Acta oto-rhino-laryngologica belg., 2000, **54**, 221-232

Minimally invasive endoscopic management of malignant sinonasal tumours

Y. Goffart, M. Jorissen**, J. Daele*, V. Vander Poorten**, J. Born***, J.-M. Deneufbourg****, A.-Fr. Zicot* and J.-M. Remacle****

Department of ENT and Head & Neck Surgery, *CHR Citadelle Liège, Belgium ; **K.U.Leuven, Leuven, Belgium ; ***CHR Citadelle Liège, Belgium ; ****CHU Sart Tilman, Liège, Belgium

Key Words. FESS ; ethmoid ; carcinoma ; paranasal sinus neoplasms ; skull base

Abstract. *Minimally invasive endoscopic management of malignant sinonasal tumours.* A large retrospective study from two belgian institutions of 78 patients who underwent minimally invasive endoscopic management for malignant sinonasal tumors from, 1992-1999 is presented. We attempt to assess the results of this less invasive approach. The spectrum of disease included adenocarcinoma, squamous cell carcinoma, olfactory neuroblastoma and other malignant tumors. All patients were treated primarily for cure. 66 patients were operated on by a purely endoscopic technique, while 9 patients had a simultaneous neurosurgical and endoscopic approach, and 3 a limited orbital approach. 16 patients (20.5%) presented with local recurrence, 6 patients (7.7%) sustained distant metastases and 7 patients (9%) presented simultaneous local recurrence and distant metastases. The 2-years and 5-years survival rates of the whole group were respectively 73.1% and 52.3%, while the adenocarcinoma group exhibits a significantly better prognosis than other histological types with 2-years and 5-years survival rates of 89.8% and 63.8%. Patients who could be treated purely endoscopically had a significantly better survival in comparison to patients treated by an external and endoscopic approach. Morbidity was minimal and the local control rate as well as survival rates were comparable to literature data. Endoscopic resection was adequate, providing clear margins and en bloc removal in most cases. Our results encourage us to use this minimally invasive approach in selected cases as a reliable alternative to the systematic use of an exclusively external approach.

Introduction

Endoscopic nasal surgery is defined as a range of procedures based on the use of endoscopes. Its main indication in the recent years has been chronic inflammatory disease of the sinuses. The concept of functional endoscopic sinus surgery (FESS) derived from the pioneering works of MESSERKLINGER, WIGAND, DRAF, STAMMBERGER, HOSEMANN, KENNEDY and others (1-11). While a great deal of attention has focused on FESS, endoscopic nasal surgery has evolved as an alternative treatment for numerous pathologic conditions affecting the nose and the sinuses.

Endoscopic techniques have created the potential to manage intranasal and intrasinusal malignancies but the part which should be played by this new technique is still a matter of debate and controversy.

Malignant neoplasms of the nasal cavity and paranasal sinuses are relatively uncommon cancers, accounting for less than 0.8% of all malignancies and 3% of head and neck neoplasms (12, 13).

Paranasal sinus carcinoma in its early stages mimics benign conditions or is asymptomatic. Thus the majority of the patients present with locally advanced tumors and represent a challenge in term of adequate resection of tumor and preservation and/or restoration of function and cosmesis.

The lateral rhinotomy technique, described by MOURE and SÉBILEAU (14), is the classical

surgical procedure for ethmoid cancer surgery. The advent of craniofacial resection allowed the surgeon to gain access to the superior part of the tumor in the case of invasion of the dura or the skull base. However both approaches encounter significant technical limitations and are associated with morbidity, mortality and long term sequelae.

The present report deals with a retrospective series of 78 non-consecutive patients operated upon in two centres in Belgium. The surgical approach was mainly endoscopic but not exclusively so. Thus we prefer the term minimally invasive endoscopic management (MIEM) of tumors of the nose, the paranasal sinuses and the skull base.

Even if it is possible to deal endoscopically with slight to moderate extension to the orbit, the dura or the skull base, technical limitations arise once the tumor has extended beyond the anatomical borders of the paranasal cavities. An external approach (neurosurgery or orbital surgery) was used in patients with extensive disease.

The purpose of this study is to demonstrate that as long as general principles of oncologic surgery are respected, a MIEM is a valuable alternative to conventional surgery in terms of local control and survival.

Material and methods

During the, 1992-1999 period 78 patients with tumours arising from the ethmoid sinus were treated by MIEM in Liege Citadelle Hospital and in University Hospital of Leuven, respectively regional and academic referral medical centres.

The average age was 62.4 years ± 14.04 (range 2-91). The mean follow-up time was 25.9 months ± 19.4 (range 2-82). There were 64 (82.1%) male patients and 14 (17.9%) female patients (M/F ratio 4.6/1).

Patient survival and disease-free survival were measured from the date of surgery to the date of death or disease recurrence, or the last follow-up assessment available in the absence of any event. The survival curves and the corresponding 2- and 5-years survival were estimated using the Kaplan-Meier method with the help of a S-Plus 2000© computer analysis by the Department of Biostatistics (Laurence Seidel, MSc,University of Liege).

Age, sex, histologic types, surgical approach, tumor staging and the number of anatomical subsites invaded were analysed as possible prognostic factors. For this purpose the Cox regression model was adopted.

