

Surgical outcomes of endoscopic management of adenocarcinoma of the sinonasal cavity*

Camille Jardeleza, Kristin Seiberling, Steve Floreani, Peter-John Wormald

Department of Otolaryngology Head and Neck Surgery, The Queen Elizabeth Hospital, University of Adelaide, Adelaide, Australia

SUMMARY

Objective: To report the surgical outcomes of endoscopic resection of adenocarcinomas of the Sinonasal cavity.

Methods: Retrospective chart review of patients presenting with adenocarcinoma of the anterior skull base between 1998-2008. All patients who underwent wholly endoscopic resection were included in the study.

Results: Twelve patients presented with adenocarcinoma involving the sino-nasal cavity. At diagnosis 6 patients were staged as a T2, 5 as a T3 and one as a T4. All of the patients had successful removal of the tumour entirely endoscopically. Three patients recurred: 2 locally and 1 with distant metastases. Overall, 11 patients are alive and free of disease and 1 patient dead of disease. We found an overall disease free survival rate and overall survival rate of 91.6%. The follow-up period ranged from 10 to 96 months with a median of 30 months.

Conclusion: Endoscopic management of adenocarcinoma of the sino-nasal cavity can be a viable treatment option to craniofacial resection. With the advancement in endoscopic equipment and surgeon skill, larger tumours may be managed wholly endoscopically.

Key words: adenocarcinoma, endonasal, craniofacial resection, sinus surgery, anterior skull base, modified lothrop, ethmoid, olfactory fossa

INTRODUCTION

Malignant tumours of the sinonasal tract are extremely rare with an estimated annual incidence of 1 in 100,000 people per year. Adenocarcinomas make up only 4-8% of all sinonasal malignancies, but account for 40-68% of all ethmoid/olfactory fossa neoplasms⁽¹⁾. Adenocarcinomas are more common in woodworkers, furniture makers and leather workers⁽²⁾, with woodworkers adenocarcinoma found to originate from the olfactory cleft⁽³⁾. Exposure to textile dusts and hydrocarbons has also been implicated⁽²⁾. Although not a primary risk factor, smoking may have a synergistic effect. Adenocarcinomas typically present in the 5th and 6th decade. Early symptoms are vague in nature and often indistinguishable from benign sinus disease resulting in many of these tumours being diagnosed at a late stage.

Given the rarity of these tumours there is a paucity of clinical studies looking at treatment and outcomes. Prospective studies are largely absent except those that look at the wide range of histologic types of sinonasal malignancies. However, a recent multicenter retrospective study looked at 418 cases of adenocarcinoma and found the five year survival rate to be only 64% and furthermore, 51% recurred locally at a median time of 28 months⁽⁴⁾. In the 418 cases, only 6 were approached entirely endoscopically, whereas, the majority was removed via a cran-

iotomy (anterior craniofacial resection). The "gold standard" treatment of malignant tumours involving the anterior skull base has traditionally been defined as an anterior craniofacial resection, which entails the removal of the cribriform plate, ethmoids and fovea ethmoidalis, anterior face of the sphenoid and septum. The skull base defect is repaired with a pericranial flap. Typically surgery is followed by postoperative radiation treatment^(5,6). Surgical resection with the intent to cure is obtained in many patients, however, not without the morbidity of a craniotomy, noticeable facial scars, prolonged hospital stay and lengthy recovery. As technology for endoscopic sinus surgery and computer assisted surgery has expanded, so has their role in the removal of both benign and malignant sinonasal tumours. The endoscopic approach enables access into areas that are difficult to reach externally, such as the sphenoid sinus, orbital apex and frontal recess. Proponents advocate better visualization of the tumour and margins with magnification by the endoscope, improved control of bleeding with early identification and ligation of the anterior and posterior ethmoid arteries intranasally. Endoscopes also provided improved postoperative surveillance with endoscopic examination performed on routine office visits. Recently, endoscopic assisted and exclusive endoscopic removal of malignant sinonasal neoplasms has been demonstrated⁽⁷⁻¹³⁾. However,

there are no universal guidelines regarding the role of endoscopic resection; the surgical approach may vary according to tumour histology, location, and size, extent of spread and the endoscopic skill and knowledge of the surgeon. Most studies to date have looked at a heterogeneous group of patients with various tumour histologies, stage and follow-up making it difficult to perform meaningful statistical analysis and give definitive treatment guidelines. The purpose of this study is to look at the treatment outcomes of sinonasal adenocarcinomas treated endoscopically.

MATERIALS AND METHODS

A retrospective review of all adenocarcinomas of the sinonasal cavity presenting to the senior authors at the Adelaide University Teaching Hospitals was conducted between 1999-2008. Thirteen patients were diagnosed with adenocarcinoma during that time frame. One patient who underwent a combined endoscopic-cranio-facial resection was excluded from the study. A total of 12 patients were included in the study and underwent endoscopic surgery. After ethics approval by the institutes review board, charts were reviewed for patient age, presenting symptoms, tumour histology, radiologic findings, surgical procedure, postoperative course, complications, adjunctive procedures or chemoradiation. Tumours were staged according to the American Joint Committee on Cancer guidelines (2007). Local recurrences and distant metastasis were recorded and overall survival noted. All patients were offered surgery with intent to cure. Surgery was performed entirely endoscopically. For tumours with intracranial extension, both an otolaryngologist and neurosurgeon operated as a 2-surgeon team to remove the tumour.

