Frontal Sinus Surgery: Indications and Outcomes in Chronic Rhinosinusitis

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This thesis is dedicated to my incredible family who have sacrificed so much, and supported me without reservation.

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Thesis declaration

This work contains no material which has been accepted for the award of any other degree or diploma in any university or other tertiary institution to Yuresh Naidoo and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text.

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Dr Yuresh Naidoo

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Long-term results after primary frontal sinus surgery

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Risk factors and outcomes for primary, revision, and modified Lothrop (Draf III) frontal sinus surgery.

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Abbreviations

ADSS	Adelaide Disease Severity Score
AFS	Allergic fungal sinusitis
AFRS	Allergic fungal rhinosinusitis
AR	Allergic rhinosinusitis
ARS	Acute rhinosinusitis
A-P	Anterior-Posterior
CL	Caldwell-Luc
CRS	Chronic rhinosinusitis
CRSsNP	Chronic rhinosinusitis without nasal polyps
CRSwNP	Chronic rhinosinusitis with nasal polyps
CFT	Canine Fossa Trephination
CT	Computed Tomography
rCRS	Refractory CRS
EM	Eosinophilic mucus
ESS	Endoscopic sinus surgery
EM-CRS	Eosinophilic Mucus Chronic Rhinosinusitis
ECRS	Eosinophilic Mucus Chronic Rhinosinusitis
EMLP	Endoscopic Modified Lothrop Procedure
FDO	Frontal Drillout
FESS	Functional Endoscopic Sinus Surgery
IgE	Immunoglobulin E

INCS	Intranasal Corticosteroids
L-M	Lund-Mackay
MMA	Middle Meatal Antrostomy
MRI	Magnetic resonance imaging
NAFES	Non Allergic Fungal Eosinophilic Sinusitis
NANFES	Non Allergic Non Fungal Eosinophilic Sinusitis
NSAID	Non-steroidal Anti-inflammatory Drug
OMU	Osteomeatal Unit
OR	Odds Ratio
P. aeruginosa	*Pseudomonas aeruginosa*
PROM	Patient Reported Outcome Measure
QoL	Quality of Life
S. aureus	*Staphylococcus aureus*
SNOT-20	Sino-nasal Outcome Test 20
VAS	Visual Analogue Scale

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Thesis summary

The research described in this PhD thesis follows an extensive literature review of the role of the medical and surgical management of CRS. Despite the utilization of surgery to alleviate the symptoms of CRS refractory to medical therapy, there are clear deficiencies in our understanding of what type of surgery to perform, and how extensive this surgery should be so as to maximize long-term symptom alleviation and control. Particular controversy exists regarding addressing the frontal sinus with a wide variety of philosophies employed, but with limited scientific rationale to support such approaches.

Chapter two describes a prospective study to validate a quality of life tool, the Adelaide Disease Severity Score. This study showed a simple 5 question tool directly related to sinus symptoms and visual analogue quality of life score correlated very highly with other more complex rhinological quality of life tools – the SNOT 20/22. It further correlated with radiological disease burden (Lund Mackay CT score) and endoscopic disease (Lund Kennedy endoscopic score) burden. This study validated our use of this tool to measure quality of life and symptom improvement in patients undergoing surgery.

Chapter three describes a detailed retrospective study of the outcomes of primary frontal sinus surgery. This is the largest study in the literature of

primary frontal surgery and forms the basis to support an approach where the diseased frontal sinus should be addressed surgically to optimize long-term outcomes. It also identified that certain anatomical factors such as a narrow frontal ostium seemed to play a role in persistence of symptoms. This raised questions as to whether these outcomes were as successful for revision and extended frontal sinus surgery. Were there identifiable risk factors for success and failure?

The fourth chapter describes the outcomes of primary and revision standard frontal sinus surgery and investigates which patient, anatomical and disease factors were poor prognostic factors for failure. It identified a select cohort of patients that would benefit not just from frontal sinus surgery, but extended frontal sinus surgery (EMLP) in the first instance.

The final chapter investigates the outcomes of extended frontal sinus surgery (EMLP) and seeks to determine the risk factors for its success and failure. This study found that the EMLP had excellent outcomes in the majority of patients, but there was a significant minority of patients that had persistence of symptoms. The relevance of the host immune system response to sinonasal microorganisms, and anatomical risk factors was also explored and lays open the basis for further study.

Systematic review of the literature

chapter 1

1.1 CHRONIC RHINOSINUSITIS - BACKGROUND

1.1.1 Rhinosinusitis defined

The term 'rhinosinusitis' describes a constellation of disease entities with a common feature - inflammation of the mucosa lining the nasal cavity and the paranasal sinuses[1,2]. Rhinosinusitis is divided temporally based on the duration of inflammation and symptoms:

1. Acute Rhinosinusitis- <4 weeks duration
2. Subacute Rhinosinusitis- 4-12 weeks
3. Recurrent Acute Rhinosinusitis- Four or more episodes per year with complete resolution between episodes. Each episode lasts at least seven days
4. Chronic Rhinosinusitis- >12 weeks

The abundance of guidelines that exist for this disease entity points to its complexity. Controversy surrounds almost every aspect of rhinosinusitis and is highlighted by a multitude of guidelines published within the past 15 years. A number of multi-national expert panels have recently published guidelines addressing the definitions, diagnosis, and management of rhinosinusitis[1-6]. These guidelines have been based on the available evidence base of published literature as well as expert opinion of leaders in the field.

Acute Rhinosinusitis (ARS) is a bacterially mediated infectious disease with *Streptococcus pneumoniae*, *Haemophilus influenzae, Moraxella catarrhalis* and *Streptococcus pyogenes*[7] the common inciting organisms. The pathologic hallmarks of acute inflammation, such as fluid exudation and neutrophil emigration, are consistently found. Key diagnostic criteria include symptoms following upper respiratory tract infection, purulent nasal discharge, unilateral maxillary sinus tenderness, maxillary tooth or facial pain (especially unilateral), and a history of initial improvement followed by a worsening of symptoms[8,9]. Complications are uncommon with the majority settling with empirical antibiotic therapy[10].

CRS shares many of the symptoms of ARS. However, distinguishing between the acute forms of rhinosinusitis and CRS has both clinical and scientific importance. In CRS, the duration of symptoms and signs persist for greater than 12 weeks. Fluctuations may occur but there is never complete resolution. This enables distinction between ARS, subacute rhinosinusitis, and recurrent ARS.

The current belief is that CRS is not one disease but a complex disease process of separate but related entities with differing clinical and pathological manifestations. According to the most recent European position paper on rhinosinusitis and nasal polyps (EP^3OS)[1,2], the term chronic rhinosinusitis describes inflammation of the nose and paranasal sinuses which is associated with two or more symptoms lasting >12

weeks. This should be supported by demonstrable disease. Symptoms must include at least one of:

- nasal blockage, obstruction or congestion, or
- nasal discharge (anterior or posterior),

and may include facial pain or pressure, and hyposmia or anosmia. Disease can be demonstrated by endoscopically or radiologically. Endoscopic evidence includes findings of polyps, mucopurulent discharge (mostly from the middle meati), mucosal oedema or obstruction. Radiological evidence includes findings on CT such as thickened mucosa within the ostiomeatal complex and / or the paranasal sinuses[1,2].

1.1.2 Epidemiology

12.5% of the American population, or 31 million people in the US alone is affected by sinusitis (acute, and chronic types) [11-13]. 9.0% of Australians suffer from CRS symptoms[14]. Europe has a significant regional variation in prevalence ranging between 6.9% Brandenburg, Germany and Helsinki, Finland to 27.1% in Coimbra, Portugal. Overall the prevalence of CRS in Europe is 10.9%.[15]. This contrasts with the prevalence in Korea, with a rate of CRS of only 1% [16].

Given its prevalence, it is not surprising CRS has significant socioeconomic implications. Annual estimated direct health care costs for CRS in the US is approximately $US 5.8 billion. This includes the costs of outpatient and emergency attendances as well as approximately half a million surgical procedures annually [17]. CRS also accounts for significant

indirect costs to the economy from decreased productivity and work absenteeism. In the US, CRS results in over 70 million days of restricted activity annually [6].

Patients with CRS visit primary care clinicians twice as often as those without the disorder, and have five times as many prescriptions filled[6]. CRS is the principal diagnosis in 14 million visits to a health care facility in the US, compared to 3 million for ARS[18]. CRS is therefore, the second most prevalent chronic health condition in the US population[11-13]. It is extremely detrimental to the quality of life of those suffering from it, and quality of life measures are similar or worse than chronic obstructive pulmonary disease (COPD), chronic back pain, and congestive cardiac failure[19,20].

1.1.3 CRS –clinical classification

Although our understanding of CRS has advanced greatly, there is still a lack of consensus as to the categorization of this disease. The simplest, and most common division of CRS is based on the presence (CRSwNP) or absence (CRSsNP) of nasal polyposis [4].

Polyps are macroscopically grape-like projections of tissue pedicled from the sinonasal mucosa. They can originate from any part of the sinonasal mucosa but are most often seen originating from the middle meatus and ostiomeatal complex.

Polyps are histologically benign, non-granulomatous inflammatory tissue. The underlying loose connective tissue consists of mixed inflammatory cells, marked stromal oedema, glands and capillaries[21]. They are usually covered with typical respiratory epithelium- ciliated pseudostratified epithelium with goblet cells. Eosinophils are the most common leukocyte within nasal polyps; however, they can also contain neutrophils, mast cells, lymphocytes, monocytes, and fibroblasts. The eosinophil content of nasal polyps is greater in the presence concomitant asthma, aspirin sensitivity, or both[22,23].

CRS patients with a Western countries are more likely to have polyps with an eosinophilic predominance whereas in Asian patients and in cystic fibrosis, neutrophils predominate [24].

Besides being a relatively simple classification based on endoscopic findings, the differentiation between CRSwNP and CRSsNP has clinical implications. Patients in the CRSwNP group tend to complain of predominantly obstructive symptoms with associated anosmia. On the other hand CRSsNP patients are more likely to complain about anterior and posterior rhinorrhea and sinus pain. The nature of the predominant inflammatory cell (eosinophilic or neutrophilic) has significant implications for treatment. Eosinophilic polyps appear to be more responsive to corticosteroid treatment than non-eosinophilic polyps[25]. The prognostic implications of nasal polyps are conflicting. The presence of nasal polyposis was shown to be the most important predictor of poor outcome following ESS in a 5-year prospective outcomes trial[26]. Another study showed that CRSwNP patients have significant symptomatic improvement following ESS, but found a higher revision rate than CRSsNP[27]. Contrary to these findings, a study of 132 patients[28] found that the success rate (based on symptom reduction) was higher in CRSsNP patients but this was not statistically significant,. Other studies have likewise found no adverse effect of nasal polyps on post-surgical outcomes[29,30].

Apart from nasal polyposis, other important differentiating factors include the presence of absence of eosinophilic mucus, and fungal hyphae or bacteria within sinus mucus[4]. A histological sub-classification based on the presence or absence of eosinophilic mucus (EM) has been proposed[31]. EM consists of necrotic eosinophils, mixed inflammatory infiltrate, and Charcot-Leyden crystals - the byproduct of eosinophils[31]. The presence of EM or peripheral eosinophilia has been shown to be a predictor of the need for revision surgery in a small study of 56 patients[32]. EM-CRS patients are often sub-classified based on the presence or absence of fungal elements in the mucus, and fungal allergy as demonstrated in Table 1.1. However a recent study has found no distinction between these subgroups on clinical or immunological grounds[33].

Table 1.1: Subdivision of EM-CRS based on the presence of fungi in the mucosa and systemic fungal allergy.

		Fungal Allergy	
		Present	Absent
Fungal presence (culture or histology)	Present	Allergic fungal sinusitis (AFS)	Non-allergic fungal eosinophilic sinusitis (NAFES)
	Absent	AFS-like	Non-allergic, non-fungal eosinophilic sinusitis (NANFES)

1.1.4 Aspirin sensitivity

In 1968, Samter described a large cohort of patients with adult onset asthma, nasal polyposis and aspirin hypersensitiviy[34]. 36%-96% of aspirin sensitive patients have nasal polyps, and a similar percentage have radiographic evidence of mucosal abnormalities consistent with CRS[35]. Furthermore, aspirin sensitive patients with nasal polyposis have a high rate of early recurrence following surgical intervention, often requiring revision surgery[36]. As a consequence surgery to control symptoms in this group has been frustratingly unsuccessful.

The pathogenesis of this condition is incompletely understood. Abnormal prostaglandin and leukotriene metabolism is thought to play a role. Arachidonic acid is converted to prostaglandins by the action of cyclo-oxygenase, or leukotrienes by leukotriene synthase. Aspirin and other non-steroidal anti-inflammatory drugs exert their effect by inhibiting cyclo-oxygenase. By blocking cyclo-oxygenase, arachidonic acid is preferentially converted to leukotrienes. Leukotrienes are powerfully bronchoconstricting, and enhance capillary permeability thereby inducing shortness of breath, rhinorrhea and nasal congestion[37,38]. The basal levels of leukotrienes in patients with Samter's triad are higher[39] than controls and these levels increase to a greater extent than normal controls after exposure to aspirin and other inhibitors of cyclo-oxgenase[40].

The diagnosis of aspirin sensitivity has implications for research and clinical outcomes for the patient, as aspirin sensitive patients may benefit from desensitization[35,41].

1.1.5 Asthma

There appears to be a clinical association between asthma and chronic rhinosinusitis Patients with chronic rhinosinusitis and asthma have a significantly higher prevalence of nasal polyps, olfactory dysfunction and nasal congestion than those without asthma[42]. Nasal polyps are statistically more common in nonallergic asthma versus allergic asthma[43] Increasing severity of asthma is associated with advancing radiological severity of CRS and a greater prevalence of allergic sensitization and nasal polyposis[44].

Szczeklik et al.[45] studied the natural history of asthma and CRS in a total of 500 patients. . Rhinitis was the first symptom of the disease appearing at a mean age of 29.7+/-12.5 yrs. Asthma, aspirin intolerance and nasal polyposis then appear.

The clinical presentation in different European countries was remarkably similar. There was a close linear association between mean age at onset of rhinitis, asthma, NSAID intolerance and nasal polyps. This strong link between asthma and CRS and its linear association adds to the growing support of the unified airway theory.

1.1.6 Allergic Fungal Rhinosinusitis

Allergic fungal rhinosinusitis (AFRS) is a distinct clinical entity, however much controversy exists over the clinical criteria for its diagnosis[46-49]. A number of authors have proposed specific diagnostic criteria, the most widely accepted being that of Bent & Kuhn[49] which incorporates a combination of clinical, radiographic, microbiological and histopathologic criteria:

1. Eosinophilic mucus containing non-invasive fungal hyphae
2. Nasal polyposis
3. Characteristic radiographic findings (unilateral disease, bony erosion and heterogeneous areas of signal intensity within affected sinuses)
4. Immunocompetence
5. Allergy to cultured fungi

The presence of eosinophilic mucus, often termed ‘allergic mucin’ or ‘fungal mucin’ is clinically the most important feature. Macroscopically, it is darkly coloured, thick and tenacious. Microscopically, it is characterized by laminations of degraded eosinophils on a background of mucus. Charcot-Leyden crystals, which are the breakdown products of eosinophils, are often seen. Fungal hyphae are present but may be scarce, requiring specific staining for identification.

