MINI-REVIEW

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The impact of modern techniques on the recurrence rate of inverted papilloma treated by endonasal surgery*

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SUMMARY

Sinonasal inverted papilloma (IP) is a benign epithelial tumour which displays aggressive local behaviour, has a high local recurrence rate and the potential for malignant transformation. It is treated by surgical excision which must be thorough to avoid recurrence. Traditionally this was done by an open approach, but since the early 1990's endoscopic techniques have been increasingly employed and are now widely accepted for the treatment of IP. This has led to debate as to whether the access afforded endoscopically is adequate to treat IP without a higher recurrence rate.

Studies comparing the recurrence rates of open to endoscopic approaches have shown similar rates but open approaches are usually considered the gold standard for advanced disease, despite the higher morbidity.

Reviewing the literature we found that the recurrence rates with endoscopic surgery have improved significantly since the technique was first introduced and conclude that to accurately compare open and endoscopic techniques historical data, from the early days of endoscopic surgery, should be excluded as it does not truly represent the outcome with modern techniques. In doing this it is apparent that endoscopic surgery is the gold standard for the treatment of the vast majority of IP.

Key words: inverted papilloma, sinonasal

INTRODUCTION

Inverted papilloma (IP) is a benign epithelial tumour composed of well-differentiated columnar or ciliated respiratory epithelium having variable squamous differentiation [(1)]. It was originally described by Ward in 1854 [(2)] and accounts for 0.5-4% of nasal tumours [(3)]. The hallmark features of IP are its aggressive local behaviour, high local recurrence rate and potential for malignant transformation. Its incidence is estimated as 0.52 per 100,000, but 0.74 per 100,000 if all histological types of sinonasal papilloma are taken into account [(2)]. It is most common in white males in their fifth to seventh decade but can affect all ages.

Ever since the emergence of endoscopic techniques for the treatment of inverted papilloma [(4)] there has been some debate in the literature over the gold standard for treatment. The debate rests on the recurrence rate experienced with open techniques and the comparison with endoscopic approaches. The argument for open techniques is that the more open the approach, the better the access and the lower the chance of recurrence. By this rational the gold standard for treatment has been lateral rhinotomy with en bloc resection of the medial maxilla and radical ethmoidectomy.

In 2006 a meta-analysis comparing endoscopic with open techniques by Busquets and Huang [(5)] found a significantly lower recurrence rate in the endoscopic cohort (12%) compared with the open cohort (19%). In the same year a systematic review by Karkos et al. [(6)] cited recurrence rates of 12% for endoscopic and 17% for open techniques. The recurrence rates for the endoscopic groups in these studies include results from 1992 to the present, with a mean follow up $>$ 20 months.

Since the early years of endoscopic surgery for IP there have been significant advances in techniques and skills, supported by modern imaging and guidance techniques. Here we systematically review the literature and compare the recurrence rates of the early endoscopic cohorts with those of recent years. We look at how advances in the technique have impacted on recurrence rates and discuss the tools available to the modern rhinologist. We also compare these results with those quoted for open surgery and ask if we should still consider open surgery as the gold standard?

LITERATURE SEARCH

A literature search was performed of MEDLINE (1950 to Oct 2007), EMBASE (1974 to Oct 2007), CINAHL (1982 to

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Table 1. Studies (in chronological order) with data from endoscopic approaches to inverted papilloma.