RESULTS

Nine out of the 12 patients (75%) had a history of prolonged wood dust exposure based on occupation (Table 1). One patient worked in a shoe factory and another as an opal miner. One patient had no mention of her occupation in the patient files. Half the number of patients (50%) had a history of smoking, 5 have since ceased and one continues to smoke. Twelve patients were treated entirely endoscopically for adeno-

carcinoma of the sino-nasal cavity (Table 2). There were 10 males and 2 females with an average age of 66 years. At presentation 6 were a stage T2, 5 a stage T3 and one a stage T4. Ten patients presented with primary disease with two patients been referred from other institutions with a local recurrence. Both patients referred with recurrence (patient 5 and 6, Table 1) were treated endoscopically. All patients had radical resection (R0), the tumours excised with a margin and histological confirmation of the margin if the margin was not bony. Where the margin was bony, this was drilled down with a diamond burr up to the anterior cranial fossa and the skull base removed, to ensure complete resection of the tumour.

The mean total operative time was 3 hours and 50 minutes (range 117-480 minutes), the longest operation being on the patient with the most advanced lesion (Patient 10). The median total hospital stay, including the day of surgery was 2.5 days (range 2-11 days). The same patient with the most advanced tumour stage also spent the most number of days in hospital. The reason for a prolonged hospital stay was due to a post-operative headache, which was further investigated and revealed only inflammatory changes consistent with post-operative findings on a head CT scan. This eventually resolved and he was discharged home with no further complications. None were admitted to the Intensive Care Unit. Three patients were admitted to the High Dependency Unit (ICU step-down) post-operatively, including Patient 10, and the other 2 patients in view of existing medical co-morbidities but had uncomplicated stays and were discharged at day 2 and 4 respectively (Table 1).

The most common postoperative complication was prolonged crusting (50%, n = 6). In four patients during removal of the tumour from the cribriform plate an intraoperative cerebral spinal fluid (CSF) leak was noted and repaired at the time of surgery with a free mucosal graft. There were no postoperative CSF leaks. All but one patient received postoperative radiation therapy (9 xrt alone, 1 chemoradiation) with an average of 55.6 Gy. The patient who did not receive radiation therapy (XRT) refused initially and only later agreed to treatment when the tumour recurred one year later. Minor complications of XRT

Table 1. Patient demographics. Int: Intestinal, Non-int: Non-intestinal.

Patient	Sex/Age	Smoker	Occupation	Histopath	Hosp stay (days)	HDU post-op
1	F/82	Non	shoe factory worker	Non-int low grade	2	No
2	M/53	Non	panel beater/cabinet maker	Int/Well diff	3	No
3	M/52	Ex	wood machinist	Int/Mod diff	3	No
4	M/57	Non	carpenter	Int/Mucinous	2	No
5	F/75	Smoker	unknown	Non-int low grade	10	No
6	M/74	Ex	chair maker	Int/Mod diff	4	Yes
7	M/74	Ex	cabinet maker	Int/Mod diff	2	No
8	M/70	Ex	saw mill worker	Int/Mucinous	2	No
9	M/66	Ex	opal miner	Int/Poorly diff	2	No
10	M/52	Non	timber works/truck driver	Int/Mucinous	11	Yes
11	M/65	Non	ban saw mill worker	Int/Poor diff	2	Yes
12	M/70	Non	carpenter	Int/Mod diff	4	No

were frequently observed with the most common being that of nasal crusting (n = 7), skin irritation (n = 5), mucositis (n = 5) and conjunctivitis (n = 2). However, one patient after XRT lost substantial vision and is considered legally blind.

Ten patients had adenocarcinoma of the intestinal type and 2 with non-intestinal adenocarcinoma. Of the intestinal type, 1 was classified as well-differentiated, 4 moderately-differentiated, 2 poorly-differentiated and 3 were of the mucinous type (Table 1).

A total of three patients recurred, 2 locally and 1 with distant metastasis. The first patient with local recurrence recurred three times over a period of five years. The recurrence in this patient was treated each time endoscopically with the addition of topical 5-fluorouracil cream applied to the surgical site at the end of the case. The second patient with local recurrence was found to have extension into the anterior cranial fossa. This occurred in the patient who refused initial postoperative radiation therapy. Her recurrence was treated surgically with a com-

Table 2. Patient summary.