All patients were primary cases that were not treated before. Patients treated with a palliative intention (debulking or decompression surgery, or metastatic patients), or tumors whose treatment is mostly based on chemotherapy, such as lymphomas (15) or rhabdomyosarcomas, were excluded.

All patients had routine pre-operative evaluation including CT scan and/or MRI of the sinuses and skull base, chest X-rays, bone scintigraphy, lab, endoscopic biopsy under local or general anaesthesia. According to the results of the biopsy and radiological imaging, specific examinations such as serologic studies, ophthalmologic and neurosurgical consultations were obtained in some patients.

The tumours were staged retrospectively according to the UICC, 1997 classification, as before this date no classification for ethmoidal carcinomas existed (table 1).

We also assessed the number of subsites invaded, uni- or bilaterally (anterior ethmoid, posterior ethmoid, frontal sinus, maxillary sinus, sphenoidal sinus, middle turbinate, inferior turbinate, nasal septum, ethmoidal roof, rhinopharynx, pterygopalatine fossa, maxillary process, nasal bones, periorbit, posterior orbit, endocranial, endocerebral, and skin). The mean number of subsites invaded was 5.3 ± 3.6, with a range from 1-17.

Table 1

TNM staging in 78 patients

T 1	5
T 2	28
T 3	9
T 4	36

In one adenocarcinoma patient preoperative angiographic embolisation of the external maxillary artery was performed. This procedure was indicated because of excessive bleeding at the time of biopsy.

Patients were classified into five groups according to their histopathological affiliation (table 2).

Endoscopic biopsies were obtained prior to surgery in all patients. In 3 patients focal malignant transformations (SCC) of an inverted papilloma were found.

Table 2

Histopathological findings in 78 patients

Adenocarcinoma	40
Squamous cell carcinoma (SCC)	13
Malignant melanoma	7
Esthesioneuroblastoma	5
Other malignant tumors (adenoid cystic carcinoma, sarcoma, undifferentiated carcinoma, neuroendocrine tumors)	13
Total	78

Surgery was undertaken under general anaesthesia. After topical adrenaline decongestion and infiltration with xylocaine-epinephrine the tumor resection was performed according to preoperative planning. Anything from turbinate resection, anterior ethmoidectomy, to total sphenoethmoidectomy with nasal septum resection was performed. Debulking of the tumor to obtain adequate visualisation was sometimes required. In extended tumors resection of the lamina papyracea, the periorbit and the anterior bony skull base was performed. In some cases expected CSF leak occurred with drilling of the olfactory fossa or ethmoidal roof and were closed peroperatively with a mucosal flap and fibrin glue (16).

Major extension to the dura or intracranial disease were controlled by a simultaneous neurosurgical approach in 9 cases while a separate limited orbital incision was required in 3 cases to control local extension to the orbital fat tissue (*Table 3*).

Neurosurgical approach started with a coronal incision and elevation of the skin and galea. An anteriorly based pericranial flap was elevated and a frontal craniotomy was performed. A spinal catheter was used to facilitate in brain retraction. Resection of the infiltrated dura and if necessary the frontal brain was performed. Lateral osteotomies were conducted through the lateral ethmoid whereas anterior osteotomy was performed through the floor of the frontal sinus and posterior osteotomy through the roof of the sphenoidal sinus. The endoscopic procedure was the second step with resection of the septum and the ethmoid sinuses until the osteotomies were reached. The resulting skull base defect was repaired using bone powder mixed with fibrin glue or free bone graft and the peduncled pericranial flap, and careful closure of the dura.

Table 3

Surgical technique in 78 patients

Exclusive endoscopic approach	66
Endoscopic and neurosurgical approach	9
Endoscopic and limited orbital approach	3
Total	78

Peroperative and postoperative antibiotherapy was routinely given in all patients.

There were no cases of deliberate preoperative chemotherapy in primary patients. We did not perform any peroperative chemotherapy.

Anatomopathologic examination was performed on all surgical specimens. Frozen sections were not obtained systematically. Surgical margins were found to be clear in 67 patients, infiltrated in 7 patients and were interpreted as being infiltrated in 4 patients due to tearing of the surgical specimen.

Radiation therapy was used in all but 8 patients. Post-operative radiation therapy was used in 61 patients, and pre-operative radiation therapy in 9 patients. External beam megavoltage radiotherapy was started as soon possible after surgery (mean delay was 4 weeks) and patients received an average of 65 Gy in 7 weeks. There was no additional brachytherapy. No elective treatment to the neck was given.

Results

Survival

Fig. 1 shows the overall survival and disease-free survival for the whole group. 2-years and 5-years estimates were respectively 73.1% and 54.9% for overall survival, whereas DFS estimates at 2- and 5-years were 63.4% and 52.3.9%.

At univariate analysis no significant prognostic effect on survival was detected for age or sex.

A significantly better prognosis was evident for adenocarcinomas in comparison to other histologies (p = 0.016, fig. 2).