AFRS is the most common type of fungal rhinosinusitis[50]. The incidence of AFRS in a cohort of Australian CRS patients requiring surgery was 9%[51]. A similar proportion was found in the US[52,53]. Warmer climates have a much higher incidence[50,54].

The natural history of AFRS suggests a recurrence rate following treatment between 10 and 100%[55]. In one study universal recurrence was noted following endoscopic sinus surgery where rigorous post-operative medical therapy was not instituted[56]. AFRS patients undergo an average of two surgical procedures, and three courses of systemic corticosteroids per year, and despite being symptom free, endoscopy suggests that ongoing polypoid inflammation persists in many patients[57].

1.2 MANAGEMENT OF CHRONIC RHINOSINUSITIS

1.2.1 Introduction.

The aetiology of chronic rhinosinusitis is complex and multifactorial. In some cases, CRS is *secondary* to conditions that produce systemic pathology. Such secondary causes include genetic or systemic host disorders such as cystic fibrosis, Wegener's granulomatosis or primary ciliary disorders. Sinonasal mucosal inflammation is just one part of a systemic process. CRS can also be secondary to local processes such as a fungal ball or tumor.

However, the overwhelming majority of cases of CRS are not the result of clinically defined systemic disease or local pathology. CRS for the majority remains idiopathic or *primary*. A number of possible environmental and host factors have been described, including ostial obstruction, impaired mucociliary clearance, genetic susceptibility, osteitis, allergy, airborne irritants, smoking and gastroesophageal disease.

This thesis focuses on the primary form of CRS, with patients with recognizable causes of CRS intentionally excluded. Treatment of CRS is intended to reduce symptoms, improve quality of life and prevent disease recurrence or progression. In order to achieve this medical and surgical treatment is often required. A number of tools and scales have been

developed to quantify disease severity in CRS, and its impact on quality of life

1.2.2 Quantifying disease severity

Disease severity in CRS is quantified based on subjective patient symptoms and objective endoscopic and radiological findings. Assessment of CRS is based on symptoms of:

1. Nasal blockage, stuffiness or congestion
2. Nasal discharge which can be anterior or posterior
3. Reduction in smell
4. Facial pain, or pressure and headache

In addition to this, the patient may complain of distant symptoms of dysphonia, cough and a sore throat, and general symptoms of malaise, drowsiness and sleep disturbance.[58-61] All of these symptoms impact on the patients Quality of Life (QoL).

1.2.2.1 Quality of Life Scales

A number of scales have been proposed to quantify symptom severity:

- A basic description of mild, moderate or severe
- A numerical scale, for example 1-5 (as used in our department with 1 reflecting absence of symptoms and 5 maximally symptomatic)

However, for the purposes of comparing outcomes across the different population groups and for the purposes of research, standardized validated scales need to be employed. There are several validated tools available for use in CRS in the adult population.

Patient Reported Outcome Measures (PROMs) are self-reported questionnaires completed by patients themselves to give an overview of their symptoms at any given time. They can be used on initial assessment or to assess their health status pre- and post- an intervention such as a surgical procedure. They can be useful in representing a snapshot of a patient's subjective clinical condition, and can give an indication of the disease specific burden on an individual patient. Information gathered can be used as an indicator of outcome or quality of care delivered to patients following intervention [62]. Although they are generally not used as fixed criteria for decisions to treat, the ideal PROM for CRS should have the following qualities:

1. Simple and easy to use
2. Reliably quantifies the disease specific burden to the patient
3. Correlates well to objective findings of disease severity
4. Reliably reflects changes in disease specific burden after surgical and/or medical intervention.
5. Allows categorization of patients into appropriate treatment arms.

Various rhinology-specific PROMs have been reported and validated in the modern literature. Piccirillo[63] reported the use of a 31-item rhinosinusitis outcome measure in 1995 which contains both general and rhinosinusitis-specific questions. This was subsequently condensed into the Sino-Nasal Outcome Test[64], which contains 20 nose, sinus and general points that was validated as a disease-specific, health related quality of life measure for rhinosinusitis. A change to this questionnaire added in two points that were left out which were felt to be extremely important in quality of life reporting by CRS patients; nasal obstruction and loss of sense of taste and smell[65], thus the questionnaire became the SNOT-22. Both the SNOT-20 and SNOT-22 are well established methods of patient assessment in CRS[66,67] as well as other diseases including septoplasty[68], asthma and COPD [69], Wegener's Granulomatosis and other vasculitides[70,71], and following nasal tip surgery[72]. International translations of these scores have been used in Japan, Denmark and Czechoslovakia[73-75]. Other variant sino-nasal outcome questionnaires include the Sino-Nasal assessment questionnaire (SNAQ) [76], SinoNasal outcome test-16[77], Rhinosinusitis symptom inventory[78] and Rhinosinusitis utility index [79] amongst others.

Despite the interest in using the SNOT-20 or 22, it is well recognized that it has poor correlation to true clinical meaningfulness [80]. The lack of correlation between SNOT-22 scores with either the Lund-Mackay or Lund-Kennedy scores has been noted in a number of studies [66,81]. Although there have been attempts to make it more relevant to clinical

conditions such as weighting certain questions, no PROM currently exists that fulfills the ideal requirements.

1.2.2.2 Lund Mackay CT Score

A range of staging systems based on CT scanning have been described but the most commonly used and validated is the Lund-Mackay system[82-84] which is based on sinus involvement. A score is given for degree of opacification: 0 = normal, 1 = partial opacification, 2 = total opacification. These points are then applied to the maxillary, anterior ethmoid, posterior ethmoid, sphenoid, and frontal sinus on each side. The ostiomeatal complex is graded as 0 = not occluded, or 2 = occluded deriving a maximum score of 12 per side[82] .

1.2.2.3 Lund Kennedy Endoscopy Score

Scoring systems for endoscopic findings in the sinonasal cavity have been used increasingly in the literature to objectively measure outcomes following interventions for CRS. The most widely used is that proposed by The Staging and Therapy Group in 1995. An endoscopic staging system was proposed to evaluate therapeutic outcomes. Such a staging system had to be complex enough to incorporate the most important measures of the sinonasal cavity, but simple enough to facilitate regular clinical use. Characteristics are assessed endoscopically of each sinonasal cavity to provide a score – polyp disease, mucosal edema/crusting/scarring and nasal discharge each receiving a score from 0 to 2. (See Table 1.3). This

scoring system has been the instrument of choice to endoscopically evaluate outcomes of interventions in CRS prospectively over time in research and clinical practice.

Table 1.2: Lund Kennedy Endoscopy Staging System

Polyp	0=absence of polyp, 1=polyps in middle meatus only, 2=beyond middle meatus
Edema	0=absent, 1=mild, 2=severe
Discharge	0=no discharge, 1=clear, thin discharge, 2=thick, purulent discharge
Scarring	0=absent, 1=mild, 2=severe
Crusting	0=absent, 1=mild, 2=severe

1.2.2.4 Osteitis

Osteitic bone is a feature of chronic rhinosinusitis (CRS). However, its role in the pathogenesis of CRS and implications for medical and surgical treatment is unclear.

Studies in rabbits have shown sinus infections can cause transmucosal injury with initial changes of edema, loss of submucosal glands, and ulceration followed by fibroplasia and bone remodeling. Furthermore,

infectious agents may spread through enlarged Haversian canal systems to distant bony sites away from the primary site of infection[85]

A number of studies have shown a correlation between radiological severity and extent of CRS, as measured with Lund-Mackay grading system, and osteitis. However, there is no apparent correlation between clinical severity and osteitis[86]. QoL, and nasal symptoms are not correlated with the presence and degree of osteitis, but it is strongly correlated to the number of previous surgeries. This appears to be a result of a common endpoint of recalcitrant disease rather than surgery itself [86].

A recent prospective study has shown that osteitis in CRS is associated with the degree of tissue eosinophilia. It is independently associated with the need for a course of systemic corticosteroid over a 12-month period. However, the presence of osteitis did not affect overall disease control[87].

1.2.3 Medical Therapy

Medical treatment for CRS is widely accepted as first line therapy prior to any surgical intervention[88]. The aim of medical treatment is to reduce mucosal inflammation, and re-establish ventilation of the sinuses with a corresponding alleviation of symptoms. Although the term “maximum medical therapy” is often mentioned as the treatment given before surgery, there is no universal acceptance as to what this entails. There

are a number of potential treatments but only a few have evidence for its use.

Systemic corticosteroids have been shown to reduce polyp size & decrease intra-operative bleeding[55,89]. Post-operative systemic corticosteroids may also prevent early polyp recurrence[90], but their long term use is limited by significant side effects. Despite widespread use of systemic corticosteroids, no ideal treatment dose or duration has been agreed upon.

Intranasal (topical) corticosteroids (INCS) have minimal side effects and can reduce sinonasal inflammation and can reduce polyp size[53], and are currently considered the medical treatment of choice for nasal polyposis[91]. A pilot uncontrolled study suggested 0.5mg of budesonide in >100mL of saline for twice daily nasal douching can improve symptoms and CT sinus scores in patients with EM-CRS[92]. This treatment has been shown to have no effect on the hypothalamic-pituitary-adrenal axis[93]. Mometasone furoate has been shown in two large, multicentre placebo controlled trials to be effective in providing lasting symptom relief compared with placebo for nasal congestion, anterior rhinorrhea, and post-nasal drip scores in nasal polyposis patients[94,95]. Symptom relief can commence as soon as two to five days after initiation of therapy[96]. Despite their efficacy a large proportion of patients with nasal polyposis will continue to have significant symptoms whilst using INCS[97].

Leukotriene receptor antagonists, such as Montelukast have been used due to their more favorable side effect profile when compared to systemic steroids. A recent single blind placebo study showed there were significant improvements with use of 10mg of Montelukast daily for 6 weeks in the nasal symptom score and airflow limitation as well as a reduction in the inflammatory mediators in nasal lavage fluid after treatment[98]. Furthermore, reduced eosinophils in nasal smears and peripheral blood were observed 2 and 6 weeks after treatment. In another randomized control trial, Montelukast was shown to have clinical benefit as an adjunct to oral and inhaled steroid in chronic nasal polyposis, but the effects were not maintained after cessation of treatment[99].

Macrolide antibiotics have also been used for their anti-inflammatory action, but recent double blinded placebo controlled trials showed either only a small effect[100] or no effect[101] when compared with placebo.

A recent double blind, placebo-controlled, multicenter trial, demonstrated a significant effect of both oral methylprednisolone and doxycycline on size of nasal polyps, nasal symptoms, and mucosal and systemic markers of inflammation compared with placebo. The effect of methylprednisolone was greater and lasted for 8 weeks whereas the effect of doxycycline was moderate but present for 12 weeks[102].

Topical antibiotics have a theoretical advantage of high local drug concentration levels without risks of systemic absorption. Nebulized

culture directed antibiotics have been used for acute exacerbation of CRS[103]. Nebulized therapy showed a longer infection-free period (average, 17 weeks) compared with standard therapy (average, 6 weeks). Improvements in posterior nasal discharge, facial pain/pressure, and emotional consequences were noted. Endoscopic appearances also improved.

Topical mupirocin has been used for recalcitrant *S.aureus* infections with improved symptoms and endoscopic appearance.[104,105]

Delivery of topical therapy is better achieved in a post-surgical patient where widely patent sinus ostia theoretically allow for better penetration of the sinuses. In a systematic review of topical antimicrobial therapy for CRS, efficacy of topical therapy was noted in both surgical and non surgical patients although higher levels of evidence were noted for post surgical patients and with the use of culture directed topical antimicrobials[106].

1.2.4 Endoscopic Sinus Surgery

Functional endoscopic sinus surgery (FESS) is now the standard of care for CRS refractory to medical therapy. Multiple outcome studies have shown improvement in symptoms, signs and QoL after FESS. A systematic review showed substantial level 4 evidence with supporting

level 2 evidence that ESS is effective in improving symptoms and/or QOL in adult patients with CRS[107].

However, high-level evidence for surgical intervention in CRS is lacking. The Cochrane collaboration re-assessed and revised in 2009[108] the evidence for surgery in CRS. The Cochrane collaboration, using data from three randomized controlled trials, stated that "(ESS) has not been demonstrated to confer additional benefit to that obtained by medical treatment with or without antral irrigation in relieving the symptoms of chronic rhinosinusitis".

There is a major dilemma in demonstrating benefit of ESS in the treatment of CRS. Currently, the general philosophy of treating CRS is that surgical intervention is only suggested ***after*** medical therapy has failed, with medical therapy often being required post surgical intervention. A clinically relevant comparison of medical versus surgical treatment for CRS is therefore difficult, as the patient cohorts in whom these treatment modalities are indicated are different.

The medical consensus then is that functional endoscopic sinus surgery (FESS) is considered to be the gold standard in the surgical management of chronic rhinosinusitis (CRS) that has failed maximal medical therapy[109] [88].

1.2.4.1 Rationale for FESS-Historic Perspective

Historically, FESS emphasized clearance of pathology at the ostiomeatal complex (OMC)[110,111]. This concept suggests that clearing the obstruction of the common drainage pathway restores function by improving ventilation and allowing mucociliary clearance to normalize. FESS has been shown to be successful, with reported success rates of 90% for primary FESS.[109,112]. However, FESS is not successful in all patients. Patients who fail FESS and require multiple surgeries are considered to have refractory CRS (rCRS)[113]. FESS is still beneficial in this group but the success rates are lower.[114]

The theory behind FESS was based mainly on the sinonasal mucociliary physiology studies of Messerklinger and Stammberger. Consequently, FESS placed a great emphasis on sinus aeration and restoration of mucociliary function through clearance of blocked sinus ostia, with a particular focus on OMC disease. Although these concepts play a role in the disease process, they do not provide sufficient explanation as to why some patients with CRS do not benefit from functional surgery.

For example, more than 35% of patients with CRS in a recent study did not manifest OMC obstruction on computed tomography (CT) scans[115]. And although FESS does improve mucociliary function as shown in multiple studies[116-118], the exact role of mucociliary drainage is unclear. Two studies [119,120] have shown only a slight or nonsignificant improvement in mucociliary clearance. Inanli et al.[118] reported a

significant postoperative improvement in mucociliary function, but function still did not reach the level of normal healthy controls at 12 weeks. Other studies showed that that postoperative mucociliary function (as indicated by the saccharin test) did not always correlate with postoperative endoscopy. Some studies found that, although OMC blockage cleared, mucociliary clearance tended to be significantly prolonged in sinuses containing polyps when compared to sinuses without polyps [117,121,122]. Interestingly, many patients were asymptomatic, even though mucociliary function had not fully recovered.

1.2.4.2 Rationale for FESS-Current Concepts

Studies into the aetiopathogenesis of CRS suggest an increasing number of reasons for the existence of this small, but significant, subset of patients with refractory CRS (rCRS.) The original theories of FESS do not provide sufficient explanation for why these patients do not fare as well with functional surgery. On the other hand, there is increasing evidence that many patients with rCRS may benefit from more extensive or radical surgical options[123-130]. Arguably, in addition to re-establishing ventilation, radical surgery promotes topical treatment and allows more complete clearance of inflammatory mediators.