Patient	Sex/ Age	Stage	ICE	Surgery/ Date	Presentation	Complications	XRT postop	CX XRT	Recurrence	Mets	Subsequent procedure	Status/ F-up (months)
1	F/82	T2	No	Endoscopic/ 2007	L NAO, rhinorrhea, frontal HA, anosmia	None	Yes	Conjunctivitis	No	No	None	Alive/16
2	M/53	T3	No	Endoscopic/ 2003	R NAO	None	Yes	None	No	No	None	Alive/53
3	M/52	T2	No	Endoscopic/ 2003	L NAO	Intraop CSF leak, crusting	Yes	Skin, mucositis	Yes (2004,05,08) Local	No	Endoscopic resection + 5-FU (2004, 2005, 2008)	Alive/60
4	M/57	T3	No	Endoscopic/ 2001	R vision loss, NAO	Crusting	Yes	Skin	No	No	Bx 05: no recurrence	Alive/96
5	F/75	T3	No	Endoscopic/ 2002	L fronto- temporal headache	Intraop CSF leak, crusting	No- 2002 declined, Yes- 2003	Skin	Yes (2003) Local ACF	No	Combined craniotomy + endoscopic + XRT (2003)	Alive/69
6	M/74	T2	No	Endoscopic/ 2000	L NAO, epistaxis	Intraop CSF leak, crusting	Yes	Skin, conjunctivitis	No	No	None	Alive/96
7	M/74	T2	No	Endoscopic/ 2006	L NAO, epistaxis, PND, L frontal HA	Crusting	Yes	B visual loss (legally blind), mucositis	No	No	None	Alive/24
8	M/70	T2	No	Endoscopic/ 2005	R NAO, anosmia, epistaxis, frontal pain	None	Yes	None	No	No	None	Alive/36
9	M/66	T3	No	Endoscopic/ 2003	Diplopia, L facial pain, proptosis	Crusting, anosmia	Yes	Skin, mucositis	Yes (2004) Distant	Yes (bone, lungs, liver)	Palliative ctx/rtx (2004)	Died/20
10	M/52	T4a	Yes	Endoscopic/ 2008	R NAO, epistaxis, R HA	Crusting	Chemo/ xrt	Sinus infection- staph, mucositis	No	No	None	Alive/12
11	M/65	T3	No	Endoscopic/ 2007	Diplopia, proptosis	None	Yes	Mucositis, epiphora	No	No	None	Alive/12
12	M/70	T2	No	Endoscopic/ 2008	NAO	Intraop CSF leak	Yes	None	No	No	None	Alive/10

ICE: intracranial extension, NAO: nasal airway obstruction, HA: headache, CX: complication, PPS: parapharyngeal space, ACF: anterior cranial fossa.

bined craniotomy/endoscopic resection and postoperative radiation therapy. To date she is free of disease. The patient with metastasis failed to respond to palliative chemoradiation and passed away. Overall, 11 patients are alive and free of disease and 1 patient dead of disease. We found an overall disease free survival rate and overall survival rate of 91.6%. The follow-up period ranged from 10 to 96 months with a median of 30 months.

In order to illustrate the endoscopic management techniques used in this series, two illustrative cases are presented.

Case One

G.E. is a 52-year-old male who presented with long standing right sided nasal obstruction associated with recurrent epistaxis. In addition the patient complained of right-sided headaches, numbness on the right face and tearing in the right eye. Physical exam demonstrated a large nasal mass occluding the nasal cavity. A CT was obtained which showed a soft tissue density filling the right nasal cavity. The CT was followed up with an MRI which demonstrated a mass 76 x 45 x 54 mm centered in the right nasal space compression of the lateral nasal wall and erosion of the midline septum. Superiorly the mass was seen to extend through the cribriform plate into the right anterior cranial fossa with the intracranial (IC) component measuring 26 x 28 x 32 mm. Posterior to the IC extension there was a 15 x 10 x 10 mm focus of high T1/T2 signal suggestive of hemorrhage. There was associated edema of the right frontal lobe and mild subfalcine herniation of the frontal lobe/tumour (Figure 1). A biopsy was done which was consistent with nonsalivary sinonasal adenocarcinoma. A metastatic workup was completed and negative; the patient was staged as a T4aN0M0 adenocarcinoma of the sinonasal cavity. The patient was presented to the Head and Neck Tumour board and all treatment options discussed with the patient. The patient elected to have a wholly endoscopic approach. Neurosurgery was consulted and involved in the decision-mak-

ing and surgery. The patient was consented for endoscopic removal, but was also consented for a craniotomy if conversion to an open procedure was necessary. The patient underwent endoscopic removal (see surgical technique below) of the tumour. The surgery was uneventful and the tumour was removed in its entirety endoscopically. Postoperatively the patient was drowsy with a headache. A CT of the head showed only inflammatory changes consistent after brain tissue removal, expected after such surgery. He eventually recovered and subsequently underwent 6 weeks of chemoradiation without any major complications. He has had no further postoperative complications and is free of disease to date.