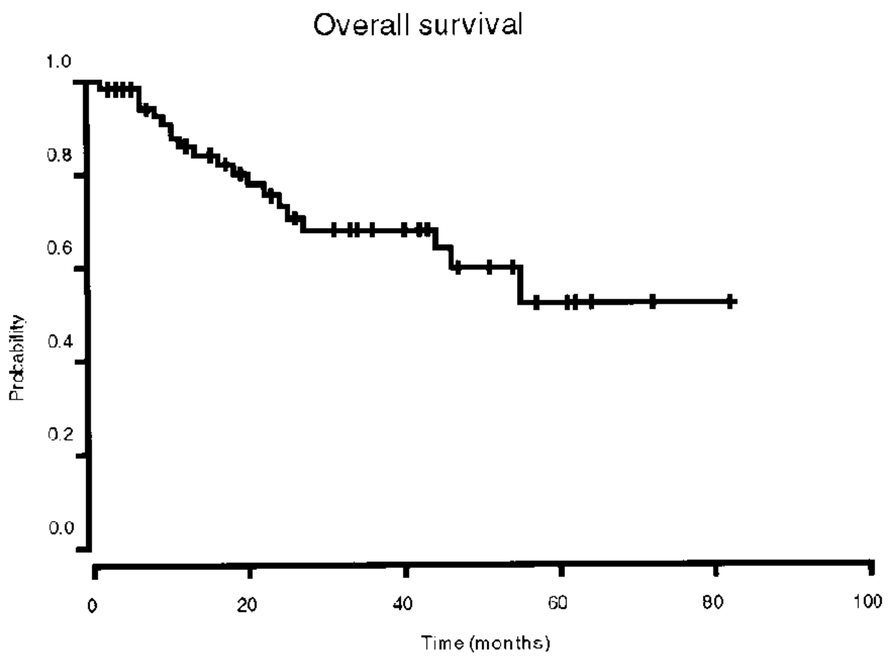

Fig. 1
Overall survival

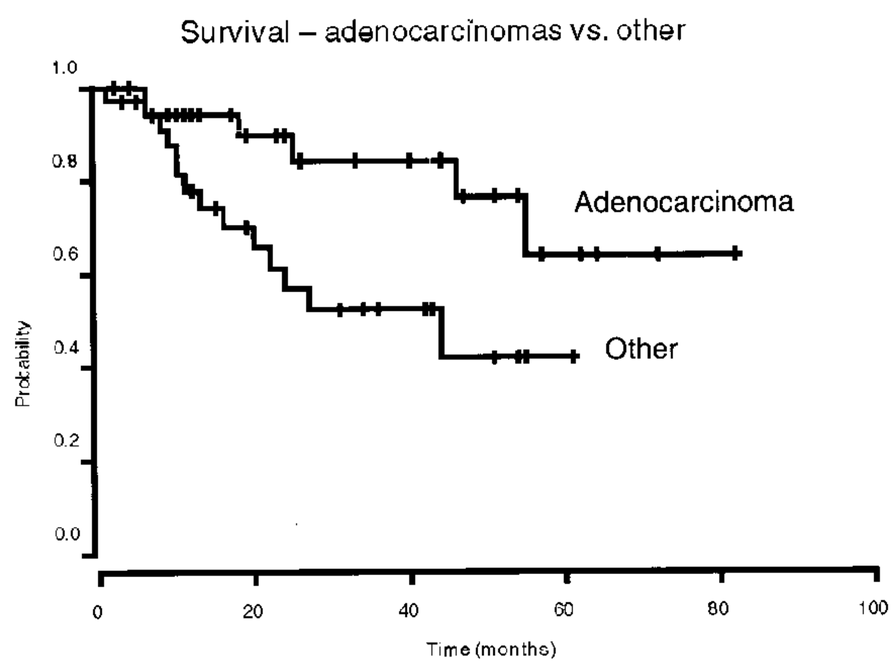

Fig. 2
Adenocarcinomas vs. other histologies

Survival estimates at 2-yearss and 5-yearss were 89.8% and 63.8% for adenocarcinoma patients, and 56.9% and 42% for other histologies.

Patients who were treated by a pure endoscopic approach displayed a better prognosis than patients operated by a combined endoscopic and external approach (p = 0.032, fig. 3). Survival estimates at 2-yearss and 5-yearss were 79% and 57.6% for endoscopic patients, and 43.7% and 29.1% for external/endoscopic patients.

In the adenocarcinoma subgroup patients who were treated by a pure endoscopic approach also displayed a better prognosis than patients operated by a combined endoscopic and external approach (p = 0.002, fig. 4). Survival estimates at 5-yearss were 67.2% for endoscopic patients, and 21.6% for external/endoscopic patients.

The staging of the tumor had little influence on survival except for T 1 lesions. Fig. 5 shows no significant survival advantage between T2, T 3 and T 4 patients (p = 0.383)

The relationship between survival and the number of subsites involved by the tumor was assessed by a Cox regression model. This number was found to be a significant factor of survival and relapse for all histologies with the exception of adenocarcinomas (p value = 0.0103).