There is a general consensus amongst clinicians treating CRS, that one of the fundamental reasons for offering patients ESS is to maximize delivery of topical medication to the sinonasal mucosa[131,132]. Multiple studies have supported the notion that ESS improves topical

delivery[133,134] Topical penetration of the unoperated sinuses is negligible, with the frontal and sphenoid sinuses particularly difficult to penetrate. For the maxillary sinus an ostial size of greater than 4mm is required[133]. With the presence of underlying mucosal edema in CRS, less than 2% of total irrigation volume penetrates the sinuses[135].

A number of studies have looked at the degree of inflammation and CRS outcomes. These studies showed that the grade of inflammation is positively correlated with disease severity. Mucosal eosinophilia correlated with disease severity as measured by CT or endoscopy scores[136-138]. From the literature, it is apparent that the patients with the highest inflammatory load are those with nasal polyposis (CRSwNP), concomitant asthma, and/or aspirin intolerance[139-141]. These patients experience worse postoperative subjective and objective outcomes, as well as higher recurrence rates and a higher need for revision surgery[142-149].

Although FESS produces excellent long-term results in patients without high-grade eosinophilic inflammation, a large proportion of patients in whom standard FESS fails have eosinophilic infiltration of the sinus mucosa. Potentially, this is a consequence of conservative surgery addressing only the sinus ostia promoting ventilation but not eliminating the significant load of eosinophils in the mucosa or the thick tenacious EM in the sinuses.

Many studies suggest that better outcomes can be achieved through a radical surgical approach. In the early days of FESS surgery, FESS was compared to the more traditional but radical surgery of Caldwell-Luc (CL) and ethmoidectomies. In 1990, McFadden et al.[123] reviewed 25 patients with Samter's triad. Sixteen patients underwent ethmoidectomies using the FESS philosophy. Of these 16 patients, six required subsequent surgery for recurrent disease. The remaining nine had radical procedures such as CL with intranasal and transantral sphenoethmoidectomies. None of these nine patients required further surgery. Another study comparing CL to FESS showed a higher revision rate in the FESS group of 18%-27% of cases, but 4.8% to 7.3% in the CL group[150]. Ragheb et al [151]also compared the CL to middle meatal antrostomies (MMAs) in 153 patients. This study showed that the subset of patients with bronchial asthma may benefit from the more radical approach offered by the CL as opposed to standard FESS. In a more recent study[124], the traditional CL (with a radical removal of the mucosa) was performed in patients who failed, on average, two prior MMAs. The response rate was 92%.

In the era of endoscopic surgery, the CL has limited indications [152]and has been almost abandoned for treatment of CRS. A more recent and slightly more conservative approach for severe maxillary sinusitis has been the canine fossa trephine (CFT)[125]. In CFT it is important to note that, contrary to CL, the mucosa is not stripped to the underlying bone. The sinus is cleared of all polypoid mucosa with the underlying basement membrane retained. As a result of improved access, this hybrid

procedure enhances clearance of polyps, pus, and tenacious EM from the sinus. This in turn led to less disease recurrence when compared to a matched historic cohort. More recently, the authors showed that the CFT did not prolong the surgical time and was often faster than performing a standard MMA. They concluded that the CFT allows for clearance of all gross disease in the maxillary sinus and appears to improve postoperative outcome at 6 and 12 months and decrease the need for revision surgery[153]. The only downside of CFT is the small incidence (~3%) of upper lip and teeth numbness from disruption of the branches of the anterior superior alveolar nerves. In most patients this recovers over a 3-6 month period as the nerves regrow[154].

Friedman et al [155] performed revision surgery for 100 patients with recurrent disease in the maxillary sinus that occurred despite functional surgery with a conventional MMA. In the revision surgery, all recurrent or residual diseased mucosa was removed, including polyps, occasional mucoceles, and hyperplastic changes that occurred inside the sinus, followed by wide marsupialization into the posterior nasal vault. The overall polyp recurrence rate at 18 to 48 months after this revision surgery was less than 5%, compared to 19.2% after the functional sphenoethmoidectomy with MMAs.

The endoscopic modified Lothrop procedure (EMLP or Draf 3/frontal drillout) is a radical but successful procedure for persistent frontal sinusitis. Wormald[128] performed the EMLP in 83 patients with a

dysfunctional frontal sinus. For an average follow-up of 21.9 months, the cure rate from the EMLP was 75%, in a cohort who had had a mean of six previous failed functional sinus operations. Possibly, this radical ostium-widening procedure breaks the cycle of persistent frontal sinusitis by enabling the surgeon to gain better access and achieve better clearance of the inflammatory load in the normally difficult-to-access frontal sinuses (which, in many cases, are blocked by osteitic new bone formation in the frontal recess).

Other radical procedures have been described for complete clearance of severe disease in the sinuses. Masterson et al.[127] reviewed CRSwNP patients who had complete removal of all polyps along with a radical ethmoidectomy and compared them to patients who underwent only anterior ethmoidectomies and found that extensive surgery led to a significant decrease in revision rate 3 years postoperatively. Denker's procedure is another radical procedure in which all walls between the nasal fossa and the paranasal sinuses are removed, creating one large cavity reaching from the ethmoid roof to the floor of the nose and maxillary sinus and from the lateral wall of the maxillary sinus to the nasal septum. Denker's procedure was originally described by Denker for sinonasal malignancies but has been performed as a last resort for rCRS. Kerrebijn et al.[130] performed it in 56 patients and reported relief of sinusitis with significant improvement in symptoms. Videler et al.[156,157] reported significant improvements in symptoms and QoL measures from Denker's procedure while Wreesmann et al.[158] reported improvement of

lower airway symptoms in asthmatic patients. These studies suggested that radical surgery should be an option for patients who fail repetitive conservative functional surgery.

Nasalization is essentially similar to Denker's procedure in that it consists of a radical ethmoidectomy with removal of all bony lamellae (including the middle turbinate), plus wide opening of all sinus ostia. This creates one large cavity with all the sinuses marsupialized (or nasalized) into the nasal cavity. Jankowski et al.[129,159] compared nasalization with functional ethmoidectomy in patients with CRSwNP and reported better long-term results with greater overall symptom improvement in the nasalization group. Recurrence rate was 22.7% in the nasalization group versus 58.3% in the functional ethmoidectomy group.

1.3 THE FRONTAL SINUS

1.3.1 Background

Development of the frontal sinus begins in the fourth foetal month when the entire nasofrontal area is represented by the frontal recess. It is the last paranasal sinus to develop. At birth, the sinus has usually not formed. At around 2 years of age, the most anterior ethmoidal sinus invaginates into the frontal bone and continues its vertical growth trajectory at an average annual rate of 1.5mm until the 15th year. Final growth is completed before 20.

The sinus is compartmentalized by the intrasinus septa, which divides the sinus into halves. The frontal sinus has the most complex and variable drainage of any paranasal sinus. The frontal recess itself can be considered to be bordered by the frontal beak anteriorly, the anterior face of the bulla ethmoidalis posteriorly, the middle turbinate medially and the lamina papyracea laterally (Figure 1.1).

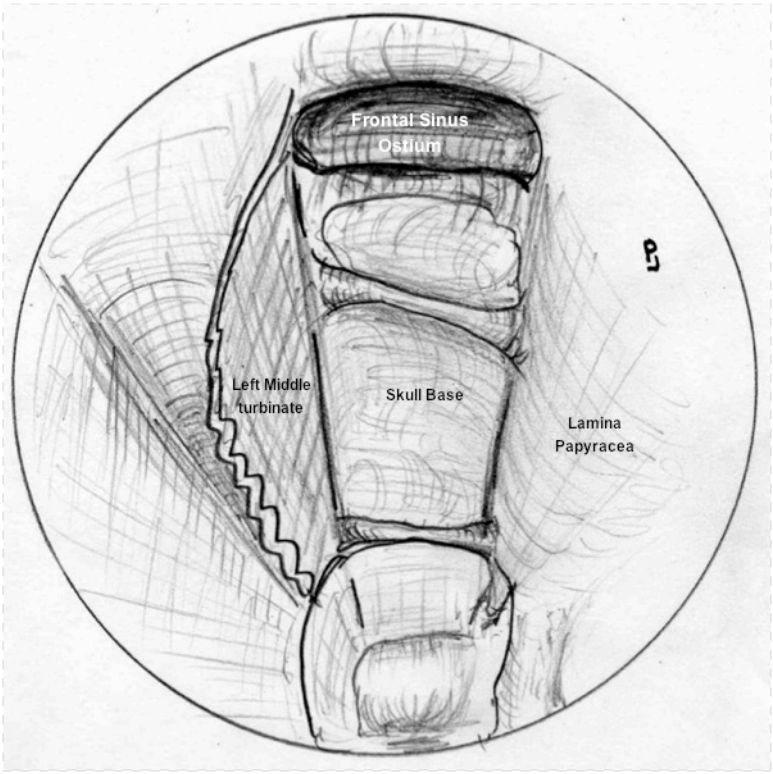


Figure 1.1: Boundaries of the frontal recess.

These limits are altered by the variable pneumatisation of anterior ethmoidal cells. Along the frontal beak, the agger nasi cell and other fronto-ethmoidal cells protrude into the frontal recess and sinus to alter the drainage pathway. Along the skull base, suprabullar cells may protrude anteriorly compressing the drainage pathway. When a suprabullar cell pneumatizes along the skull base into the frontal sinus it is called a frontal bulla cell. Frontal bulla cells can considerably narrow the frontal sinus drainage pathway.

The types and variability of cells that can be found in the frontal recess and frontal sinus, which can markedly alter the frontal sinus drainage pathway, were first described by Kuhn[160] in a landmark paper. He

described four basic cells: the agger nasi cell, the fronto-ethmoidal cell(s), the intersinus septal cell(s), and the cell/s originating from the bulla ethmoidalis/suprabullar region. This classification was modified by Wormald[161] who more clearly defined the fronto-ethmoidal cell and redefined type 3 and 4 cells. (See Table 1.3 and Figures 1.2-1.7 for examples)

Table 1.3: Wormald Classification of Frontal Recess and Frontal Sinus Cells (adapted from the Kuhn classification)

Cell		Description
Agger Nasi		Cell that is either anterior to the origin of the middle turbinate or sits directly above the most anterior insertion of the middle turbinate into the lateral nasal wall
Frontal ethmoidal cells		Anterior ethmoidal cell that needs to be in close proximity or touching the frontal process of the maxilla
	Type 1	Single cell above agger nasi, not extending above the frontal beak
	Type 2	Tier of frontal ethmoidal cells above agger nasi, not extending above the frontal beak
	Type 3	Frontal ethmoidal cell pneumatising cephalad into the frontal sinus but extending less than 50% of the vertical height of the frontal sinus
	Type 4	Frontal ethmoidal cell that extends more than 50% of the vertical height of the frontal sinus
Frontal bulla cell		Suprabullar cell that pneumatises along the skull base into the frontal sinus along its posterior wall
Suprabullar cells		Cells above the ethmoid bulla that do not extend into the frontal sinus
Intersinus Septal Cell		A medially based cell related to the frontal sinus septum which opens into the frontal recess

Examples of Frontoethmoidal Cells

Below are some radiological examples of frontoethmoidal cells and their influence on the frontal sinus drainage pathway.

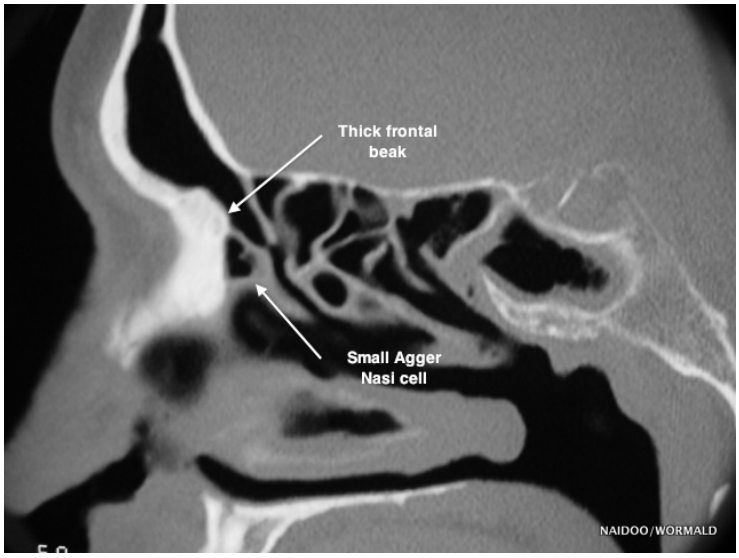


Figure 1.2: Small Agger cell

In this example, a small agger cell is associated with a thick frontal beak

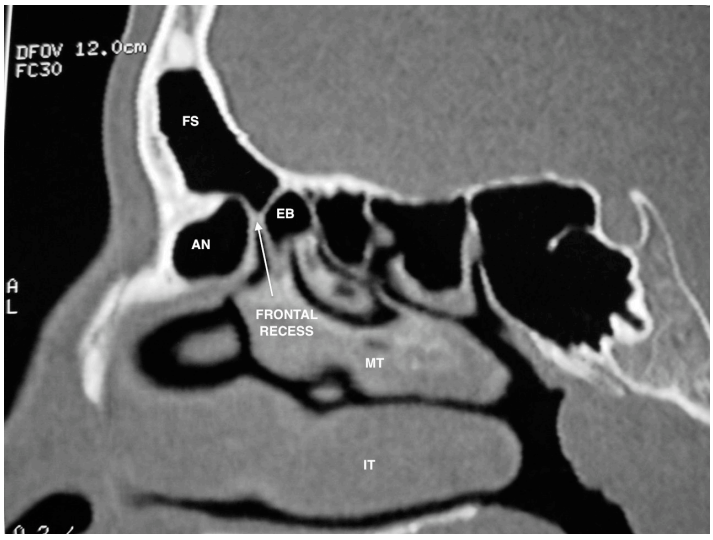


Figure 1.3: Large Agger

In Figure 1.3, a large agger cell is extending up to the floor of the frontal sinus. The frontal recess lies between the Agger Nasi cell (AN) and ethmoid bulla (EB). MT-Middle turbinate, IT-inferior turbinate

Figure 1.4-1.8 describes and gives examples Type 1-4 Fronto-ethmoidal cells (Kuhn Cells)

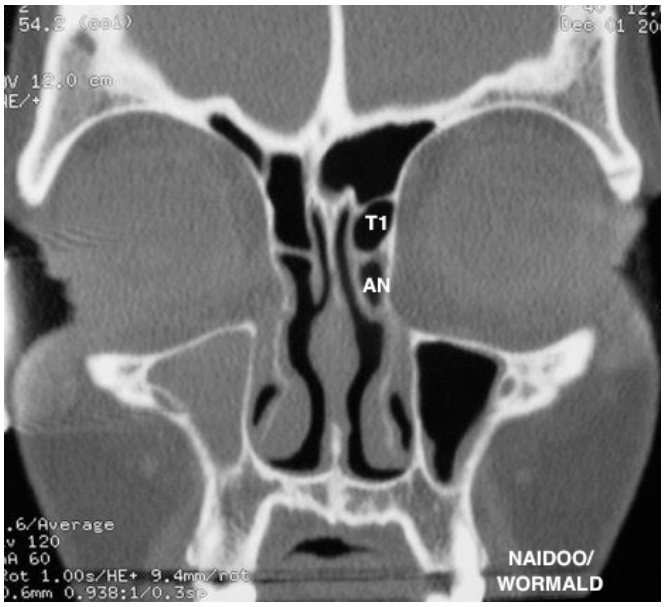


Figure 1.4: T1 cell.