Surgical technique

After decongestion and infiltration of the nose with local anesthetic and adrenalin the tumour was debulked with a microdebrider with removal of only the pedicled portion of the tumour. A septoplasty was performed with raising of a large left septal flap pedicled posteriorly on the sphenopalatine artery. Care was taken to ensure that a margin of at least 1 cm was left between the tumour on the septum and the edge of the septal flap. Tumour was visualized eroding through the superior aspect of the septum. The tumour was further reduced with a microdebrider until the attachment of the tumour on the skull base could be visualized (Figure 2A). Bilateral sphenoidotomy and ethmoidectomy with clearance of the skull base around the tumour was performed. An endoscopic modified Lothrop (frontal drillout) was performed to delineate the skull base anteriorly. The anterior and posterior ethmoid arteries were identified by drilling with a diamond burr on the skull base and cauterized bilaterally. Osteotomies of the skull base and crista galli were made with a 25-degree DCR diamond bur (Medtronic ENT, Jacksonville, USA). The osteotomies were done around the skull base attachment of the adenocarcinoma. Anteriorly the falx was cut with skull base scissors (Medtronic ENT). The skull base was dropped into the nasal cavity and removed resulting in an "en bloc"



Figure 1. (A) Parasagittal T1 weighted MRI with contrast demonstrates a large nasal mass extending through the cribriform plate into the anterior cranial fossa. (B) Coronal T1 MRI with contrast shows the tumour with associated edema of the frontal lobe. (C) Axial T1 MRI with contrast shows the tumour filling the nasal cavity with fluid in the sphenoid sinus.

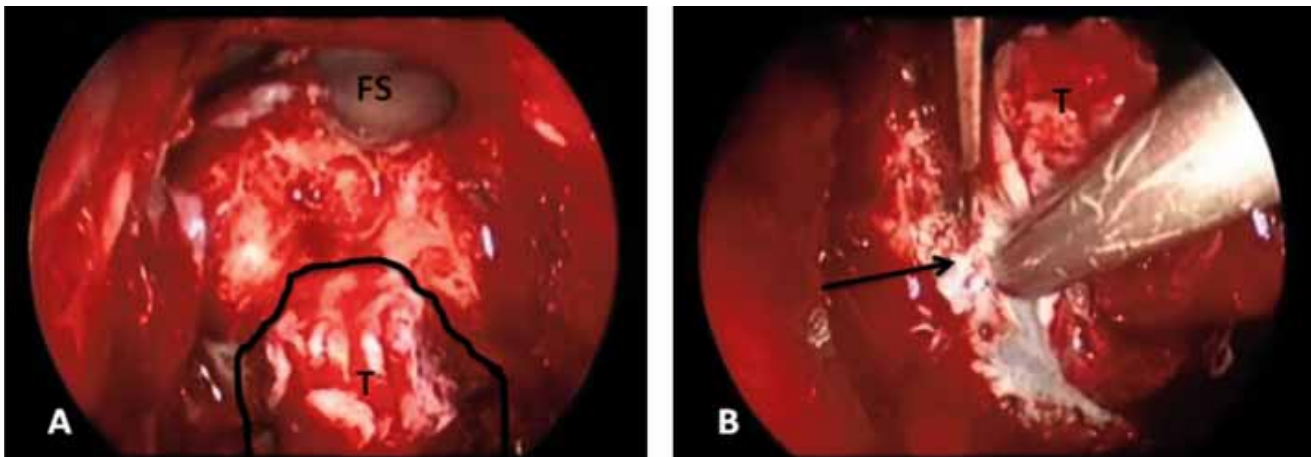


Figure 2. (A) The tumour (T) can be seen eroding through the cribriform plate extending intracranially. The solid black line represents the outline of the tumour. (B) Osteotomies through the skull base (black arrow) have been made and the dura incised. FS - frontal sinus.

removal of the adenocarcinomas attachment to the skull base (Figure 2B). This exposed the intracranial tumour, which was meticulously dissected and removed with the 2 surgeon (ENT and neurosurgeon) approach. The skull base was repaired with two layers of fascia lata. The first layer was riveted anteriorly through the remaining posterior table of the frontal sinus to prevent posterior migration of the graft (Figure 3). The graft was tucked under the edges of the skull base defect and flattened out so that no folds were present. Two strips of titanium mesh were placed horizontally and secured under the edges of the skull base defect to prevent prolapse of intra-cranial contents (Figure 4). The second layer of fascia was placed over this in an overlay fashion followed by the pedicled septal mucosal flap. The closure was sealed with polyethyleanglycol glue and covered with two pieces of Gelfoam and the nasal cavity packed with Bismuth Iodoform Paraffin Paste (BIPP) soaked nasal gauze. A lumbar drain was not used in the pre or postoperative period.