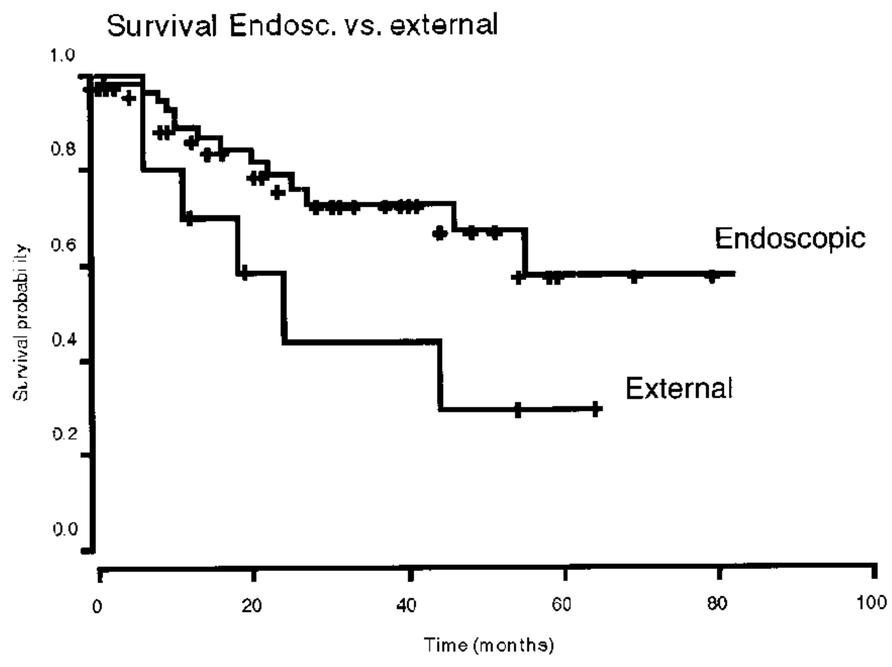

Fig. 3
Endoscopic approach vs. external approach

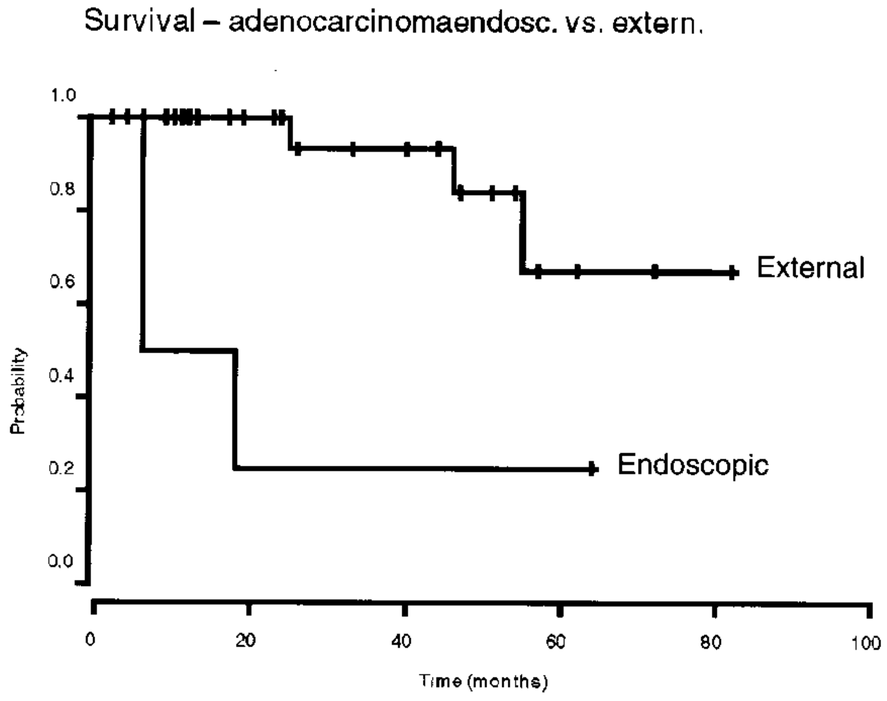

Fig. 4
Adenocarcinoma. Endosc. vs. extern

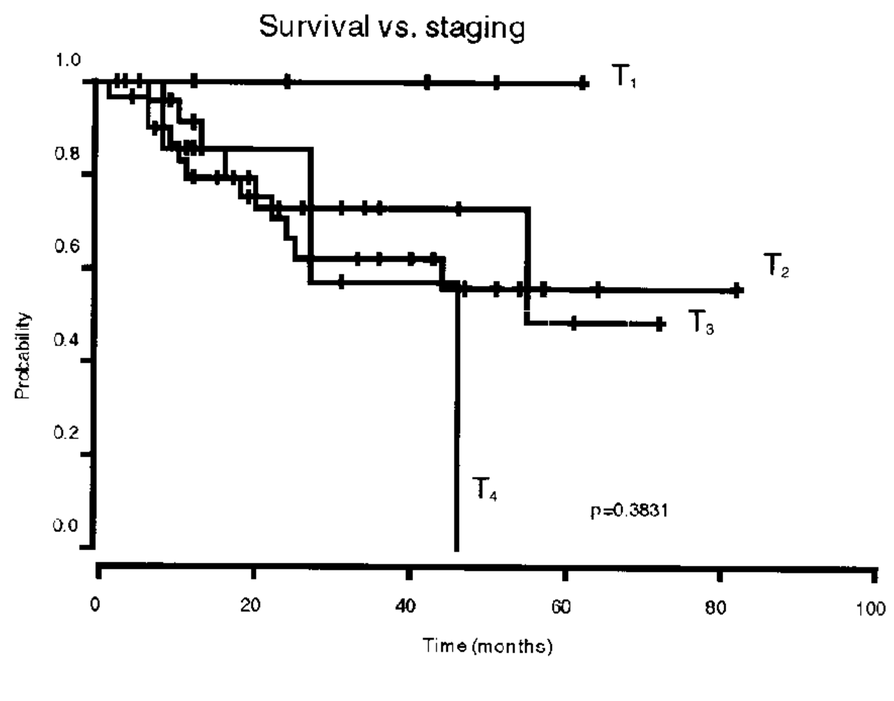

Fig. 5
Survival vs. TNM

Local control

Of the 78 patients 49 (62.8%) remained free of disease (Table 4).