Name of first author	Date published	No. of patients	Recurrence rate (%)	Follow up (mths)	Dates of surgery	No. patients with recurrence
Waitz [4]	1992	35	17	46	1976-1991	6
Stankiewicz [28]	1993	15	33	36	1988-1992	5
McCary [29]	1994	4	0	30		0
Buchwald [3]	1995	5	0	24		0
Raveh [30]	1996	9	22	26		2
Xu [31]	1996	14	7	>24		1
Peter [32]	1997	18	31	52		6
Sham [33]	1998	22	27	53	1990-1995	6
Chee [34]	1999	18	5.5	32.8	1993-1996	1
Tufano [35]	1999	33	15	20	1992-1997	5
Bertrand [36]	2000	85	17.6	41.9	1991-2000	15
Lund [37]	2000	37	8	45	1992-1998	3
Sukenik [22]	2000	19	21	36		4
Klimek [38]	2000	33	18	36		6
Han [17]	2001	19	10	50	1986-1999	2
Schlosser [39]	2001	21	19	41.9	1990-1996	4
Thorp [40]	2001	2	0	32		0
Krouse [16]	2001	7	14	40		1
Keles [41]	2001	13	23	27		3
Kuhn [42]	2001	28	7	22		2
Kraft [21]	2003	26	8	62	1990-1997	2
Lawson [43]	2003	30	12	62	1973-2001	4
Wormald [44]	2003	17	6	39.5	1993-2001	1
Baruah [45]	2003	6	17	21		1
Kaza [46]	2003	51	14	30		7
Llorente [47]	2003	26	8	60		2
Eviatar [48]	2004	40	18	26.8	1996-2003	7
Lee [25]	2004	43	9.3	25.3	1991-2002	4
Tomenzoli [49]	2004	47	0	55	1992-2002	0
Wolfe [50]	2004	50	14	31.1	1992-2001	7
Pasquini [51]	2004	36	3	74		1
Kamel [18]	2005	70	5.8	64	1990-2003	4
Busquets [5]	2006	28	11	22	1998-2004	3
Minovi [52]	2006	61	10	74	1989-2004	6
Zhang [53]	2007	19	16	23	1996-2002	3
Mirza [54]	2007	36	14	60	1985-2005	5

Oct 2007) using the key words "sinonasal inverted papilloma." Although Stammberger and Benninger published results of intranasal resection prior to 1992, the first results of truly endoscopic techniques were not published until this time.
A table was therefore constructed of all reports or case series published in the English language from 1992 to the present day. Studies where the mean follow-up was less than 20 months were excluded.

Two cohorts were constructed from this table. The historical cohort consisted of all those series published from 1992 to 2001, inclusive. The contemporary cohort was those series published from 2004 to the present day. These cohorts were chosen as they had similar numbers of patients. The recurrence rates for both cohorts were calculated and compared.
The overall recurrence rate was also calculated.

RESULTS

The recurrence rate for the historical cohort was 16.5% (72 out of 437 patients had recurrence, 95% CI: 13.0%- 20.0%) compared to 9.3% (40 out of 430 patients, 95% CI: 6.6%-12.0%) for the contemporary cohort. This demonstrates a statistically significant improvement in outcome as endonasal techniques have developed with time.

The overall recurrence rate derived from all studies from 1992 to the present day was 13% (129 out of 1023 patients), which is in line with recent reviews and analyses.

DISCUSSION

There is obvious overlap between the cohorts as the contemporary cohort includes cases operated on in the historical period. It was not possible to exclude this factor without the exact dates of surgery of each case, which were not available. This results in dilution of the contemporary results with historical data. In addition the historical cohort extends up to 2001 when some of the modern techniques had already come into use. Despite these factors that act to diminish the difference between the cohorts, there is still a statistically significant improvement in recurrence rates.

It was not possible to eliminate selection bias but one would suppose that as endoscopic techniques have improved increasingly complex cases would be attempted endoscopically. If this were the case it would again favour the historical cohort and diminish the magnitude of the improvement observed. It was also not possible to rule out a follow up bias and the percentage of cases lost to follow up has not been ascertained.

In this study we found a recurrence rate of 9% in the contemporary cohort. Recent meta-analyses [5,6] reported recurrence rates of 12% for endoscopic resection of IP and we found the overall recurrence rate to be 13%. We feel that the overall recurrence rate figure is an outdated figure as it includes results from as far back as 1992 when endoscopic sinus surgery was in its infancy. We suggest that this figure is abandoned as it no longer reflects the outcome with modern endonasal approaches. It would seem that a more realistic figure is probably less than 9%. We suggest it is likely that the recurrence rates with endoscopic surgery is less than 9% as our calculation for the contemporary cohort was still significantly tainted with historical data with a higher recurrence rate. Based on these findings it would seem that modern endoscopic techniques offer a significantly lower recurrence rate than open techniques which have been found to have rates of 17-20% [5,6].

The world of endonasal surgery continues to evolve at great pace. We now have the tools to deal with previously inaccessible sites. Angled endoscopes allow direct inspection of the most inaccessible areas facilitated by lens cleaning systems.

Camera systems now have far better magnification, monitors have better resolution and image guidance is available. Straight and angled microdebriders and burrs have been developed alongside malleable suction instruments and curettes.