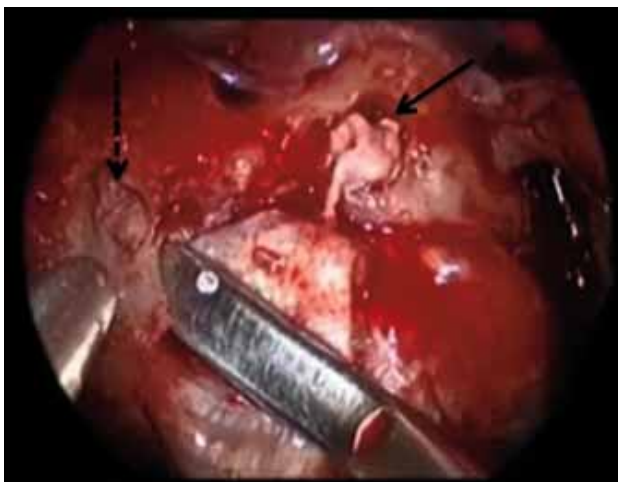


Figure 3. Two holes in the skull base superiorly were created with a 70-degree diamond burr (dotted black arrow). The fascia lata graft was pulled through each hole (solid black arrow).

Case Two

A 74-year-old previous chairmaker was referred to one of the senior authors after a recurrence of his nasal adenocarcinoma in 2000. He presented with left nasal obstruction and epistaxis to his GP and was referred to an ENT surgeon in 1999. Initial sinuscopy revealed granulation tissue on the left lateral nasal wall at the level of the middle turbinate and middle meatus. CT scan showed opacification of the left sphenoid, posterior ethmoids and maxillary antrum. He underwent a “removal of a left sphenothmoidal polyp, middle meatal antrostomy & intranasal ethmoidectomy” in 1999. Histopathology revealed moderately differentiated adenocarcinoma. Staging CT chest and abdomen were negative. He had then had a Left lateral rhinotomy, external ethmoidectomy and repair of CSF leak. There was no residual tumour on pathology. In subsequent follow-ups however, a repeat MRI of the brain and sinuses demonstrated a 20x15mm mass occupying the anterior aspect of the left ethmoid sinuses adjacent to the cribriform plate and

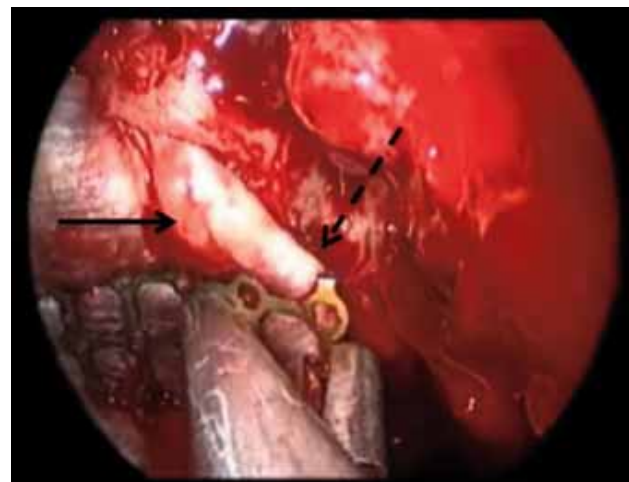


Figure 4. A titanium mesh plate was placed over the fascia lata graft (black arrow) and under the skull base edges (dotted black arrow).

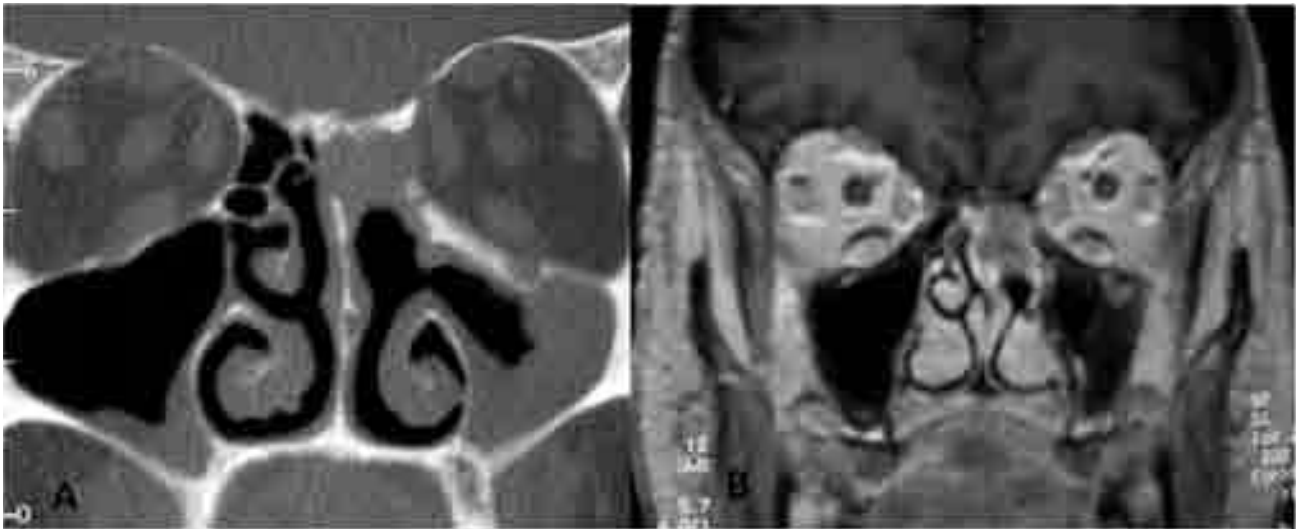


Figure 5. (A) Coronal CT shows a soft tissue density in superior aspect of the ethmoids adjacent to the cribriform plate and lamina papyracea. (B) T1 MRI with contrast demonstrates the mass without any evidence of intracranial penetration or erosion.

posterior orbit. There was no evidence of intracranial extension. (Figure 5B).

