significant difference in margin-positive status in the final histopathology report between piecemeal vs en bloc resection [16]. The same evidence is supported by a recent study by Cohen et al. [17].

Regarding the second concern, the focus is on addressing the reconstruction of a significant defect in the skull base. Gil et al. conducted a comprehensive study involving 100 patients who underwent reconstruction of the anterior cranial base after the removal of ASB tumors [18]. The study specifically analyzed 120 cases of anterior skull base resections (52 malignant (43%), 68 benign (57%)) performed using an endoscopic approach. For cases with small dural defects, primary closure or reconstruction using temporalis fascia was employed. However, in instances of large anterior skull base defects, a double-layer fascia lata graft was utilized. In situations where the tumor affected the frontal, nasal, or orbital bones, a split calvarial bone graft, posterior frontal sinus wall, or three-dimensional titanium mesh was employed. For cases involving eye globe exenteration, a

temporalis muscle flap was used to cover the orbital socket, while a rectus abdominis free flap was employed for subcranial-orbitomaxillary resection. Vascularized flaps such as Hadad-Bassagasteguy (HBG) flaps are workhorse of ASB reconstruction. Wardas et al. conducted a retrospective analysis to evaluate the criteria used for qualification such as relative and absolute indications for the HBG flap reconstructive techniques [19]. The study concluded that absolute indications for HBG flap harvesting prior to resection are reoperations in the case of a previous open approach, preoperative CSF leakage, intradural localization of a tumor related to its etiopathogenesis, and suspicion of intradural diffusion of a neoplasm in magnetic resonance imaging if the etiopathogenesis cannot clarify the tumor's relation to the meninges. Relative indications concern mostly pituitary macroadenomas of at least 2.5 cm in diameter.

Complications vary from bleeding to irreversible vision loss. In our study, complication rates were similar between the two groups. The most common complication was bleeding, especially in the open approach assuming to be from osteotomy. In open approaches, the internal maxillary artery which is a major blood supply to the nose and paranasal sinuses is usually not ligated. Rather, ipsilateral external carotid artery control is taken by neck incision. This is different from endoscopic, where visualization is paramount and depends on meticulous hemostasis. As expected, the higher blood loss found in the open group translated into a relatively higher percentage of transfusions in these patients. Nonetheless, this observation did not reach statistical significance.

We found no significant differences in metastatic and recurrence rates between the two groups; given the differences in stage and histology, it is difficult to reach definitive conclusions. We observed recurrence in one patient from each group. For the endoscopic group, the patient underwent salvage endoscopic CFR, for recurrence after primary endoscopic resection of sinonasal adenocarcinoma of intestinal type and adjuvant RT, whereas in the open group, one patient had a histopathology of myoepithelial carcinoma. These findings can be further supported by homogeneity in the stage of the disease. Llorente et al. published their findings in 32 patients, of whom only 3 had recurrence [20]. Conversely, an Asian study comparing the outcomes of open and endoscopic CFR showed no recurrence in the open group whereas 55% of patients in the endoscopic group had recurrence [12]. This significant disparity may be explained by many limitations of these studies such as inherent lower level evidence attributed to the retrospective study, single surgeon vs multi surgeons, and significant heterogeneity in the stage and histopathology.

In a European study of 32 patients, the mean survival rate was 70% at 5 years, while disease-free survival was 85% at 5 years. They calculated the survival rate in adenocarcinomas; that is, the mean survival rate at 5 years and disease-free survival were 70% and 80%, respectively [20]. In our study, there were no significant differences observed between the two groups in terms of survival, which was similar to Eloy et al.'s findings.

Based on our expertise, we firmly believe that experienced and skilled endoscopic skull base surgeons can effectively and safely treat early and intermediate-stage malignancies of the anterior skull base using endoscopic resection, while adhering to proper oncologic principles. This technique offers excellent visualization for tumor removal and is associated with faster recovery, shorter hospital stays, and potentially lower local recurrence rates in carefully selected cases, compared to traditional open CFR. For large tumors that extensively invade the intracranial, dermal, or orbital regions, requiring substantial intracranial tumor resection, skin excision, or orbital exenteration respectively, endoscopic-assisted CFR is a viable option. However, in cases where tumors are extensive and involve the skin and orbital regions beyond the capabilities of a purely endoscopic approach, open CFR becomes necessary. In such instances, the use of endoscopic equipment alongside open surgery can provide improved visualization during tumor removal. Endoscopic skull base surgeons who perform TER for malignancies should possess proficiency in CFR, as a backup plan in case complete tumor removal cannot be achieved endoscopically, necessitating conversion to an open procedure. Similarly, surgeons with extensive experience in open CFR can integrate endoscopic techniques into their surgical repertoire.

Conclusion

In summary, the traditional approach of open craniofacial resection (CFR) has been the standard for managing malignancies involving the anterior skull base. However, it is accompanied by significant perioperative risks and complications. The emergence of endoscopic techniques has provided a safer and more efficient alternative for managing these tumors. Endoscopic CFR has been found to be effective and safe for benign tumors and has shown promising results in select cases of malignant sinonasal tumors. It offers advantages such as improved visualization, shorter hospital stays, and potentially lower local recurrence rates. However, there are still concerns about en bloc resection and reconstruction of large skull base defects using endoscopic approaches. Surgeons should have proficiency in both open and endoscopic techniques to ensure optimal outcomes for patients.

Author Contribution All authors were equally involved in the conception of the work, data collection, data analysis and interpretation, drafting of the article, critical revision of the article, and final approval of the version to be published.

Data Availability The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics Approval Approved by Institutional Ethical Committee, All India Institute of Medical Sciences, Jodhpur (AIIMS/IEC/2018/827)

Consent for Publication Cases were selected after obtaining informed consent of the patient for publication.

Competing Interests The authors declare no competing interests.

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Main Points - Anterior skull base (ASB) malignancies traditionally treated with craniofacial resection (CFR) have high morbidity and mortality rates.

- Recent advances in endoscopic surgical techniques present a promising alternative to open CFR.

- Out of 24 patients, 18 underwent craniofacial resection (CFR), with 13 receiving endoscopic CFR and 5 undergoing open CFR.

- There was a male predominance, with a mean age of 40.8 years, and squamous cell carcinoma was common among the patients.

- Endoscopic CFR showed favorable outcomes compared to open CFR in terms of visualization during surgery.

- Endoscopic CFR also demonstrated advantages in terms of reduced bleeding, shorter surgery duration, and improved cosmesis.

- All patients who underwent endoscopic CFR had piecemeal resection, with 12 achieving negative margins.

- Postoperative radiotherapy was administered to all patients regardless of the surgical approach.

- Mean survival time was similar between the endoscopic (709 ± 5.5 days) and open (707 ± 7 days) CFR groups, with no significant difference in recurrence rates observed between the two groups in short-term follow-up.