These tools have been combined with a greater understanding of the disease, although the principles of surgery for IP are the same for open and endoscopic techniques. Case selection and pre-operative planning of the approach, assisted by CT and /or MRI to determine the exact site of origin of the tumour is essential. CT findings of IP can be non-specific as contrast resolution is insufficient to characterise the lesion or distinguish it from retained secretions within a sinus, although Yousuf et al. [7] found that areas of hyperostosis within the paranasal sinuses can be used to predict the site of origin of the tumour with a high degree of accuracy. Maroldi et al. [8], however, have shown that MRI has a positive predictive value of 95.8% for IP compared with 66% for CT [9]. This is based on the detection of the columnar pattern characteristic of IP seen on enhanced spin echo T1-weighted and turbo spin echo T2-weighted images on MRI. In the absence of extended bone erosion, this characteristic was also shown to distinguish IP from malignant tumours. In addition they were able to differentiate foci of carcinoma within an inverted papilloma. MRI is also invaluable to assess intracranial or intraorbital extension pre-operatively. Several studies have concluded, however, that MRI cannot consistently distinguish scar tissue from recurrent tumour [10-12].

Nasal contact endoscopy was introduced by Andrea et al. [13] into otolaryngology as a technique for the non-invasive differential of IP from inflammatory polyps. A prospective study by Romano et al. [14] showed the technique to have a good rate of correct diagnosis even in the case of inexperienced examiners.

Table 2. Krouse's staging system (2000) for inverted papilloma.

T1	Tumour totally confined to the nasal cavity, without extension into the sinuses. The tumour can be localised to one wall or region of the nasal cavity, or can be bulky and extensive within the nasal cavity but must not extend into the sinuses or into extranasal compartment. There must be no concurrent malignancy.
T2	Tumour involving the ostiomeatal complex and ethmoid sinuses and/or the medial portion of the maxillary sinus, with or without involvement of the nasal cavity. There must be no concurrent malignancy.
T3	Tumour involving the lateral, inferior, superior, anterior, or posterior walls of the maxillary sinus, the sphenoid sinus, and/or the frontal sinus, with or without involvement of the medial portion of the maxillary sinus, the ethmoid sinuses or the nasal cavity. There must be no concurrent malignancy.
T4	All tumours with any extranasal/extrasinus extension to involve adjacent, contiguous structures such as the orbit, the intracranial compartment, or the pterygomaxillary space. All tumours associated with malignancy.

Results from this technique can be combined with radiological findings to optimise the pre-operative diagnosis and surgical planning.

Several staging systems have been proposed, with the Krouse system probably the most commonly in use. The TNM [15], Krouse [16] (Table 2) and Han [17] systems focus on the extent of the disease whereas the Kamel [18] staging system focuses entirely on whether or not the tumour originates in the maxillary sinus. In 2007, Cannady et al. [19] proposed a new staging system based on the recurrence rates associated with different tumour sites and designed to provide "prognostic information in the endoscopic era". These staging sytems allow the data to be more closely scrutinised as demonstrated by Sautter et al. [20] who showed no statistical difference in recurrence for open versus endoscopic cases when classified by Krouse staging, although when all cases were analysed together by Krouse stage, there was a significantly higher recurrence rate for more advanced disease. They conclude that the risk of recurrence is more likely related to extent and biological features of the tumour than to whether an endoscopic or open approach is used. In addition they found that the significantly higher recurrence rate for secondary compared to primary IP was independent of whether an endoscopic or open approach was used. This was also the conclusion of Han et al. [17] and supports the use of endoscopic techniques as the primary surgical approach given its lower morbidity.

Some studies advocate the use of pre-operative antibiotics and steroids [21-23] which are thought to reduce concurrent oedema and infection and can make identification of the site of the tumour origin easier. Intra-operatively the diseased mucosa should be resected with a wide margin and the underlying bone drilled with a diamond burr to remove microscopic mucosal remnants. Suspicious areas can be submitted for frozen section and further resection performed if necessary. The result should be a marsupialised sinus that is easy to inspect at follow up in the out-patient clinic. All tissue should be sent for histology which is made possible by the use of suction traps and socks with the microdebrider. A study by McGarry et al. [24] confirmed that it is possible to use these specimens for a reliable histological diagnosis, although there are studies that do not share this opinion. Lee et al. [25] advocate the use of sequential segmental endoscopic surgery (SSES) as a technique of removing bulky tumours, not amenable to en bloc resection, usually in three segments. This technique avoids the use of the microdebrider to debulk large tumours and provides a more conventional histological specimen, albeit in several sections.