He was then referred to one of the senior authors for further management. Nasal endoscopy revealed a polypoid mass superiorly in the left nasal cavity. A CT of the sinus was performed which showed a mass along the left cribriform plate with evidence of bony destruction (Figure 5A). A biopsy again confirmed adenocarcinoma. The patient was staged as a T2N0M0 adenocarcinoma of the sino-nasal cavity. The patient was taken to the theater for endoscopic removal of the tumour (see surgical technique below). Postoperatively the patient received radiation therapy for a total dose of 55.8Gy. Except for a prolonged period of crusting, the patient experienced no postoperative complications. He had no recurrences and to date he is free of disease (8 years later).

Surgical Technique

After decongestion and infiltration of the nose a left uncinectomy and antrostomy was performed. The dependant portion of the tumour was debulked but its attachment to the olfactory fossa and superior turbinate left untouched. A complete anterior and posterior ethmoidectomy was performed leaving the tumour attachment to the skull base untouched. The natural ostium of the sphenoid was identified and widened. The middle turbinate was cut flush with the skull base. The mucosa about one cm away from the tumour edge was incised with a scalpel blade. This was carried down to the underlying skull base bone and orbital periosteum laterally. The tumour was dissected off the cribriform, fovea ethmoidalis and lamina papyracea in the subperiosteal plane. The bone of the olfactory fossa was eroded in the region of the anterior ethmoidal artery with exposed dura and a small CSF leak. The bone of the rest of the olfactory fossa and fovea ethmoidalis was intact, although each individual olfactory nerve needed to be cut to

allow dissection in the subperiosteal plane. In addition there was no attachment to orbital periosteum and this allowed a complete macroscopic resection to be achieved. The exposed dura in the region of the CSF leak was macroscopically clear of tumour. A fat graft was harvested from the right ear lobe and a bath-plug closure of the CSF leak was performed. The closure was sealed with fibrin glue and supported with Gelfoam. No nasal packing or lumbar drain was used.

DISCUSSION

In this series, we were able to focus on the outcomes after endoscopic resection of adenocarcinoma. With 12 patients included, we found an overall survival of 91.6%. Overall, 75% of these patients had a significant exposure to wood dust in their lives, supporting the findings of previous studies that woodworkers have a higher risk of developing nasal adenocarcinoma^(1,2). All patients were treated entirely endoscopically. Offering patients a purely endoscopic resection relies on recent data demonstrating equal local control rates and overall survival rates with less functional morbidity as compared to craniofacial resection (CFR). This only holds true though if complete tumour extirpation is achieved endoscopically, which is dependent not only on tumour size and extent of spread but also on surgeon comfort level and skill. Adenocarcinoma of the sino-nasal cavity has been traditionally treated with craniofacial resection (CFR) and postoperative radiation therapy. With CFR, adenocarcinomas have a 5-year survival of 39-57%^(5,14,15). CFR is not thought to be a benign surgical procedure with an overall mortality rate of 4.5% and complication rate of 33%⁽¹⁶⁾. Subsequently there has been a trend over the last decade to approach certain tumours endoscopically or with endoscopic assistance. In late 1999, Thaler et al. published four cases of endoscopically assisted CFR⁽⁷⁾. In more recent years, endoscopic resection of anterior skull base tumours has

become more prevalent with the advances in endoscopic technology and training. In 2001, Casiano published the first report in which anterior skull base tumours (ASB) with intracranial extension were removed entirely endoscopically⁽¹⁷⁾. Batra et al. compared results of patients treated with a CFR (n = 16) to those who underwent purely endoscopic resection (n = 9) for ASB tumours with intracranial extension. In this study there appeared to be no statistical difference between the two groups⁽¹⁸⁾. There were, however, advantages noted with the purely endoscopic approach including improved visualization, decreased operative time, shorter hospital stay, decreased post-operative pain and fewer complications. The mean operative time and median hospital stay in this study is lower compared to other results involving CFR⁽¹³⁾. In 2007, Dave et al. reported 17 cases of malignant ASB tumours treated entirely endoscopically with an overall local control rate of 94.1% with a mean follow-up of 34.3 months⁽¹³⁾. This study, like the previous ones mentioned, looked at a heterogenous population of ASB tumours including, esthesioneuroblastoma, adenocarcinoma, sinonasal undifferentiated carcinoma, adenoid cystic carcinoma and hemangiopericytoma.