A T1 cell is single frontoethmoidal cell above the agger nasi cell (AN).

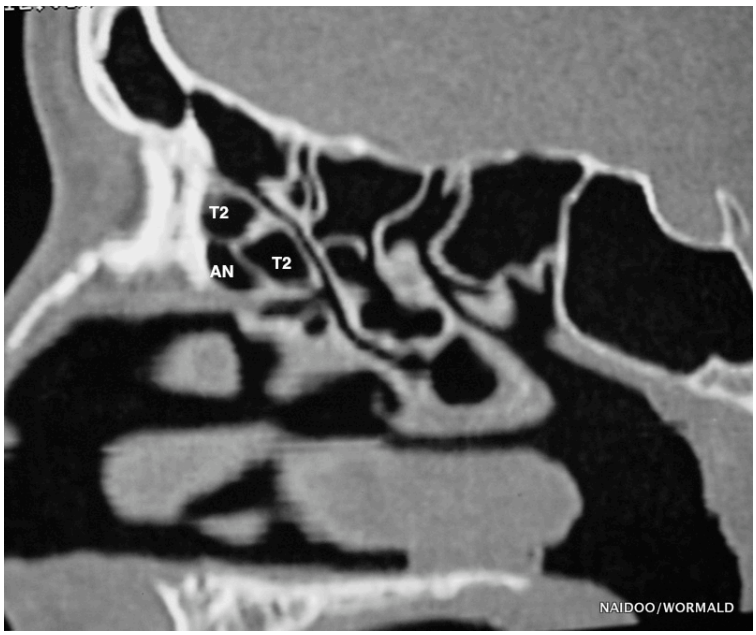


Figure 1.5: T2 cell

A tier of fronto-ethmoidal cells (T2) is seen above the agger nasi cell (AN) but not extending above the frontal beak

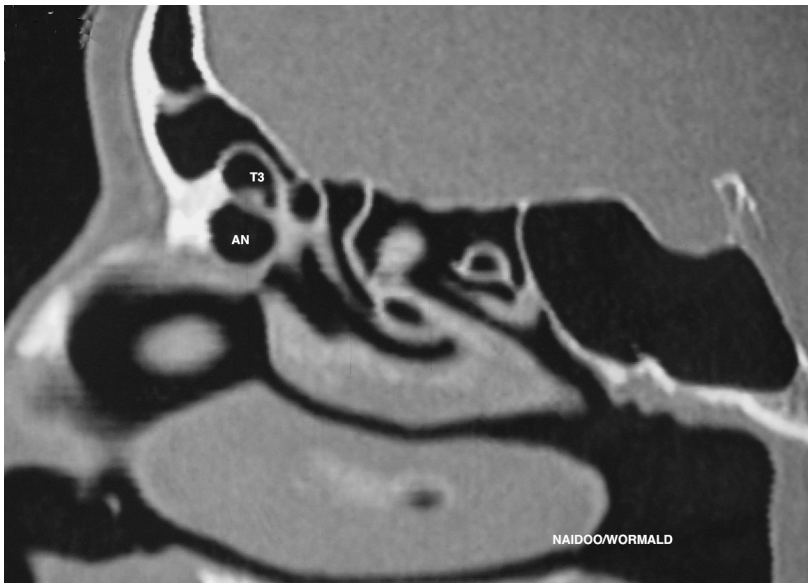
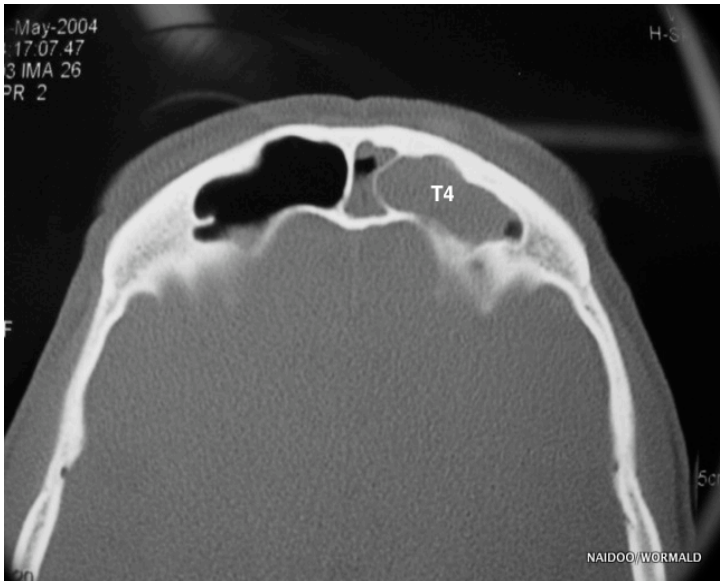


Figure 1.6: T3 cell

This is a fronto-ethmoidal cell extending above the frontal beak but extending less than 50% of the vertical height of the frontal sinus. A T4 cell, however, extends greater than 50% of the vertical height of the frontal sinus and is shown below in Figure 1.7.



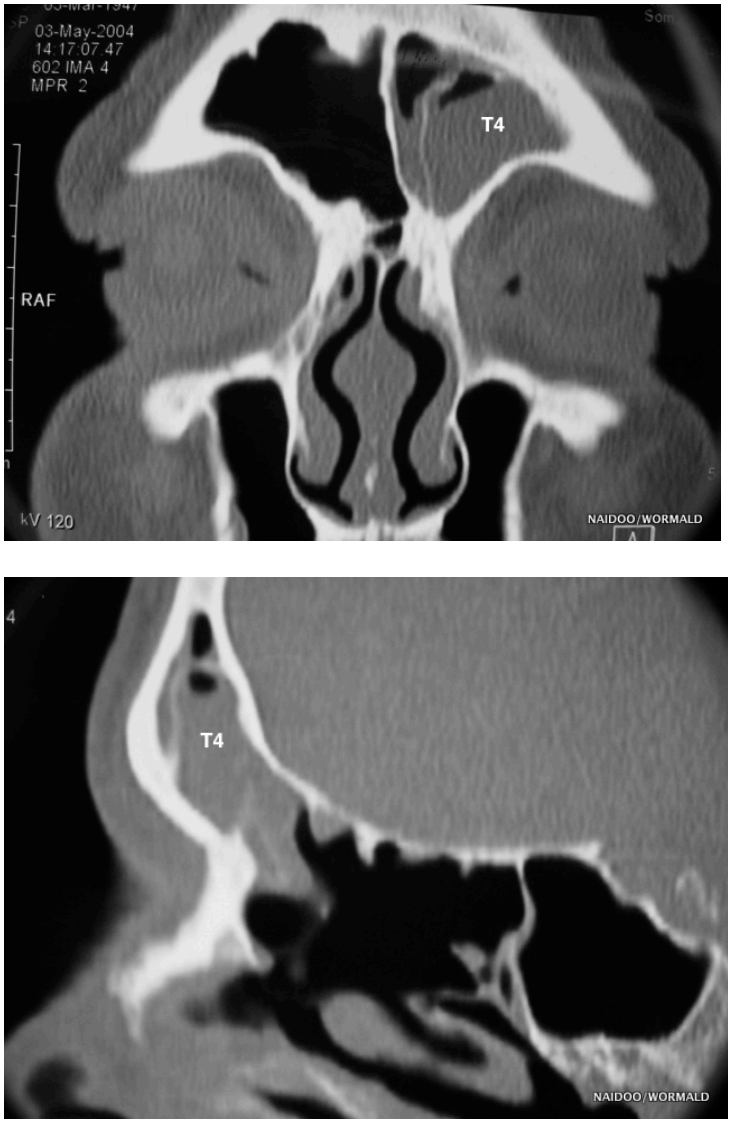


Figure 1.7: Axial, Coronal and Parasagittal views of a T4 cell

Suprabullar cells are cells that lie above the ethmoid bulla but do not extend into the frontal sinus. In Figure 1.8 there is an associated T3 cell. Both these cells are compressing the frontal sinus drainage pathway.

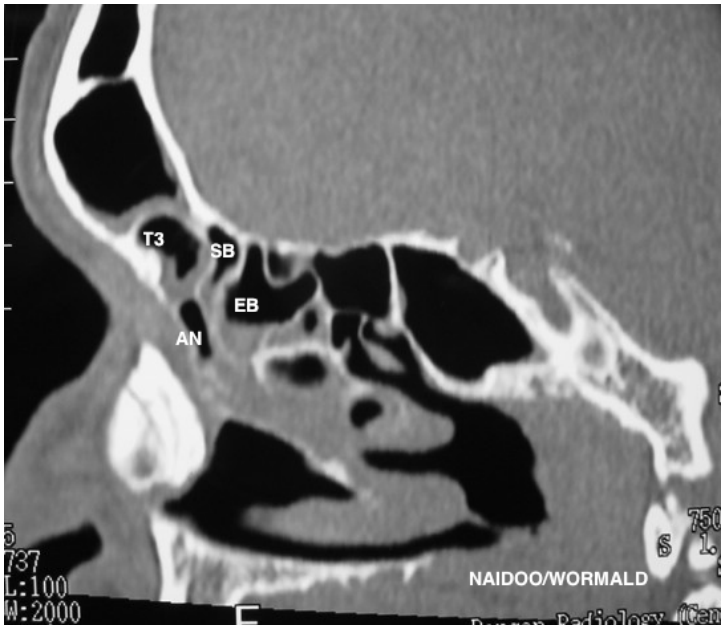


Figure 1.8: Suprabullar cell

This is an ethmoid cell above the ethmoid bulla that does not extend into frontal sinus. (AN-Agger Nasi cell, SB – suprabullar cell, EB-ethmoid bulla, T3- type 3 frontoethmoidal cell)

In Figure 1.9 below a frontal bulla cell (FB) is shown. The FB cell is pneumatising along the skull base into the frontal sinus along its posterior wall. (AN-Agger Nasi cell, SB-suprabullar cell, EB-ethmoid bulla)

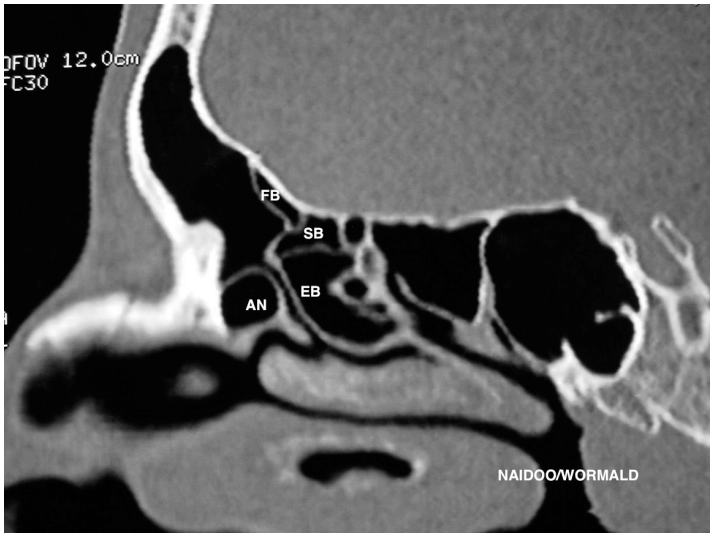


Figure 1.9:Parasagittal scans showing a Frontal bulla cell.

Finally, the intersinus septum itself might pneumatize in the midline and push the frontal recess laterally. This is known as an Intersinus Septal Cell (ISSC) as shown below in Figure 1.10).

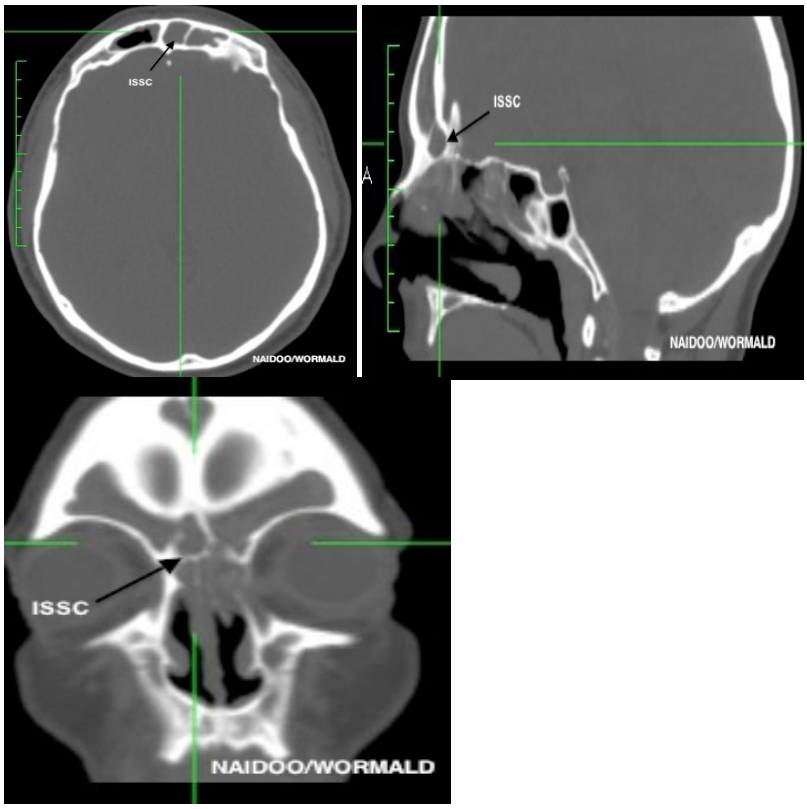


Figure 1.10: Intersinus septal cell

1.3.2 Frontal Sinus Surgery

Although endoscopic sinus surgery has been accepted as the treatment of choice for chronic sinusitis refractory to medical treatment, frontal sinus surgery and the extent of frontal sinus surgery remain controversial.

Surgery on the diseased frontal sinus surgery has evolved from quite radical, and morbid open procedures to endoscopic techniques which are minimally invasive[162]. However, controversy still rages regarding the most appropriate surgical approach as a number of endoscopic techniques have been advocated and long-term efficacy of these techniques is still not known or of low clinical evidence[163].

The osteoplastic flap frontal sinus obliteration procedure was historically accepted as the gold standard for treatment of frontal sinus disease until the advent of endoscopic sinus surgery[162] The rationale for the development of the osteoplastic flap frontal sinus obliteration procedure was the high failure rate associated with earlier external techniques such as the Lynch and Lothrop procedures. These procedures were associated with short-term patency rates up to 90% but at least 20% failed over a 7-year follow-up period[162,163]. This led to the prevailing dogma that trauma to the mucosa of the frontal recess invariably leads to scarring and obstruction of the frontal sinus ostium. As a result, any surgical manipulation of the frontal recess was discouraged[163,164].

Although widely regarded as the gold standard treatment, osteoplastic flap surgery with fat obliteration also has a reported long-term failure rate of up to 25%. In addition, it is associated with significant morbidity including frontal bossing, supraorbital neuralgia, donor site complications after abdominal fat grafting, and difficulties with postoperative imaging[128].