16 patients (20.5%) presented with local recurrence.

6 patients (7.7%) suffered a metastatic failure without evidence of local relapse.

7 patients (9%) presented a simultaneous local and metastatic failure.

16 patients (20.5%) developed local recurrence. Among them 12 patients had adenocarcinoma.

The mean delay for observing local relapse was 14.7 months ±15.9m. Of these patients five were operated for limited recurrence by endoscopic management and remained free of disease. Six patients were operated by an external approach and four of them were salvaged. Five patients were not suitable for secondary surgery (table 5).

Table 4
Results and site of recurrence

	All histological types (n = 78)	Adenocarcinoma (n = 40)
NED	49 (62.8%)	26 (65%)
Local recurrence	16 (20.5%)	12 (30%)
Metastatic recurrence	6 (7.7%)	2 (5%)
Metastatic and local recurrence	7 (9%)	0 (0%)

Table 5
Modalities of treatment for local recurrence and results

Salvage treatment	All histological types	Adenocarcinoma	Delay of recurrence after initial surgery	Control of recurrence	Disease free interval after salvage surgery
Endoscopic surgery	5	5	12.8 ± 7.7	5 (100%)	48 ± 19.7 (5 patients)
External surgery	6	6	24.3 ± 21.9	4 (66%)	51.5 ± 29.4 (4 patients)
No surgery	5	1	5 ± 4.5	0 (0%)	0
Total			14.7 ± 15.9	9 (56%)	

In the adenocarcinoma group 12 patients out of 40 presented with local relapse (30%). The mean delay for these recurrence was long as indicated in table 5.

Nine out of these 12 patients (75%) were salvaged either by another endoscopic procedure or by external surgery and remained free of disease after an appreciable follow-up. A delayed recurrence resulted in a better long term prognosis.

Distant failures (table 6) occurred in 13 patients (16.6%).

Table 6

Distant failures

Metastatic	6	Adenocarcinoma = 2 Malignant melanoma = 2 Others = 2
Metastatic and local	7	Esthesioneuroblastoma = 1 Squamous cell carcinoma = 2 Malignant melanoma = 1 Others = 3

Positive surgical margins (table 7) were clearly associated with a bad prognosis as all these patients but one presented a local or a local plus metastatic relapse.

Table 7

Surgical margins

	Local failure	Metastatic and local	Metastatic
Negative *n = 67*	10 *(14.9%)*	3 *(4.5%)*	5 *(7.4%)*
Positive *n = 11*	6 *(54.6%)*	4 *(36.4%)*	1 *(9%)*
P value			

Complications

There was no postoperative death. Non-lethal complications were pneumocephalus, diplopia, and personality change. One patient operated by a combined approach developed acute postoperative tension pneumocephalus with severe neurological depression and required repeated needle aspiration of intracranial air. The patient recovered incompletely and died from respiratory infection at 3 months postoperatively. One patient with frontal brain resection had personality changes noticed by the family. One patient suffered radiation optic neuropathy with unilateral blindness.

Diplopia was mainly mild and transient. Nasal crusting was frequent but with local care, gradually improved over the weeks after radiation therapy. No postoperative bleeding occurred.

There was no meningitis, cranial bone infection, orbital cellulitis or frontal sinus infection.

Cosmetic results were excellent.

Discussion

The time-honoured lateral rhinotomy approach, as described by MOURE and SÉBILEAU (14), associated with radiotherapy, remained for a long time the cornerstone in the management of ethmoidal carcinoma (17). This classic transfacial approach provides through an osteoplastic maxillectomy good access to the maxillary sinus, ethmoid sinus, nasal fossa and orbit.

Reported 5-years survival rates range from 25% to 65% (17-20). Since the advent of the craniofacial approach there have been few recent reports of conventional surgery and radiotherapy. TIWARI *et al.* (20) reported in, 1999 their retrospective experience on 50 patients with ethmoid carcinoma previously untreated who were operated through a transfacial approach (with the exception of three patients operated by a craniofacial resection) and underwent a subsequent radiotherapy and brachytherapy. The overall 5-years survival was 65%. Adenocarcinoma patients had a 5-years survival of 59%. The morbidity was minimal and there was no mortality associated with treatment. A 38% local recurrence rate was observed whereas 24% of the patients developed distant metastases.

Complications of lateral rhinotomy include cosmetic deformities of the skin or of the upper jaw as a result of scar contraction, pain in the infraorbital area, radionecrosis of the nasal bones, epiphora and lacrymal dysfunction (8, 21).

Advances in surgical techniques that lessen cosmetic damage such as midface degloving, subfrontal approaches and endoscopic surgery may lead to better patient acceptance.

The midface degloving was initially described by Portmann and Retrouvey in 1927 (22), and then modified by MANIGLIA, CONLEY and PRICE (23). This approach allows good cosmesis and functional results if careful technique is applied but the approach to the superior boundary is limited. Simultaneous subcranial and midfacial degloving technique has been described for tumours involving the anterior skull base (24).