All of the patients in this series were assessed by the Head and Neck Tumour Board. This included a thorough review of pre-operative imaging as well as the input of neurosurgery in the cases where the tumour had breached the anterior skull base. Both surgeons must be comfortable approaching the tumour through the nose and also be able to convert to an open procedure if necessary. Skill in skull base reconstruction is a must, as closure is a critical component of the case. When the anterior skull base has been removed, we prefer to use a two-layer closure with fascia lata and more recently have adopted the Hadad-Bassagasteguy pedicled septal flap as an additional adjuvant⁽¹⁹⁾. None of our patients experienced a postoperative CSF leak. Using the riveting technique is believed to decrease the risk of postoperative CSF leak.

Studies support the role of postoperative radiation therapy in anterior skull base tumours. All of our patients were offered postoperative radiation therapy and received the conventional technique, the most common being 3-dimensional conformal radiotherapy. Newer techniques such as Intensity Modulated Radiotherapy, have improved dose distributions and are associated with lesser complications⁽²³⁾, but are not yet available in South Australia. The most common complication seen in outpatients was prolonged crusting as a consequence of the impaired mucociliary clearance from post-operative radiotherapy. The other two most common complications experienced in our cohort with radiation therapy were skin changes and mucositis. However, radiation therapy to an area in close proximity to the orbit and brain is not without the risk of significant morbidity such as blindness, frontal lobe necrosis and radiation induced malignancies. In one of our patients, bilateral vision impairment occurred after radiation therapy. Although the patient still has some vision he has been classi-

fied as legally blind. The risks and benefits must be discussed with the patient and thoroughly understood. As technology in radiation therapy advances, these risks decrease but are still present⁽²⁰⁾.

According to the WHO Classification of Tumours (Pathology and Genetics, Head & Neck Tumours), the histological type of the adenocarcinoma plays an important part in the prognosis, aggressiveness and clinical behavior of the tumour^(20,23). They can be classified into intestinal and non-intestinal, the latter further classified into low-grade and high-grade subtypes. Intestinal adenocarcinomas are associated with wood dust and leather dust exposure. The results of this study are consistent with this finding. Well-differentiated (Papillary) types are associated with better prognosis and are more indolent, whereas poorly differentiated (Solid) and mucinous types have a lower survival rate and tend to be more aggressive. Risk of distant metastasis is 20%. These predictive factors seem to correlate well to the findings of this study. The only patient who died (Patient 9) had a poorly differentiated type and eventually had distant metastasis. One patient with recurrence had a moderately differentiated type, while the other had well differentiated type, although she initially refused post-operative radiotherapy. Two patients were classified as non-intestinal of the low-grade type, associated with an excellent prognosis if complete surgical excision is achieved.

Recurrence occurred in three of our patients (25%) including the patient who initially refused postoperative radiation therapy after excision of the primary tumour. Two recurred locally while the other one presented with distant metastasis despite a disease free primary site. The recurrences were treated with endoscopic removal in one, combined approach in one and palliative chemoradiation in the last. One patient had local recurrence 3 times, each treated with endoscopic removal and topical 5-fluorouracil (5-FU) application. To date this patient is disease free. Topical 5-FU may have a role in the treatment of primary and recurrent adenocarcinoma. Knekt et al. reported an 87% 5 year survival for adenocarcinoma of the ethmoid sinus treated with recurrent endoscopic debridement and topical 5-FU application⁽²¹⁾.

In managing patients with adenocarcinoma of the sino-nasal cavity, long term follow-up and surveillance for tumour recurrence is imperative. These tumours have been known to recur several years later. One of the limitations in our study is the short follow-up in some of the patients. As more of these tumours are approached endoscopically, further data can be collected with long-term follow-up. Further studies with larger patient numbers and longer follow-up are needed to better define the outcomes of endoscopic resection of anterior skull base tumours.

CONCLUSION

Endoscopic resection of adenocarcinoma of the ethmoid sinuses can be a viable alternative to CFR, depending on a sur-

geon's comfort, level and skill in endoscopic surgery. It is demonstrated in this study that complete endoscopic removal of both large and small tumours of the anterior skull base is possible.

CONFLICT OF INTEREST

PJ Wormald receives royalties from Medtronics for instruments he has designed.