Endoscopic frontal sinus surgery is perhaps the most technically demanding of all endoscopic sinus surgery. The complex and varied anatomy, acute nasofrontal angle and proximity to critical structures such as the olfactory fossa, skull base and orbit contribute to the surgical difficulty. These narrow confines, and a penchant for postoperative scarring, make surgical treatment of chronic frontal sinusitis challenging.

The literature and evolution of endoscopic frontal sinus surgery supports a graduated step-wise approach to tackling disease in the frontal sinus[165-168]. A wide spectrum of defined endonasal surgical procedures of the frontal sinus has been developed. These are based on the drainage or sinusotomy classification of Draf[165].

Table 1.4: Draf Classification of Endonasal Frontal Sinus Procedures[165]

Type	Extent of Surgery	Indication
I	Anterior ethmoidectomy with drainage of the frontal recess by removal of obstructing disease inferior to the frontal ostium. The frontal ostium itself and any cells protruding into it are not touched.	• History, endoscopy and CT findings suggest chronic frontal sinusitis is due to sinus outflow tract obstruction at the level of the frontal recess
IIA	Removal of all ethmoidal cells protruding into the frontal sinus thereby creating an opening between the middle turbinate medially and the lamina papyracea laterally	• Complicated frontal sinusitis or failed Draf I • Recommended in frontal sinuses with a large anterior–posterior (A–P) diameter (anticipated minimum diameter of frontal neo-ostium 5 mm or more), hypoplastic internal nasal spine (small frontal beak), and a broad ethmoid.
IIB	Removal of the frontal sinus floor between the nasal septum medially and the lamina papyracea laterally	• Complicated frontal sinusitis in frontal sinuses with a small A–P diameter, hyperplastic internal nasal spine (i.e. large frontal beak), or narrow ethmoid
III	Bilateral Draf IIB with removal of the upper part of the nasal septum and intersinus septum	• As for Draf IIB • Recommended over type II sinusotomy for cases with severe polyposis

Short-term outcomes after endoscopic frontal sinus surgery have previously been reported in the literature [164,169,170]. However, there is only a limited number of studies that have examined long-term frontal ostium patency[165] and improvement in patient symptoms[168].

The extent of endoscopic frontal recess dissection varies from surgeon to surgeon across the world with some surgeons only performing endoscopic frontal sinusotomy when patients have symptoms of frontal headache or congestion.

Our institution's philosophy is that the frontal sinus should be treated no differently to any of the other sinuses. Mucosal disease in the frontal sinus without symptoms of headache can still contribute to the other symptoms of CRS such as nasal obstruction, anosmia, postnasal drip and rhinorrhea. The surgical philosophy therefore is based on an all-or-nothing approach to frontal sinus surgery once maximum medical treatment has failed. Limited surgery in the frontal recess places raw surfaces in close proximity to each other, which increases the likelihood of scarring and failure. Draf IIA sinusotomies are performed for primary surgery on the frontal sinus. Failed frontal sinus surgery is treated with a Draf III sinusotomy (otherwise know as endoscopic Modified Lothrop (EMLP) or frontal drillout procedure).

At present, a ***primary*** EMLP is ***not*** performed for chronic rhinosinusitis. One of the primary aims of this thesis is to validate this approach. The secondary

aims are to assess risk factors for failure, and determine if there are patients that would benefit from more radical endoscopic frontal sinus surgery –such as an EMLP in the first instance.

1.3.3 Evidence for Frontal Sinus Surgery

In patients with CRS involving the frontal sinus and frontal recess, surgeons historically limited surgery to the OMC - even with proven involvement of the frontal sinus. This was largely driven by historical studies noting the extraordinary propensity for scarring in the frontal sinus as discussed earlier, as well as the notion the functionally addressing the anterior ethmoid sinuses would facilitate spontaneous healing of frontal mucositis. However, the evidence does not support this approach.

Franzen et al [171]showed that the mucosa of the frontal sinuses does not respond to the desired extent with such an approach, with no change in the appearance of the frontal sinus mucosal inflammation on postoperative CT imaging.

Ramadan[172] showed frontal sinus ostium stenosis was the third leading cause of failure in a series of 398 patients. Stenosis within the frontal recess typically occurs due to inadequate removal of agger nasi and frontal cells, lateralization of the middle turbinate or scarring due to mucosal stripping and/or osteoneogenesis[173]. Infact, secondary frontal sinusitis has been shown to

occur with an incidence of 1.5% after even minor intervention in the middle meatus[174].

Jacobs et al.[175] showed that 39 of 40 (97.5%) patients undergoing surgery for chronic diffuse hyperplastic frontal sinus and nasofrontal duct disease had persistence of mucosal disease on endoscopic evaluation post ESS. In all these cases Draf 2 surgery was not performed. The authors felt that such mucosal inflammation was of limited clinical significance and cited fears of nasofrontal duct stenosis as a rationale for not addressing the nasofrontal mucosal disease. Endoscopic surveillance and medical treatment was suggested for this persistence disease.

Suprabullar cells, supraorbital ethmoid cells, frontal bullar cells, and recessus terminalis are significantly associated with the development of frontal sinusitis by multiple logistic regression models[176]. Other sinonasal anatomical variants, specifically infraorbital and frontal intersinus cells, are associated with development of CRS in patients with Allergic Rhinitis (AR). Frontal intersinus cells in particular greatly increase the risk of developing CRS[177] (Odds Ratio 18.4). It stands to reason therefore, that Draf 1 surgery which does not remove these cells are predisposing patients to a greater chance of recidivism.

Techniques such as Balloon Sinuplasty™ (Acclarent), offer a minimally invasive approach to the sinuses but is not, as yet, supported by the literature[178,179]. Plaza et al.[179] performed a double-blind randomized clinical

trial of functional endoscopic sinus surgery assisted by balloon dilation versus conventional functional endoscopic sinus surgery in the treatment of chronic rhinosinusitis involving the frontal sinus. 40 patients were randomly allocated to balloon dilation or to conventional frontal sinus drainage with a Draf I procedure. 32 patients concluded the trial. A statistically significant reduction in the Lund-Mackay stage was seen in both groups. However, there was no statistically significant difference between the two groups in resolution of the frontal sinus disease as seen by CT scanning. The authors noted that "permeability" of the frontal recess on endoscopy was statistically more frequently after balloon treatment (73% versus 62.5%).

One of the major concerns of this technique is the ability to successfully cannulate the frontal sinus and dilate the frontal recess outflow tract. In the study by Plaza et al.[179] a 21% failure rate was noted. Heimgartner et al.[180] specifically looked at the intraoperative technical failure rate of patients undergoing balloon sinuplasty between 2007 and 2010 at three different ENT centres. Dilatation of 12 of 104 (12%) frontal sinuses failed. Analysis of the failed cases revealed complex frontal sinus anatomy including the presence of frontoethmoidal-cells, frontal-bulla-cells, agger-nasi-cells or osteoneogenesis. They also highlighted the case of one patient, in which a lymphoma was overlooked during a balloon only procedure. The lymphoma was diagnosed 6 months later with a biopsy during functional endoscopic sinus surgery. The authors concluded that in patients with complex frontal recess anatomy, balloon sinuplasty may be challenging or impossible. Another disadvantage of a balloon only procedure was of not including a histopathologic exam, with

potentially life threatening consequences. Tomazic et al.[181] reviewed the Graz experience with balloon sinusplasty in the treatment of patients with CRS. Patients with CRS refractory to medical therapy who had been scheduled for endoscopic sinus surgery between 2009 and 2011 were included in this study. Forty-five consecutive patients were included in whom 112 sinuses were approached by balloon sinuplasty. Of the 112 sinuses, 68 (60%) were planned as a "Balloon-Only" procedure and 44 (40%) were planned as a "Hybrid" procedure. 44 of 68 sinuses in the "Balloon-Only" group failed, equating to a failure rate of 65%. 29 of 44 sinuses in the "Hybrid" group failed, giving a failure rate of 66%. The authors who had planned to review 200 consecutive patients abandoned the study due to an “unacceptable” failure rate. A recent Cochrane review of the technology concluded “At present there is no convincing evidence supporting the use of endoscopic balloon sinus ostial dilation compared to conventional surgical modalities in the management of CRS refractory to medical treatment”[178].

The literature therefore supports a view that the frontal sinus should be addressed with proven endoscopic or radiological disease affecting the frontal sinus after failure of medical treatment. The literature also supports the Draf IIA frontal sinus approach when compared with Draf I surgery or newer techniques such as balloon dilation.

1.3.4 Extended Frontal Sinus Surgery

Although the literature appears to support addressing the disease frontal sinus surgically, such surgery is not universally successful. A small but significant number of patients have recalcitrant frontal sinusitis.

A review of 118 patients with severe polyposis undergoing ESS with a minimum Lund-McKay score of 16, showed 71 patients (60%) developed recurrent polyposis[182]. Furthermore, 60/100 patients (60%) undergoing frontal sinusotomy developed recurrent frontal polyposis. A history of previous sinus surgery or asthma or allergy predicted higher recurrence and revision surgery rates.

Unlu et al.[183] looked at postoperative CT scans of all symptomatic patients during their least symptomatic period or after maximal medical therapy. Multivariate analysis of all potential risk factors revealed that postoperative frontal sinus opacification was affected only by sinonasal polyposis (odds ratio [OR] 3.32) and extension of disease (OR 16.93; 95%).

Chan et al[173] showed that 32.5% of their patients underwent at least one revision procedure after initial frontal sinus surgery, with a revision rate for ECRS patients (36%) slightly higher than that of the CRS patients without eosinophilia (32%). This was despite a frontal sinus patency rate of 88% overall. The authors thought this was a reflection of the inflammatory nature of the disease as demonstrated by the presence of nasal polyps in the ECRS

group of patients compared to the non-ECRS patients (75.9% in the ECRS group vs. 9.7% in the non-ECRS group).

This is consistent with findings by Hosemann et al. [164]where patients with marked polyposis demonstrated a tendency for the frontal neoostia to narrow compared to the patients with chronic sinusitis without polyps[164].

A marked difference was noted in the revision rates for the non-ECRS group in the study by Chan[173]. 81% of revision cases were revised compared with 23% of primary cases. Such a stark difference was not noted in the ECRS group. This suggests that in the absence of polypoid edema, the frontal recess and sinus which fails to remain patent, is much more difficult to rehabilitate[173].

The endoscopic modified Lothrop procedure (EMLP, also known as Draf III or frontal drillout) has recently been used as minimally invasive alternative to frontal sinus obliteration for recalcitrant frontal sinusitis.

Multiple studies have reported on its effectiveness. Wormald[128] performed the EMLP in 83 patients with a dysfunctional frontal sinus. For an average follow-up of 21.9 months, the cure rate from the EMLP was 75%, in a cohort who had had a mean of six previous failed functional sinus operations.

A meta-analysis of 18 studies containing data from 612 patients showed that the EMLP is a safe and efficacious procedure that is well tolerated[184]. The most common indications for EMLP were chronic frontal sinusitis (75.2%) and

mucocele (21.3%). The rate of major and minor complications was <1% and 4%, respectively. Frontal sinus patency was >95%. Symptoms improved in over 82% of patients, with 16% reporting no significant change, and 1.2% reporting worsening of symptoms. Failure (defined as requiring further surgery) was 13.9% (85/612). Of the failures, 80% underwent revision EMLP, whereas 20% elected osteoplastic frontal sinus obliteration. However, the average follow-up in this review was only 28.5 months, which may underestimate the rate of surgical failure, as recurrent frontal sinusitis may develop many years after initial surgical treatment[185]. The longest period of follow-up among studies included in the meta-analysis was a report from 2003 by Samaha[186] who described outcomes in 100 patients who underwent frontal drillout surgery but only 66 patients underwent bilateral frontal drillouts i.e. EMLP. They were followed for an average of 4.1 years with a surgical failure rate of 20% as defined by the need for further frontal surgery.

Ting et al.[185] recently retrospectively examined the long-term results of the EMLP for the treatment of advanced frontal sinus disease. A total of 143 patients underwent the EMLP over the 16-year period. Mean follow-up was 10.2 years (range 0.9 to 17 years). Symptomatic re-obstruction of the frontal sinus requiring revision surgery occurred in 61 (29.9%) patients. The majority of surgical failures (61%) occurred within two years of surgery. However, failures were observed up to 12 years after drillout.

Conflicting risk factors for failure of the EMLP have been reported. Tran et al.[187] found re-stenosis and revision surgery are partly predicted by the presence of eosinophilic mucous chronic rhinosinusitis as demonstrated by logistic regression analysis. Furthermore, the intraoperative frontal ostium size determined the frontal ostium area at 1 year, and hence maximizing the frontal neo-ostium intraoperatively was a key component to success.

In contrast, Ting et al.[185] found there was no correlation between outcome and a history of smoking, asthma, nasal allergy, aspirin sensitivity, prior sinus surgery, nasal polyposis or the presence of eosinophilic mucous. Similarly, Schlosser et al.[188] found that nasal polyposis, asthma, aspirin triad, or nasal allergies did not impact on the surgical outcomes after frontal drillout. Casiano et al.[189] reported that in their series of 21 patients, a history of hayfever and the use of either prior oral or topical corticosteroid treatment were factors that significantly contributed to the rate of stenosis. Georgalas et al.[190] found a weak association between allergy and frontal stenosis.

Surgical failure after the EMLP is frequently defined as the need for revision surgery on the frontal sinus. Although, frontal stenosis is often noted in these cases, re-stenosis is not necessarily an indication for revision frontal surgery. Ting et al.[185] showed 3.5 % of patients in their series had completely obstructed frontal neo-ostia and were asymptomatic. A further 25.2% had stenosed neo-ostia without symptoms. Schlosser et al.[188] found 2 patients (out of 44 patients undergoing the EMLP) with significant stenosis but that did not require further surgery. Georgalas et al.[190] on the other hand found 10

patients (out of 103) that had patent frontal ostia and persistent symptoms and 3 of 12 patients with stenosed ostia without symptoms.

Summary of the Literature Review

Chronic rhinosinusitis is a disorder that has a significant prevalence in society. It results in a massive financial and social burden. The pathogenesis and treatment of this disorder remains unclear. A significant research effort has been dedicated to unraveling the aetiology, pathogenesis and treatment of idiopathic CRS. Surgery is considered a treatment option for failed medical treatment. The extent of surgery required for optimal treatment is debatable.

Proving the efficacy of Endoscopic Sinus Surgery is almost impossible to do with high-level scientific studies. Blinded randomized controlled trials in surgery are always difficult. However, in the treatment of CRS it is even more difficult because surgery is only considered once medical management has failed to control patient symptoms. Furthermore, endoscopic sinus surgery is often used as an adjunct to ongoing medical treatment. The surgery performed and the medical treatment instituted prior to, during and post surgical intervention varies greatly.

The historic concept of Functional Endoscopic Sinus Surgery has been shown to have a number of limitations. The concept of improving mucociliary function by improving drainage at the OMU makes sense. But a significant proportion of patients with CRS have no disease in the OMU, and improving mucociliary function does not necessarily correlate with patient symptom improvement. Therefore, surgically addressing ***only*** the OMU, does not have appear to

have a rational basis. Surgery focused only on this area appears to have a high failure rate especially where disease extends into the frontal recess and frontal sinus. Residual cells left in the frontal recess as well as instrumenting the OMU appears increases the risk of recalcitrant frontal sinusitis.