Maxillary swing approach (25-26) realises an extended osteoplastic maxillotomy and provides good exposure to the nasopharynx, the central skull base and infratemporal fossa.

The limitations of transfacial approach are encountered for lesions close to the ethmoidal roof, cribriform plate or invading the anterior skull base.

In this area craniofacial resection sees its main advantage with the ability to gain access to the superior boundary of the tumor. SMITH (27) in 1954 and KETCHAM (28) in 1963 first described this approach as allowing en-bloc resection in most cases. Since that time the technique has gained wide acceptance (29-40). Technical difficulties will be encountered when tumours have extension into areas that are difficult to access externally, such as the sphenoid sinus, orbital apex and frontal recess.

Reported survival rates at 3- and 5-yearss vary from 52 to 74% and 49 to 70%. However the incidence of major complications, including postoperative death is high, ranging from 4 -31% (20,31-39).

The psychosocial and functional effects of craniofacial surgery may be profound and the quality of life of these patients is often altered (41). JONES *et al.* (42) showed that among head and neck cancer patients those who had undergone craniofacial resection scored poorly in terms of quality of life. They reported persisting complaints in several aspects including headaches, altered vision, fatigue, anosmia, pain and anxiety.

Non-surgical treatments have been evaluated in the management of sinonasal neoplasms but at the present time are considered poorly effective.

The role of adjuvant chemotherapy in previously untreated, locally advanced patients is yet not well established (44-49). Some authors advocate the role of neoadjuvant chemotherapy in extended adenocarcinomas invading the skull base to help enhancing local control (47). However it does not allow them to perform a more conservative resection. Some studies have assessed the role of intraarterial chemotherapy with good local response in SCC (45). High local response rates have been described in SCC patients with neoadjunvant chemotherapy with a cisplatin based regimen (46, 48).

In 1985 KNEGT (49) reported his experience using topical 5-Fu in place of intraarterial 5-Fu, combined with low-dose radiation therapy and surgery. Should this approach prove itself effective, it would be a valuable adjunct in endoscopic sinus surgery for cancer.

Radiation therapy as a single technique has been shown to be relatively ineffective. In contrast the difference in 5-years survival rate after radiation alone and treatment involving excision of the tumor (with or without radiotherapy) is highly significant (43, 44, 50, 51).

As survival results have not dramatically improved over the 30 past years (52) lessening the sequelae associated with treatment seemed of utmost importance and our MIEM study was undertaken in this quality of life oriented approach..

Endoscopic procedures have been described for benign tumors such as inverted papillomas with a recurrence rate around 20-30% (53-56), for fibro-osseous lesions (57). Endoscopic skills developed by surgeons have allowed some difficult tumors such as angiofibromas (58) to be removed by this endoscopic approach.

HEFFNER (59) has reported favourable results from local resection or polypectomy in low-grade adenocarcinoma of the ethmoid sinus.

Early reports from STAMMBERGER (53) and ARNHOLD-SCHNEIDER (60), followed by

HOSEMANN (61), DRAF (62), JORISSEN (63), DAELE (64), ANDERHUBER (58), STAMMBERGER (65), SHAH (66) have indicated successful endoscopic management for malignant tumors in selected cases.

The MIEM of ethmoidal tumours requiring a simultaneous neurosurgical approach has also been described (64, 67, 68).

In contrast some authors regard endoscopic nasal surgery as having no place at all in malignancy, considering its main value to be in diagnostic biopsy and postresection follow-up (69-71). These authors consider it unlikely that patients with malignant lesions can be cured by endoscopic technique and state that the use of endoscopes should be to control bleeding or for palliation.

The statement that monobloc resection requires wide exposure is not confirmed by our surgical findings. Wide exposure does not mean wide margins, as ethmoid sinus cancer surgery cannot be a wide margin cancer surgery. We were able in most cases to gain circumferential access to the tumor through MIEM in the nose and the paranasal sinuses. In limited invasion of the floor of the anterior cranial fossa careful fraisage of the bone was performed and the anticipated CSF fistula was immediately closed by mucosal graft and fibrin glue (16) (fig. 6-7). However, when the floor of the anterior cranial fossa is widely invaded by tumor any nasal approach would be insufficient leaving portions of tumor adherent to the frontal dura or spreading along the olfactory rootlets at the cribriform plate. We then employed a modified procedure using an endoscopic and neurosurgical approach, already reported by us and others (64, 67, 68) (fig. 8).