It has been demonstrated that tumours originating in the nasal cavity tend to be pedunculated with a narrow base compared to those originating in the maxillary sinus, which tend to have a more diffuse origin. This unfortunate fact, combined with

the difficulty in accessing this area, contributes to the higher risk of recurrence of tumours originating in the maxillary sinus. This is the basis of the Kamel staging system [18] which advocates a radical medial maxillectomy for tumours arising in the maxillary sinus, based on a series of 70 patients. In Transnasal Endoscopic Medial Maxillectomy (TEMM) there is endoscopic en bloc resection of the tumour with the lateral nasal wall and entire lining of the superior, lateral, inferior, anterior and posterior walls of the maxillary sinus and/or the lamina papyracea and adjacent medial wall of the orbit. The most challenging area to access is the anterior wall of the maxillary sinus. Techniques such as a contralateral transeptal approach may offer the angle required to access the anterior wall. To enable maximum exposure of this region the frontal process of the maxilla (anterior buttress) is removed with a cutting burr. It is important to drill away the anterior buttress. The medial wall of the sinus is lowered level with the floor of the nasal cavity preserving the mucosa of the nasal cavity if healthy. A canine fossa puncture may be considered as an alternative to aid an endoscopic approach but can result in prolonged facial swelling and check discomfort and there is a risk of oroantral fistula. TEMM also allows thorough examination of the sinus at follow up but may carry the complication of reflux through the nasolacrimal duct (a minor problem) and some patients complain of the "empty nose syndrome". Although some studies advocate performing a formal dacryocystorhinostomy our experience suggests that this is not necessary providing the nasolacrimal duct is identified and cleanly sectioned.

Safe resection in the frontal recess and sinuses has been facilitated by image guidance and the use of angled burrs including the Rad 55, Frontal Finesse and 70-degree diamond burr (Medtronic). Tumours extending beyond the frontal recess can be safely resected with the modified Lothrop (Draf III) procedure where necessary. By using a 70-degree diamond burr and front angled Kerrisons the area from the lamina papyracea to the middle turbinate lamella can be resected. A 45- or 70-degree endoscope is used to visualise the procedure which results in excellent access to the sinus with minimal damage to the surrounding normal tissue. Where there is gross lateral extension of the sinus and the disease or the anterior wall of the sinus is widely involved, a combined endoscopic and osteoplastic flap approach may be considered.

A hyperpneumatised sphenoid sinus containing IP may present an access problem which may be overcome by adopting an expanded approach such as an endoscopic transethmoidal/pterygoidal approach. This is particularly useful for tumours extending into the pterygopalatine fossa and those extending in a laterally pnematised sphenoid.

Advances in the fields of radiology and immunohistochemistry are having an equal impact on our understanding and management of this condition. The incidence of Squamous Cell Carcinoma associated with IP has been reported to be less than 2% by Woodson et al. [26] but as high as 17% by Bielamowicz et al. [27] but greater understanding of the gene expression, including p53, p63, p21, p27, and Ki-67, as well as surface markers such as CD44, will help us to identify those at risk of malignancy and target treatment appropriately.

There is no denying that open procedures can offer good surgical access but this should be weighed against the significant morbidity associated. Common complications include epiphora, epicanthal scarring or webbing, dacrocystitis, telecanthus, diplopia, infraorbital hyperaesthesia and external scars.

We believe that endoscopic surgery by an experienced rhinologist with the full armoury of modern equipment is now the gold standard. The limit for the endoscopic approach is the periorbita when there is intraorbital extension but this can be combined with external techniques if necessary. Endoscopic duroplasty is possible for intracranial extension although neurosurgical support must be available. It should also be pointed out that it is always possible to convert from an endoscopic to an open procedure, as it is also possible to utilise endoscopic equipment and techniques in a planned open procedure.

CONCLUSION

Since the introduction of endoscopic approaches to IP in 1992 the technique has radically improved with advancements in the technology available. This has lead to its widespread use in increasingly complex cases of IP. In this study we show that the recurrence rates associated with the endoscopic approach have fallen significantly despite its use in more advanced disease.

However, to calculate an accurate figure for this it would be necessary to obtain exact dates of surgery and the stage of the disease for each endoscopic case referred to in the literature.

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