The frontal sinus has traditionally not been addressed without symptoms specific to the frontal sinus. However, facial pain and headaches localized to a particular sinus are considered minor symptoms in CRS. Surgery is often advocated for other more accessible sinuses such as the maxillary sinus, without there being necessarily pain localized to the maxillary sinus. In other words, the frontal sinus appears to be managed differently by some surgeons, even though the underlying pathophysiology is exactly the same.

There is no doubt that there are legitimate concerns regarding iatrogenic frontal sinusitis due to stenosis of the frontal sinus ostium or the frontal sinus drainage pathway. However, there is increasing evidence that shows more surgery is required for recalcitrant CRS (rCRS), not less. The reasons for this are not clear, but appear to be a combination of maximally ventilating the sinuses, removing inflammatory mediators intraoperatively and facilitating topical medical treatment postoperatively.

A systematic review of the literature raises a number of topical issues, which will be addressed within this thesis:

- Endoscopic Sinus Surgery has been performed for CRS refractory to medical treatment. However, surgery on the frontal sinus has historically been frowned upon unless symptoms of frontal headaches existed. The question if the diseased frontal sinus should be addressed surgically in every case of medically refractory frontal sinus disease is still unknown.
- Frontal sinus surgery has been performed and the outcomes have been reported on in a number of studies. However, the potential success factors and risk factors for failure are still unknown.
- Extended endoscopic frontal sinus surgery and in particular the EMLP has been employed as an alternative to the osteoplastic flap for recalcitrant frontal sinusitis. The short-term outcomes of this procedure have been reported on and it appears safe and efficacious. However, the long-term success of this procedure is still unknown. Further, the risk factors for success and failure over the long term are not clear.
- Extended surgery on sinuses other than the frontal sinus have been used to great effect for rCRS. For the ethmoid sinuses-nasalization; for the maxillary sinus, CFT, mega-antrostomies and modified medial maxillectomies have been employed with reportedly good success rates. The question therefore is whether the EMLP should be similarly used for rCRS affecting the frontal

sinus. Currently the EMLP is used only after failure of standard frontal sinus surgery. The role of performing the EMLP as primary surgical treatment is unknown, and which particular patient would benefit most from this approach is similarly unclear.

Aims

1. Validate a new Patient Reported Outcome Measure to quantify changes following surgical intervention.
2. Investigate the role of surgical intervention in addressing primary frontal sinus disease
3. Identify risk factors for failure of frontal sinus surgery by identifying the type of patient most likely to require extended frontal sinus surgery (EMLP) for symptom alleviation and control
4. Investigate the outcome of EMLP surgery, and identify risk factors for failure

Quality of life assessment in Chronic Rhinosinusitis using the Adelaide Disease Severity Score

Conducted in the Department of Otolaryngology Head and Neck Surgery,

University of Adelaide, Adelaide, Australia

chapter 2

The Journal of Laryngology & Otology, 1 of 5.

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MAIN ARTICLE

Chronic rhinosinusitis assessment using the Adelaide Disease Severity Score

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Abstract

Aim: This study aimed to validate the use of the Adelaide Disease Severity Score for the assessment of chronic rhinosinusitis.

Study design: A prospective cohort study supplying level 2b evidence.

Methods: Forty-eight patients, scheduled for endoscopic sinus surgery for failed management of chronic rhinosinusitis, completed the Sino-Nasal Outcome Test 22 and the Adelaide Disease Severity Score tool (the latter assessing symptoms (i.e. nasal obstruction, rhinorrhoea, post-nasal drip, headache or facial pain, and olfaction) and quality of life). Lund–Mackay computed tomography scores and Lund–Kennedy endoscopic scores were also recorded. The Adelaide Disease Severity Score results were then compared with those of the other three tools to assess correlation.

Results: Mean scores (95 per cent confidence intervals) were 22.31 (21.47–24.15) for the Adelaide Disease Severity Score and 30.6 (27.15–34.05) for the Sino-Nasal Outcome Test 22; there was a statistically significant correlation (Spearman coefficient = 0.45; $p = 0.0015$). A statistically significant correlation was also noted with the Lund–Mackay score ($p = 0.04$) and with the Lund–Kennedy score ($p = 0.03$).

Conclusion: The Adelaide Disease Severity Score is a simple, valid tool for clinical assessment of chronic rhinosinusitis, which correlates well with the Sino-Nasal Outcome Test 22, Lund–Mackay and Lund–Kennedy tools.

Key words: Quality of Life; Outcomes Assessment; Sinusitis; Endoscopic Surgical Procedures

Introduction

Chronic rhinosinusitis is an extremely common clinical condition affecting up to 15 per cent of the population in the UK and Australia. It has a significant impact on patients' quality of life as well as a substantial economic cost to society.

Assessment of chronic rhinosinusitis patients involves clinical history-taking and examination as well as, increasingly, the use of patient-reported scoring systems, disease severity markers and validated outcome measures.

Patient-reported outcome measures are questionnaires completed by patients which give an overview of symptoms at any given time. They can be used during initial assessment or to assess a patient's health status before and after an intervention (e.g. surgery). They can give a useful 'snap-shot' of a patient's subjective clinical condition, as well as an indication of the specific disease burden in that individual patient. The information obtained can be used as an indicator of the treatment outcomes and/or the quality of post-treatment care.[1]

Although patient-reported outcome measures are generally not used as fixed criteria when making treatment decisions, the ideal such measure for chronic rhinosinusitis should have the following qualities: (1) simplicity and ease of use; (2) reliable quantification of the patient's disease-specific burden; (3) good correlation with objective assessment of disease severity; (4) reliable response to changes in disease-specific burden after treatment interventions; and (5) enabling categorisation of patients into appropriate treatment arms. For example, the ideal patient-reported outcome measure would classify chronic rhinosinusitis patients into distinct disease 'stages', in a manner analogous to the staging of head and neck cancer patients prior to treatment.

Various rhinology-specific patient-reported outcome measures have been reported and validated in the literature. One of the most popular is the Sino-Nasal Outcome Test 20 questionnaire.[2] This has been modified to create the Sino-Nasal Outcome Test 22,[3] which includes symptoms involving taste, smell and nasal congestion. These two patient-reported outcome measures assess both general and rhinosinusitis-

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2.1 ABSTRACT

Objective: The aim of this study was to validate the use of a simple and reproducible Patient Reported Outcome Measure in the assessment of Chronic Rhinosinusitis.

Study Design: Prospective cohort study

Level of Evidence: 2b

Methods: Forty-eight patients listed for endoscopic sinus surgery for failed management of chronic rhinosinusitis completed a SNOT-22 score and the Adelaide Disease Severity Score (ADSS). The ADSS is a combination of a symptom score and a quality of life score. This system graded on a scale of 1-5 the symptoms of nasal obstruction, rhinorrhoea, post-nasal drip, headache or facial pain and sense of smell as well as a general quality of life visual analogue scale from 0-7. Lund-Mackay (LM) CT scores and Lund-Kennedy (LK) endoscopic scores were also recorded. The ADSS was then compared with the SNOT-22, LM and LK scores to assess its correlation to these subjective and objective markers of disease severity.

Results: Mean SNOT-22 scores were 30.6 (95% confidence interval 27.15 – 34.05) and ADSS were 22.31 (95% CI 21.47 – 24.15). The Spearman correlation coefficient was 0.45 with a statistically significant correlation between the two scores (p-value=0.0015). A statistically significant correlation was also noted between ADSS vs LM score (p-value = 0.04) and ADSS vs LK score (p-value = 0.03).

Conclusions: This study demonstrates that the ADSS correlates well to the SNOT-22 score, LM score and Lund Kennedy score. It is a simple and valid method of clinical assessment of chronic rhinosinusitis.

Key Words: Quality of Life, Outcome Assessment, Sinusitis, Endoscopic Sinus Surgery

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2.2 INTRODUCTION

Chronic rhinosinusitis (CRS) is an extremely common clinical condition affecting up to 15% of the population within the United Kingdom and Australia. It has a significant impact on patient's quality of life as well as an economic cost to society. Patient assessment in CRS includes clinical history and examination, and increasingly, the use of patient reported scoring systems, disease severity markers and validated outcome measures.

Patient Reported Outcome Measures (PROMs) are self-reported questionnaires completed by patients themselves to give an overview of their symptoms at any given time. They can be used on initial assessment or to assess their health status pre- and post- an intervention such as a surgical procedure. They can be useful in representing a snap-shot of a patient's subjective clinical condition, and can give an indication of the disease specific burden on an individual patient. Information gathered can be used as an indicator of outcome or quality of care delivered to patients following intervention [62]. Although they are generally not used as fixed criteria for decisions to treat, the ideal PROM for CRS should have the following qualities:

- Simple and easy to use
- Reliably quantifies the disease specific burden to the patient
- Correlates well to objective findings of disease severity

- Reliably reflects changes in disease specific burden after surgical and/or medical intervention.
- Allows categorization of patients into appropriate treatment arms. For example, the ideal PROM would classify patients into a disease "stage" for CRS in a manner anomalous to the staging of head and neck cancer patients prior to treatment.

Various rhinology-specific PROMs have been reported and validated in the modern literature. One of the most popular questionnaires is the Sino-Nasal Outcome Test-20 (Snot 20)[64]. This was modified to create the Snot 22 [65] to include the symptoms of taste/smell and nasal congestion. These PROMs assess both rhinosinusitis specific and general points. However, as a CRS assessment tool it has a few shortcomings. Firstly, its length means that it is more difficult to collect at the time of consultation. Secondly, we feel it is not specific enough to rhinosinusitis with the quality of life subsections often related to numerous other confounding conditions such as sleep apnoea. Finally, it does not correlate well with objective findings of disease severity.

We aimed to produce a simple and reproducible scoring system that can be easily used in directly assessing the patient's clinical status, but which would have an appropriate correlation to the SNOT-22 and objective findings of disease severity.

We propose the Adelaide Disease Severity Score (ADSS); a simplified scoring system that includes the five most significant sino-nasal symptoms

counted as major criteria for CRS by the Rhinosinusitis Task Force [191], together with a general quality of life visual analogue scale [65] (Figure 2.1). We assessed the validity of this simplified scoring system against the SNOT-22, and objective measures of disease severity such as the Lund Kennedy Endoscopic Score and Lund Mackay CT score.

The Adelaide Symptom Severity Score

	1 = absence of symptoms, 2 = mild, 3 = moderate, 4 = Severe, 5 = Extreme
Nasal Obstruction	1 2 3 4 5
Rhinorrhoea	1 2 3 4 5
Post Nasal Drip	1 2 3 4 5
Headache/Facial Pain	1 2 3 4 5
Sense of Smell	1 2 3 4 5

	0 = no effect, 7 = maximal effect
How do your symptoms affect your quality of life	0 ——— 7

Figure 2.1 Adelaide Symptom Severity Score

2.3 MATERIALS AND METHODS

2.3.1 Study Design

This was a prospective cohort study of patients listed for endoscopic sinus surgery for failed medical management of chronic rhinosinusitis in the tertiary rhinology practice of the senior author (P.J.W.) based in Adelaide, South Australia, Australia. The institution's Human Ethics Committee approved the study and all patients provided their consent to participate in the study.

There were 48 consecutive patients in an 11 month period between November 2007 and October 2008. Patients who were from interstate or overseas were excluded. All patients met the American Academy of Otolaryngology-Head and Neck Surgery diagnostic criteria for CRS [191]. All patients were treated by the senior author, and received exactly the same medical and surgical management.

2.3.2 Data Collection

Preoperative demographic data was collected in all patients including age, sex and medical history. As part of the clinical history a standard symptom scoring system was used (Figure 2.1).

The treating surgeon would record on a scale of 1 to 5 (with 5 being the most severe), the severity of the following symptoms as reported by the patient: nasal obstruction, rhinorrhoea, post-nasal drip, headache or facial pain and sense of smell. These were added to give a total out of 25. A visual analogue

scale (VAS) was filled in by the patient, recording their general quality of life on a score between 0-7. These two scores were added to give a total out of 32. In addition to these questions, the SNOT-22 was also completed by the patient. During clinical examination a Lund-Kennedy (LK) endoscopic score was recorded and all patients underwent preoperative CT scans, from which a Lund-Mackay (LM) score was recorded.

2.3.3 Data analysis

Statistical analysis was performed using two-tailed Spearman Correlation for non-parametric data using GraphPad Prism 5.0 software (GraphPad Software, San Diego, CA). Statistical significance was accepted when $P < .05$

2.4 RESULTS

A total of 48 patients fulfilled the criteria for entry into this study. The group consisted of 24 female and 24 male subjects with a median age of 54 years (range 22-80).

SNOT-22 versus ADSS

Mean SNOT-22 scores were 30.6 (95% confidence interval 27.15 – 34.05) and ADSS were 22.31 (95% CI 21.47 – 24.15). The Spearman correlation coefficient was 0.45 with a statistically significant correlation between the two scores (p-value = 0.0015).

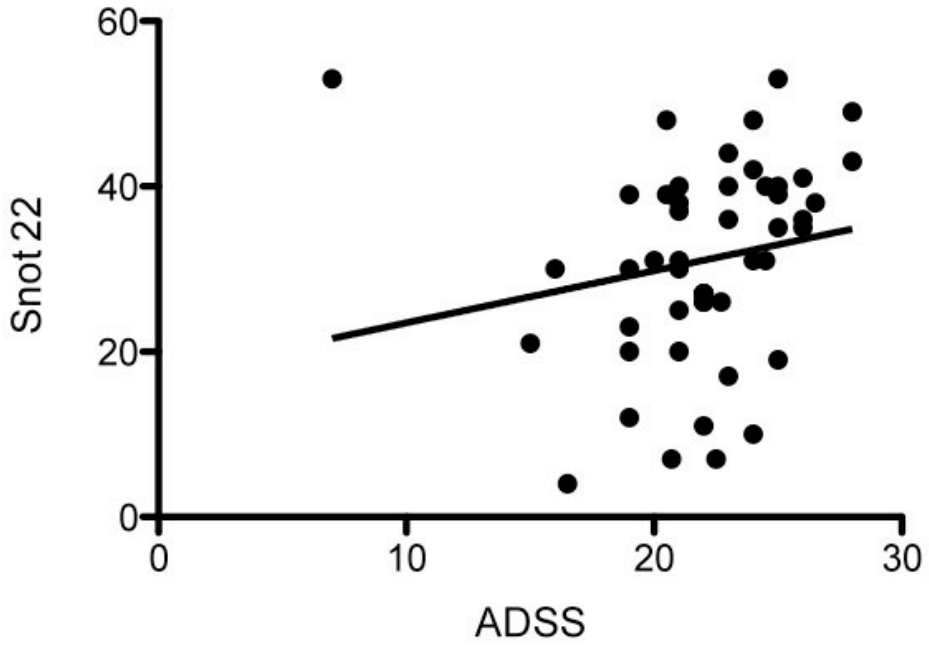

Figure 2.2: SNOT-22 and ADSS versus Lund-Mackay CT score and Lund-Kennedy Endoscopy Score

There was no statistical correlation noted between SNOT-22 scores and both Lund-Mackay (p=0.40) and Lund-Kennedy scores (p=0.57). However, there was a statistical correlation seen between ADSS and both Lund-Mackay and Lund-Kennedy scores. The Spearman correlation coefficient was 0.29 (p=0.04) and 0.31 (p=0.03) respectively.