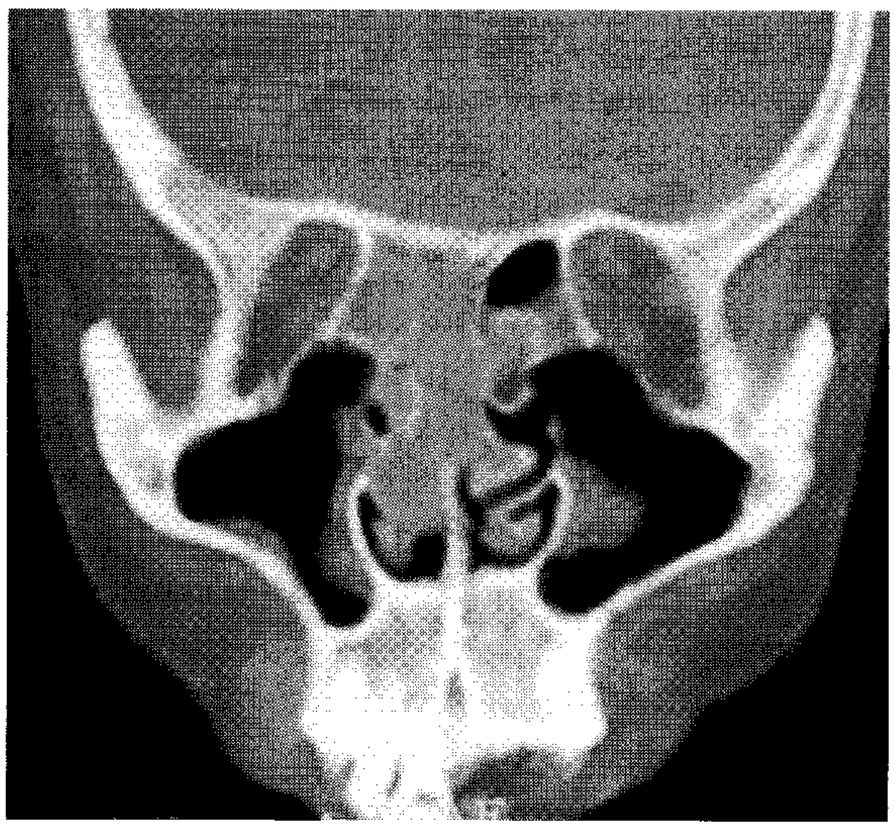

Fig. 6
Pre-operative view of ethmoidal carcinoma

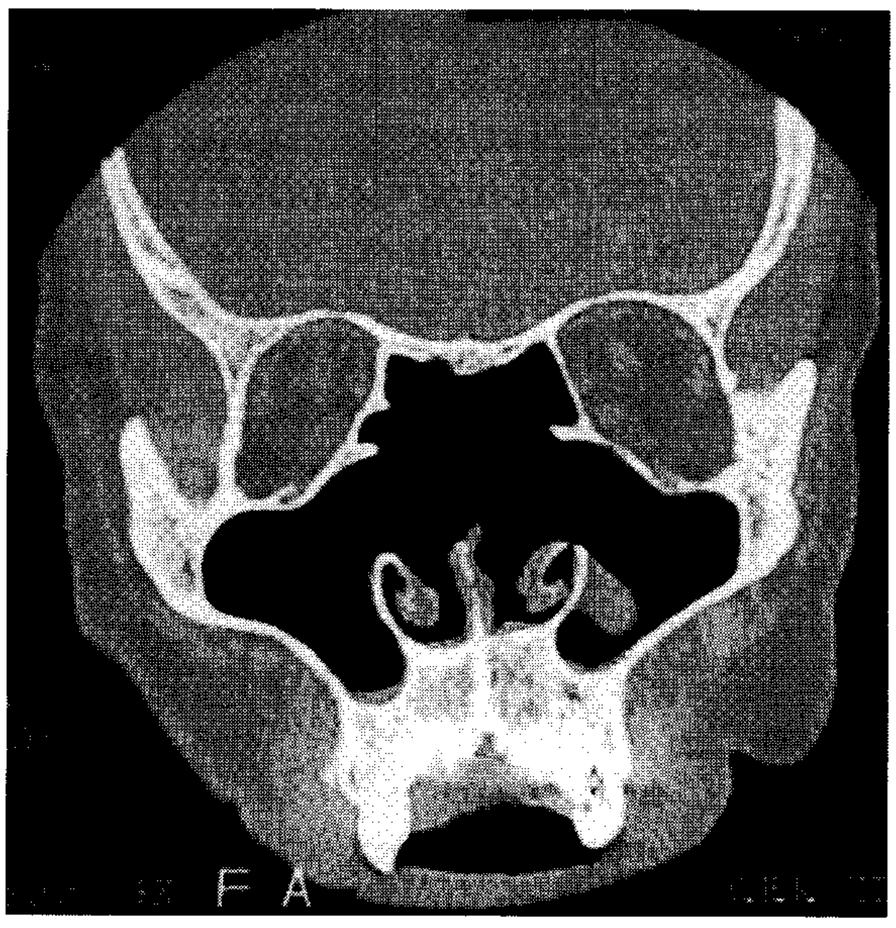

Fig. 7
Post-operative scan one-year after endoscopic resection

The need and the questionable reality of *en bloc* resection has been challenged by many authors (20, 31, 33, 35, 68, 71, 72).