REFERENCES

- Shah UK, Hybels RL, Dugan J. Endoscopic management of low-grade papillary adenocarcinoma of the ethmoid sinus: case report and review of the literature. *Am J Otolaryngol* 1999; 20: 190-194.
- d'Errico A, Pasian S, Baratti A, Zanelli R, Alfonzo S, Gilardi L, Beatrice F, Bena A, Costa G. A Case-control Study on Occupational Risk Factors for Sino-nasal Cancer. *Occup Environ Med* 2009 Jan 19. E-Pub ahead of Print.
- Jankowski R, Georgel T, Vignaud JM, Hemmaoui B, Toussaint B, Graff P, Geoffrois L, Henrot P, Kaminsky MC. Endoscopic surgery reveals that woodworkers' adenocarcinomas originate in the olfactory cleft. *Rhinology*. 2007; 45: 308-314.
- Choussy O, Ferron C, Vedrine PO et al. Adenocarcinoma of Ethmoid: a GETTEC retrospective multicenter study of 418 cases. *Laryngoscope* 2008; 118: 437-443.
- Shah JP, Kraus DH, Bilsky MH, Gutin PH, Harrison LH, Strong EW. Craniofacial resection for malignant tumours involving the anterior skull base. *Arch Otolaryngol Head Neck Surg* 1997; 123: 1312-1317.
- Bridger GP, Kwok B, Baldwin M, Williams JR, Smees RI. Craniofacial resection for paranasal sinus cancers. *Head Neck* 2000; 22: 772-780.
- Thaler ER, Kotapka M, Lanza DC, Kennedy DW. Endoscopically assisted anterior cranial skull base resection of sinonasal tumours. *Am J Rhinol* 1999; 13: 303-310.
- Castelnuovo PG, Belli E, Bignami M, Battaglia P, Sberze F, Tomei G. Endoscopic nasal and anterior craniotomy resection for malignant nasoethmoid tumours involving the anterior skull base. *Skull Base* 2006; 16: 15-18.
- Lund V, Howard DJ, Wei WI. Endoscopic resection of malignant tumours of the nose and sinuses. *Am J Rhinol* 2007; 21: 89-94.
- Shipchandler TZ, Batra PS, Citardi MJ, Bolger WE, Lanza DC. Outcomes for endoscopic resection of sinonasal squamous cell carcinoma. *Laryngoscope* 2005; 115: 1983-1987.
- Podboj J, Smid L. Endoscopic surgery with curative intent for malignant tumours of the nose and paranasal sinuses. *Eur J Surg Oncol* 2007; 33: 1081-1086.
- Buchmann L, Larsen C, Pollack A, Tawfik O, Sykes K, Hoover LA. Endoscopic techniques in resection of anterior skull base/paranasal sinus malignancies. *Laryngoscope* 2006; 116: 1749-1754.
- Dave SP, Bared A, Casiano RR. Surgical outcomes and safety of transnasal endoscopic resection for anterior skull tumours. *Otolaryngol Head Neck Surg* 2007; 136: 920-927.
- Lund VJ, Howard DJ, Wei WI, Cheesman AD. Craniofacial resection for tumours of the nasal cavity and paranasal sinuses--a 17-year experience. *Head Neck* 1998; 20: 97-105.
- Salvan D, Julieron M, Marandas Pet al. Combined transfacial and neurosurgical approach to malignant tumours of the ethmoid sinus. *J Laryngol Otol* 1998; 112: 446-450.
- Ganly I, Patel SG, Singh Bet al. Complications of craniofacial resection for malignant tumours of the skull base: report of an International Collaborative Study. *Head Neck* 2005; 27: 445-451.
- Casiano RR, Numa WA, Falquez AM. Endoscopic resection of esthesioneuroblastoma. *Am J Rhinol* 2001; 15: 271-279.
- Batra PS, Citardi MJ, Worley S, Lee J, Lanza DC. Resection of anterior skull base tumours: comparison of combined traditional and endoscopic techniques. *Am J Rhinol* 2005; 19: 521-528.
- Hadad G, Bassagasteguy L, Carrau R et al. A novel reconstructive technique after endoscopic expanded endonasal approaches: vascular pedicle nasoseptal flap. *Laryngoscope* 2006; 116: 1882-1886.
- Hoppe BS, Stegman LD, Zelefsky MJ et al. Treatment of nasal cavity and paranasal sinus cancer with modern radiotherapy techniques in the postoperative setting--the MSKCC experience. *Int J Radiat Oncol Biol Phys* 2007; 67: 691-702.
- Knecht PP, Ah-See KW, vd Velden LA, Kerrebijn J. Adenocarcinoma of the ethmoidal sinus complex: surgical debulking and topical fluorouracil may be the optimal treatment. *Arch Otolaryngol Head Neck Surg* 2001; 127: 141-146.
- Barnes L, Eveson J, Reichart P, Sidransky D. World Health Organization Classification of Tumours, Pathology and Genetics, Head and Neck Tumours. WHO Publications Center, Albany NY. 2005; 20-23.
- Daly M, Chen A, Bucci K, El-Sayed I, Xia P, Kaplan M, Eisele D. Intensity-Modulated Radiation Therapy for Malignancies of the Nasal Cavity and Paranasal Sinuses. *Int. J. Radiation Oncology Biol. Phys.* 2007; 67:151-157.

Peter-John Wormald
 Department of Otolaryngology Head and Neck Surgery
 The Queen Elizabeth Hospital
 28 Woodville Road
 Woodville South 5011
 South Australia
 Australia

E-mail: peter.wormald@adelaide.edu.au