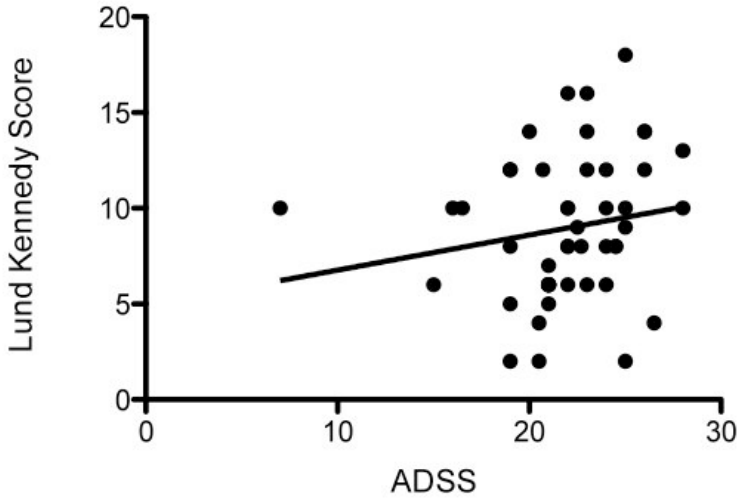

Figure 2.3: ADSS vs Lund Kennedy Score

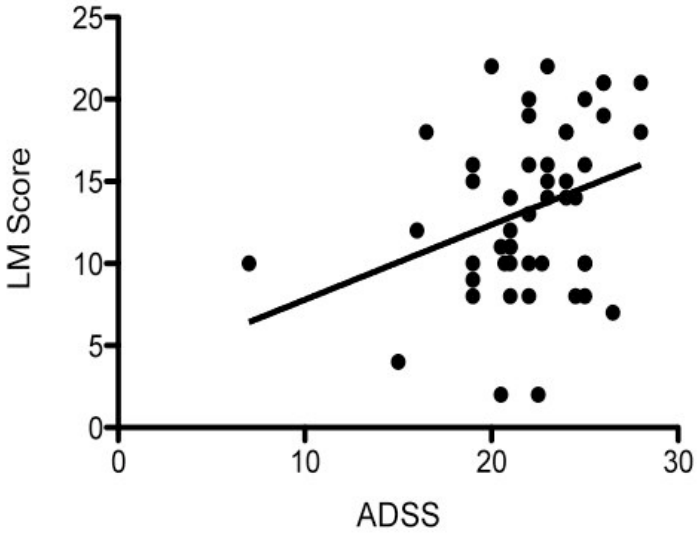

Figure 2.4:ADSS vs Lund Mackay Score

2.5 DISCUSSION

This study demonstrates that the ADSS correlates well to the SNOT-22, as well as to objective markers of disease severity. To our knowledge it is the first PROM to do so. Its use simplifies data gathering in clinical practice while retaining relevance and validity.

Various rhinology-specific PROMs have been reported and validated in the modern literature. Piccirillo[63] reported the use of a 31-item rhinosinusitis outcome measure in 1995 which contains both general and rhinosinusitis-specific questions. This was subsequently condensed into the Sino-Nasal Outcome Test [64] which contains 20 nose, sinus and general points that was validated as a disease-specific, health related quality of life measure for rhinosinusitis. A change to this questionnaire added in two points that were left out which were felt to be extremely important in quality of life reporting by CRS patients; nasal obstruction and loss of sense of taste and smell [65], thus the questionnaire became the SNOT-22. Both the SNOT-20 and SNOT-22 are well established methods of patient assessment in CRS[66,67] as well as other diseases including septoplasty[68], asthma and COPD[69], Wegners Granulomatosis and other vasculitides [70,71], and following nasal tip surgery [72]. International translations of these scores have been used in Japan, Denmark and Czechslovakia[73-75]. Other variant sino-nasal outcome questionnaires include the Sino-Nasal assessment questionnaire (SNAQ)[76], SinoNasal outcome test-16[77], Rhinosinusitis symptom inventory[78] and Rhinosinusitis utilitiy index[79] amongst others.

Despite the interest in using the SNOT-20 or 22, it is well recognised that it has poor correlation to true clinical meaningfulness[80] and although there have been attempts to make it more relevant to clinical conditions such as weighting certain questions, we suggest an alternative scoring system that is specific to CRS symptoms alone and one overall quality of life score.

Our simplified scoring system includes the five most significant sino-nasal criteria which correspond to the major criteria defined by the Rhinosinusitis Task Force [191] along with a general quality of life visual analogue score .

Headache and facial pain is combined into a single measure as patients can find difficulty in differentiating between these two symptoms. It is recognised that these five symptoms are the most important symptoms in terms of prevalence and severity as recorded in patients undergoing ESS for CRS [192]. The two remaining major criteria were excluded as purulence in the nasal cavity is an examination finding and fever pertains to acute rhinosinusitis only. The simplicity of our scoring system leads to greater compliance and less patient misunderstanding when answering the questions.

One drawback in the SNOT 22 scoring system is that the points relating to falling asleep, waking at night, lack of sleep and feeling tired can easily be related to other clinical conditions including obstructive sleep apnoea, COPD, heart failure or depression. Patients completing the questionnaire are often confused by these questions and are unable to differentiate between

rhinosinusitis or other conditions as the cause for their symptoms, and whether or not they should make that differentiation at all when completing the questionnaire.

The use of all major and minor Rhinosinusitis Task Force symptoms has been reported in the pre- and post- surgical assessment of patients undergoing ESS[78] but we have demonstrated that, refining this down to the major symptoms as listed, as well as the VAS gives a valid score that correlates well to the SNOT-22.

The lack of correlation between SNOT-22 scores with either the Lund-Mackay or Lund-Kennedy scores has been noted in a number of studies [66,81]. However, this study demonstrates a statistically significant correlation between the ADSS and two objective measures of disease severity: the Lund-Mackay and Lund-Kennedy scores. This is possibly as a result of the individual questions being more heavily weighted to CRS specific symptoms. It may therefore give a better indication of rhinological disease status at that point in time.

The results suggest that the ADSS satisfies most of the criteria of the ideal PROM. It is simple to use and, despite its simplicity, retains the validity of the SNOT-22 with regards to measuring disease specific burden. As the SNOT-22 has been validated for both pre and post treatment we propose that this simplified scoring system will also correlate to the SNOT-22 after intervention. The ADSS also correlates well with objective findings of disease severity,

which is in contrast to the more complex SNOT-22. Further work, however, is required to assess whether the ADSS can successfully “stage” CRS patients. This would allow the treating physician to tailor management, based on the disease stage.

The strength of these results lie in the fact that there are no confounding surgical or medical factors and that this prospective cohort is made up of consecutive unselected patients operated upon over the study period. All patients were treated by the senior author and received identical medical and surgical management.

2.6 CONCLUSION

Patient reported questionnaires are an important part of assessment and outcome reporting. This study demonstrates that the ADSS correlates well to the SNOT-22 score, LM score and LK score. It can therefore be confidently used as a valid method of clinical assessment pre and post treatment. Further work is required to ascertain whether the ADSS, either on its own, or in conjunction with other indicators, can successfully “stage” CRS patients in much the same way as head and neck cancer patients are staged prior to receiving treatment. Such a tool would optimise patient care by tailoring management based on disease stage.

Summary:

- The ADSS is a simplified Quality of Life assessment tool in the assessment of Chronic Rhinosinusitis
- It correlates well with other well-validated assessment tools in chronic rhinosinusitis such as the SNOT-22, Lund Mackay and Lund Kennedy scores.
- With further work, these assessment tools might be able to successfully “stage” CRS patients and optimise care by tailoring management based on disease stage

Long Term Results After

Primary Frontal Sinus Surgery

chapter 3

Conducted in the Department of Otolaryngology Head and Neck Surgery,

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Naidoo, Y., Wen, D., Bassiouni, A., Keen, M. & Wormald, P.J. (2012) Long-term results after primary frontal sinus surgery.
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3.1 ABSTRACT

Objectives/Hypothesis: To evaluate the long-term frontal ostium patency rate and symptom improvement in patients undergoing ***primary*** endoscopic frontal sinusotomy (Draf 2A) and to assess the impact of patient factors, disease factors and frontal ostium size on surgical outcomes.

Study Design: Retrospective Case Series

Level of Evidence: Level 4

Methods: Retrospective chart review. Endoscopic assessment of frontal ostium patency and patient reported symptoms were prospectively collected on patients who underwent primary frontal sinusotomy between January 2003 and December 2009

Results: 109 patients underwent ***primary*** endoscopic surgery on 210 frontal sinuses over the study period. The overall patency rate was 92%. Complete resolution of symptoms was noted in 85 patients (78%). Stenosis of the frontal sinus ostium correlated significantly with persistence of symptoms, infection or polyp recurrence ($p=0.0066$) and frontal ostium size ($p<0.03$). No significant correlation could be found between the presence of eosinophilic mucin, asthma, polyposis, and smoking on patency or resolution of symptoms.

Conclusions: To our knowledge, this is the largest study of ***primary*** endoscopic frontal sinus surgery in the literature. The technical and subjective measures of success are high. Frontal ostium size correlates with risk of stenosis of the frontal sinus. Patients with a stenosed frontal ostium and

residual frontal sinus disease are more likely to be symptomatic or have endoscopic evidence of polyp recurrence or endoscopic evidence of persistent infection. Asthma, EMCRS, allergy and smoking do not appear to affect outcomes.

Key Words: Frontal sinusotomy, endoscopic sinus surgery, patency, outcomes, frontal drillout

3.2 INTRODUCTION

Endoscopic sinus surgery has been accepted as the treatment of choice for chronic rhinosinusitis (CRS) refractory to medical treatment. However, surgery of the frontal sinus is the most technically demanding aspect of this surgery. The complex and varied anatomy, acute nasofrontal angle and proximity to critical structures such as the olfactory fossa, skull base and orbit contribute to the technical difficulty of this surgery. These narrow confines, and a tendency to postoperative scarring with subsequent stenosis of the frontal ostium, make surgical treatment of chronic *frontal* sinusitis challenging.

Endoscopic frontal sinus surgery is technically demanding. Surgical dissection of the frontal recess has, in the past, been discouraged[193], even when there is CT scan evidence of mucosal disease in frontal sinus and recess. The concern was that inappropriate mucosal trauma would lead to scarring and obstruction of the frontal sinus ostium leading to iatrogenic frontal disease. The risks of such iatrogenic disease are often emphasized in textbooks[193] even though the incidence of iatrogenic frontal sinus disease is unknown. For many years, the prevailing paradigm was to treat the osteo-meatal complex and anterior ethmoid sinus (bulla ethmoidalis), with the hope that resolution of disease in this area would improve the mucosa of the frontal sinus and recess.

Short-term outcomes after endoscopic frontal sinus surgery have previously

been reported in the literature [164,169,170]. However, there is only a limited number of studies that have examined long-term frontal ostium patency[165] and improvement in patient symptoms[168].

The primary objective of this study, is to evaluate quantitative and qualitative measures of success through long-term frontal ostium patency and improvement in patient symptoms after primary endoscopic frontal sinusotomy. A secondary objective is to analyse the impact of patient factors (asthma, allergy and smoking), disease factors (polyps, eosinophilic mucin) and frontal ostium size on surgical outcomes.

3.3 MATERIALS AND METHODS

3.3.1 Study Design

This retrospective review of prospectively collected data was undertaken in the tertiary referral rhinology practice of the senior author (PJW) based in Adelaide, South Australia, Australia. Enrolment occurred between January 2003 and December 2009. The institution's Human Ethics Committee approved the study (Application Number 2011021).

3.3.2 Inclusion and Exclusion Criteria

All patients who underwent surgery had previously failed at least a 2 month course of maximal medical treatment that included culture directed antibiotics, saline douches, topical nasal steroids and oral steroids. All patients had persistent symptoms of nasal blockage (NAO), facial pain/headache (FP), rhinorrhea, postnasal drip (PND), and/or anosmia . In addition, Draf 2A frontal sinusotomy was performed **only if there was objective evidence of persistent post-treatment mucosal thickening in the frontal recess or frontal sinus on paranasal CT scans**, and endoscopic evidence of ongoing disease such as polyposis, mucosal edema and/or muco-purulence.

Patients without objective evidence of post-treatment mucosal thickening in the frontal recess or frontal sinus were excluded. Patients undergoing endoscopic sinus surgery for reasons other then chronic sinusitis were also excluded. This included patients undergoing surgery for benign and malignant paranasal sinus tumors, mucoceles, trauma, cystic fibrosis, Kartagener's syndrome or other primary muco-ciliary abnormalities. Finally, any patient not available for long term follow up was excluded from this analysis. This includes interstate and overseas patients referred to the senior author for primary surgical intervention but who received post-operative care from the referring physician.

3.3.3 Recording of Data

Patient symptoms that were recorded on a scale of 1 to 5 (Table 3.1) included nasal obstruction, rhinorrhoea, post-nasal drip, headache or facial pain and anosmia. These scores were added to give a total out of 25.

Table 3.1: Patient Reported, Surgeon Recorded Symptom Scores

Score	Description
1	Absence of symptoms
2	Mild
3	Moderate
4	Severe
5	Extreme

Intraoperative findings of fungus, mucous, polyps and mucopurulence were documented. The dimension of each frontal sinus ostium was documented intraoperatively using a standardized 4mm olive tipped probe or measuring tool designed specifically to record ostium dimensions.

Postoperatively, persistence of symptoms was noted and endoscopy performed on each visit. Postoperative endoscopic evaluation involved assessment of the maxillary sinus, ethmoid cavity, frontal ostium and sphenoid sinus, for evidence of stenosis, crusting, scarring, edema, polyposis or purulent discharge. The frontal sinus was defined as being patent if the ostium could be visualized endoscopically, and stenosed if there was scarring, edema or polyposis occluding the frontal ostium. A sinus was deemed to be infected if there was evidence of mucopurulence on endoscopy, regardless of whether there was a positive culture result.

Demographic and clinical information was compiled by reviewing each patient's chart. Potential prognostic factors for CRS such as asthma, aspirin sensitivity, allergies, and history of smoking was collected. In addition, disease specific prognostic factors such as the presence of eosinophilic mucin, fungal and bacterial cultures from intraoperative samples were recorded.

Finally, long term symptom improvement was obtained by means of a patient

reported questionnaire using the same preoperative scale to document symptoms.

3.3.4 Surgical Technique

The extent of sinus surgery was determined by reference to preoperative CT scans and intraoperative findings. All sinuses with evidence of mucosal inflammation, infection, or polyposis were opened surgically and any diseased mucosa debrided carefully without stripping or exposing underlying bone. The sinuses were irrigated meticulously with saline to remove inflammatory mediators. The size of the maxillary antrostomy was determined by the degree of inflammation within the sinus and canine fossa trephination[125,194] performed when necessary to completely clear severely diseased maxillary sinuses. The sphenoid sinuses were opened from the skull base to the floor of the sinus in cranio-caudal extent and from septum medially to the junction with the orbit laterally. The ethmoid cells were completely removed in every case. All frontal sinusotomies were performed using the axillary flap technique and 3-D building block model of the frontal recess[195,196].