Because of the inherent structure of the paranasal sinuses and skull base, a tearing of the surgical specimen or a cancer transection may happen, especially in the posterior ethmoid area and in the sphenoid sinus before clear margins are obtained. This is not a specific drawback of MIEM as these limitations are also encountered with transfacial approaches and even with the craniofacial approach. In some cases the location of the disease indicates that no meaningful *en bloc* resection is possible. As an example, an *en bloc* resection for invasion of the sphenoid sinus would require sacrifice of the internal carotid artery, as underlined by CLAYMAN (72). The nature of

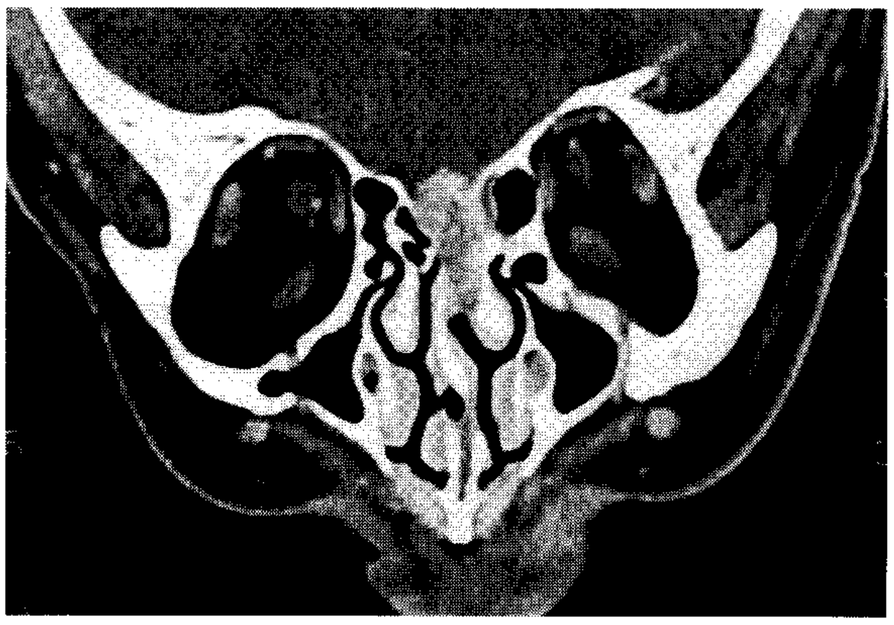

Fig. 8
Ethmoidal carcinoma with intracranial invasion, treated by endoscopic resection and neurosurgical approach

the surgical specimen may cause trouble in assessing the histologic margins and this was the main reason for not performing a systematic frozen section analysis.

Shah (30) reported that the local control rate in-patients with positive and negative frozen section examination was similar, but surgical excision could be completed with frozen section.

Early diagnosis, adequate staging, and careful preoperative planning of surgery with complete resection and healthy margins influence the survival rates. We observed with MIEM that outcomes in term of survival and local control are at least equal to standard external techniques. Moreover, excellent functional results and better overall quality of life are obtained and are important endpoints when assessing the validity of the technique. With MIEM, complications of external surgery by lateral rhinotomy, such as late cosmetic deformities or radionecrosis of the nasal bones were not observed.

The rationale for a limited orbital approach in three of our patients was to enhance the post-treatment quality of life. CHEESMAN (38), and SHAH (30) in refuting previous authors (74), state that there is no increased survival in patients subjected to orbital exenteration.

Comparison of literature data dealing with MIEM is difficult as most authors report spo-

Table 8
Advantages and limiting factors for endoscopic tumour surgery

Advantages	'Quality of life' approach : low morbidity, excellent cosmetic results
	Similar local control rate and survival rate
	Good access to sphenoid sinus, orbital apex in comparison to external approach
	Minimal blood loss
	Prevention of sequelae associated with RXT
Limitations	Bone resection
	Difficulty in controlling the superior margin (also with external surgery)
	Massive infiltration of surrounding soft tissues, the orbit or the skull base
	Extension to the frontal sinus
	Not a 'no-touch' surgery
	Possible transsection of surgical specimen (also with external surgery)
	Technical difficulties

radic cases with good long-term results (58-64). ANDERHUBER *et al.* (58) reported a series of 23 patients with malignancy of the ethmoid and skull base. They observed a 26.6% local recurrence rate with a relatively short follow-up. STAMMBERGER (65) reported on the same continued series of 36 patients, some of them (5) being treated with a palliative intention. 7 local recurrences were observed in the curative group (22.6% recurrence rate).

It is no surprise that T 1 lesions have an excellent prognosis and seem ideally suitable for endoscopic resection.

For tumors of other stages, we believe that the choice between a wide external rhinological procedure and an endoscopically assisted one should not depend on previously accepted guidelines. A safe, en bloc tumor resection by MIEM with its advantages and limitations (table 8) should be based on a precise definition of the extension of the tumor and surgical experience of the operator.

Conclusion

Functional results as well as cosmetic considerations are of importance but the main goal of cancer surgery is to obtain adequate resection of disease with clear margins. The comparison

of outcomes in the literature and in our MIEM study, the largest reported to date, is an indication that adequate cancer surgery of the paranasal sinus and skull base is feasible under endoscopic guidance. As a consequence the MIEM approach should be regarded as an important adjunct in the skull base surgeon's armamentarium and should be performed by experienced endoscopists – the first surgical treatment being of paramount importance in the prognosis of the disease.

This technique is not applicable to all cases and must be tailored to the individual patient after careful pre-operative evaluation. The establishement of precise operative planning is a necessity.

When feasible MIEM results in low postoperative morbidity rate and a shorter hospital stay. The excellent cosmetic and functional results create better patient tolerance and a better quality of life.

Our study also emphasises the importance of long-term follow-up, especially in adenocarcinoma, as late recurrence may occur and as salvage surgery is often feasible in these patients.

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Yves Goffart, M.D.
ENT Department
CHR Citadelle
Bd XII de Ligne
B-4000 Liege, Belgium