The surgical technique for Draf 2A frontal sinusotomy focuses on two key aspects: ostium size maximization and mucosal preservation.

The frontal ostium is maximized by complete clearance of all cells in the frontal recess and removal of cells migrating through the ostium. As a first

step, a 3-dimensional reconstruction of the frontal recess anatomy using the building block model[196] is created. Each block represents a cell within the frontal recess and allows the surgeon to carefully plan the surgical approach and to identify each cell to be dissected. With a comprehensive understanding of the drainage pathway of the frontal sinus, dissecting instruments can be placed along the drainage pathway, facilitating a safe dissection while minimizing mucosal trauma. This allows a step-wise cell removal with complete exposure of the frontal ostium. Note, the bone forming the natural frontal ostium is not removed – only the cells below and in the ostium are removed.

Mucosal trauma in this critical area is also reduced by using the axillary flap[195] technique to dissect the frontal recess. The axillary flap technique allows use of a 0 degree endoscope to approach the frontal sinus. By improving (reducing) the angle of attack and the distance to the frontal ostium, cells pneumatising into the frontal sinus, are more easily removed with standard endoscopes and instruments. A similar technique without preservation of mucosa was described by Pletcher et al [197]for accessing the frontal recess.

Routine postoperative medical therapy was used. This consisted of oral antibiotic therapy for 7 days, and a tapering dose of oral prednisolone (25mg daily for 7 days, 12.5mg daily for 7 days, 12.5mg every second day for seven days) for cases with diffuse nasal polyposis. All patients were encouraged to start saline douching of the nose on the first postoperative day. The first postoperative visit was scheduled two weeks after surgery and the sinonasal

cavity was debrided at this time. The second postoperative visit was scheduled 6 weeks after surgery. Regular 6 monthly follow up was performed thereafter.

3.3.5 Statistical Analysis

Statistical analysis was performed using GraphPad Prism 5.0 software (San Diego, CA). Continuous data are displayed as mean ± SD. Characteristics of the success and failure groups were compared using chi-square, Fisher exact, and t tests where appropriate. Statistical significance was accepted when $P < .05$. Multivariate analysis was performed but did not change the statistical outcome.

3.4 RESULTS

1. Patient Demographics

Primary endoscopic frontal sinus surgery was performed on 118 patients. Nine patients received their postoperative care from their referring interstate ENT physician and were excluded from the analysis. There were no significant differences between the group lost to follow up and the remaining 109 patients.

Table 3.2: Comparison between Included and Excluded Groups.

`	Analysis Group	Patients Lost to Follow Up	Statistically Different
Total No of Patients	109	9	
Male	69	6	No
Female	40	3	No
Age	48	39	No
Asthma	32	2	No
CRSwNP	74	4	No
EMCRS	45	2	No
ASA	2	0	No
Smoker	10	1	No
Total Symptom Score	15.28	15.22	No
LM Score	15.14	14.5	No

The average age was 48.5 years (SD 15.2, range 14-78 years). There were 69 male patients and 30 female patients. A total of 210 Draf 2A frontal sinusotomies were performed on these 109 patients. The average follow up period was 16.2 months (95% confidence interval 13.0-19.3 months, sd=16.6 months).

83/109 (76%) patients were allergic on RAST (Immunocap®), and/or Skin prick testing. 29% were asthmatic and 2% were aspirin or acetylsalicylic acid intolerant (ASA). Intraoperatively, nasal polyposis was found in 74 patients (68%), and eosinophilic mucous in 45 patients (41%). These patients were classified as CRSwNP (chronic rhinosinusitis *with* nasal polyposis) and EMCRS (eosinophilic mucin chronic rhinosinusitis) respectively.

2. Radiological Severity

The average Lund-Mackay (LM) score for all patients was 15.1(SD = 4.0, range 6-24, 95% CI 14.1-16.2), with the mean right frontal sinus score being 1.2 (SD =0.5), and left frontal sinus 1.2(SD=0.5) out of a maximum of 2.

The LM scores was significantly greater for the CRSwNP group only. (Table III).

Table 3.3: Lund-Mackay (LM) scores for each cohort.

(Key: FO- frontal ostium, FDO – frontal drillout procedure, CRSwNP- chronic sinusitis *with* nasal polyposis, CRSsNP-chronic rhinosinusitis *sans* nasal polyposis, EMCRS-eosinophilic mucin chronic rhinosinusitis)

Group	LM Score	Difference	P-value
All patients	15.1		
Asthma	16.6	2.0	0.071
No Asthma	14.6		
CRSwNP	15.7	2.4	0.049
CRSsNP	13.3		
EMCRS	16.1	1.9	0.065
Non EMCRS	14.2		
Stenosed FO	15.9	0.9	0.57
Patent FO	15.0		

3. Symptom Resolution

The total preoperative symptom score for all patients was 15.3 (95% CI 14.8-15.9, SD = 2.6). Nasal obstruction (NAO) was the most severe reported symptom and anosmia was least symptomatic (Figure 3.1).

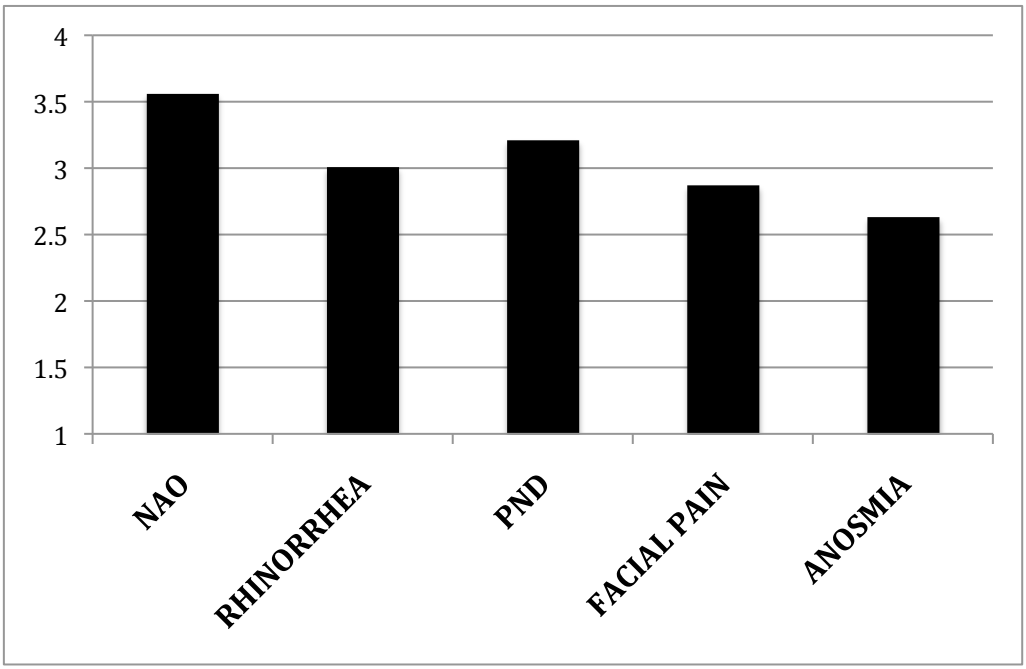

Figure 3.1: Preoperative Symptom Score

(NAO=nasal obstruction, PND=post nasal drip, 1=asymptomatic, 5= extremely symptomatic)

At their last follow up (mean 16.2 months) 85/109 (78%) patients had a complete resolution of their symptoms. 24/109 patients noted an improvement in their symptoms but were still somewhat symptomatic. No patients reported a worsening of symptoms after surgery.

Incomplete symptom resolution or abnormal endoscopy was noted in 9/11 patients with stenosis of the frontal sinus compared with 35/98 in the patent frontal sinus group (p=0.0066). Asthma, EMCRS and CRSwNP were not statistically associated with persistence of symptoms or abnormal endoscopic findings.

69/109 patients returned the post-treatment questionnaires at an average of 54 months post operatively (range 17-96 months, 95% CI 49.8 -58.8 months). Pre and post surgical treatment symptom scores for each cohort are shown in Figure 2. This showed substantial long-term improvement across all cohorts.

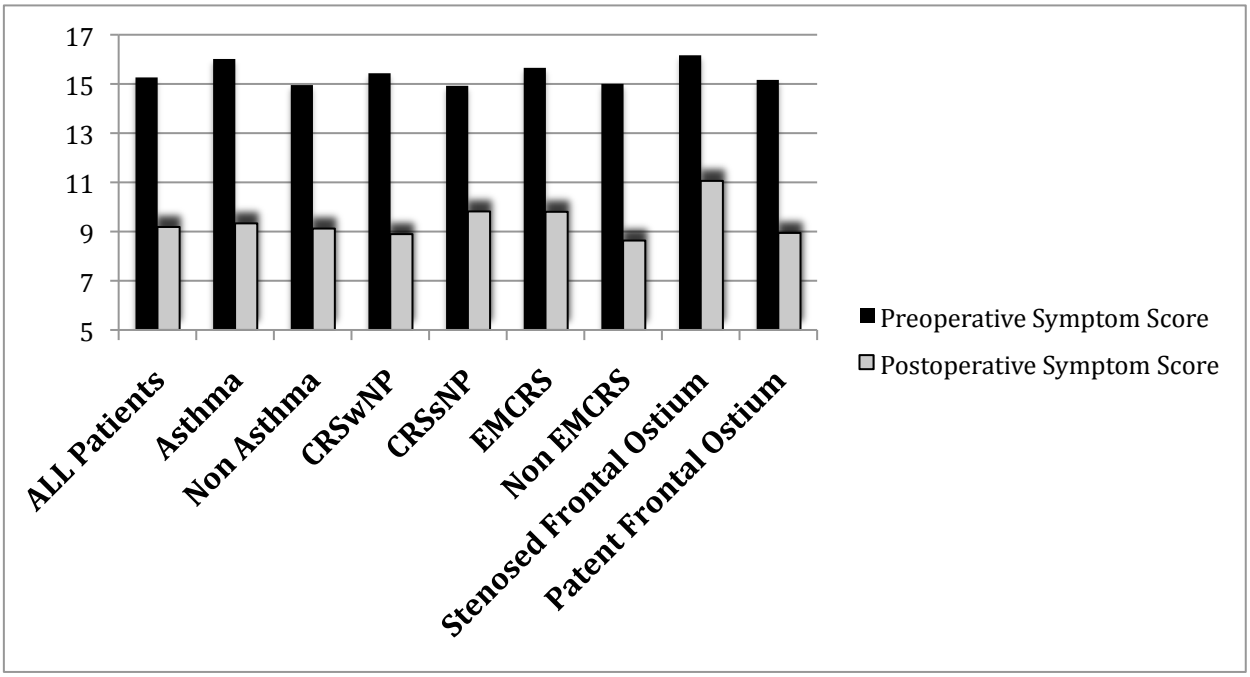

Figure 3.2: Pre and Post-operative Symptom Scores.

(All cohorts obtained significant long-term improvement in symptoms. Note on this scale, a score of 5 is asymptomatic.)

4. Frontal Sinus Outcomes

4.1 Frontal Sinus Patency

The overall patency rate was 92% with 193 of 210 frontal sinuses remaining patent on endoscopy. 17 stenosed frontal sinuses were found in 11 patients (6 bilaterally stenosed frontal sinuses, 5 unilaterally stenosed) representing a 8% postoperative stenosis rate due to scarring or edema of the frontal recess. The mean follow up period of this cohort was 22.9 months (range 6-60 months, SD 20.0 months). Of these 11 patients, 2 were completely asymptomatic. Of the remaining 9 patients, 3 had recurrence of polyposis affecting the frontal ostium, 2 had persistent infections and adhesion formation, 2 complained of persistent post-nasal drip and 2 had troublesome nasal obstruction. Although all of these patients had endoscopic evidence of frontal ostium stenosis, only 4 patients (33%) with documented evidence of stenosis proceeded to salvage surgery with the Frontal Sinus Drillout procedure (FDO) or Draf 3. The others were successfully managed with medical treatment alone. 5 other patients with patent frontal ostia required salvage FDO for persistence of frontal sinus disease, despite endoscopically patent frontal ostia.

There was no statistical difference in the preoperative symptom score between the stenosed and patent frontal ostium groups. There was also no statistical difference found in the prevalence of allergy, nasal polyposis,

eosinophilic mucin, asthma, or in the Lund Mackay (overall and frontal sinus specific) score between the stenosed and patent groups.

4.2 Frontal ostium size

The dimensions of the intraoperative frontal ostium were statistically smaller in the stenosed group ($p<0.0068$), as seen in Table 3.4. A minimum dimension of >4.8mm appeared to be critical for maintaining long-term patency, whereas there is a strong correlation with stenosis if either the lateral or AP diameter is less than 3.7mm.

Table 3.4: Impact of Frontal Ostium Size on Patency.

(AP-antero-posterior dimension of frontal sinus ostium, Minimum Dimension is the smaller of the AP and Lateral dimension)

	AP Dimension-Stenosed Group	AP Dimension-Patent Group	Lateral Dimension Stenosed Group	Lateral Dimension-Patent Group	Minimum Dimension of Frontal Ostium-Stenosed Group	Minimum Dimension of Frontal Ostium (Patent Group)
Number of values	17	162	17	162	17	162
Mean (mm)	4	5.049	4.529	6.025	3.706	4.87
Std. Deviation	1.458	1.779	2.503	2.319	1.49	1.787
Lower 95% CI	3.251	4.773	3.243	5.665	2.94	4.593
Upper 95% CI	4.749	5.325	5.816	6.385	4.472	5.148
P value	0.0117		0.0298		0.0068	

4.3 Frontal Drillout

9 patients in total proceeded to a FDO procedure after further medical treatment failed to resolve persistent frontal sinus disease. Stenosis of the frontal sinus was strongly correlated with the risk of FDO (p=0.0057, Fisher exact test). 4/11 patients with a stenosed frontal ostium required a FDO, whereas only 5/98 with a patent frontal ostium required FDO. Patients undergoing FDO with a patent frontal ostium had residual endoscopic and radiological evidence of frontal sinus disease despite appropriate medical management.

3.5 DISCUSSION

The results of this study suggest that endoscopic frontal sinus surgery for medically recalcitrant frontal sinus disease is successful when performed by an experienced sinus surgeon. The technical and subjective measures of success are high, with a frontal ostium patency rate of 92%, revision surgery rate of less than 9% and complete resolution of symptoms noted in 78%. Symptom improvement appears to persist long term.

This study shows that 92% of frontal sinus ostia remain patent after endoscopic frontal sinusotomy at a mean follow up time of 17 months. This technical measure of success compares favourably with the literature with short term reported patency rates of 69% to 90%[164,168-170,173], falling to 67%[168] after 4 years.

Symptom improvement is noted long term for all patient groups.

One of the difficulties in comparing technical outcomes is the similarity of patient groups in each study. One objective measure of disease load is the Lund Mackay score, which measures radiological severity. Chan[173] and Philpot[198] in their series of patients undergoing frontal sinus surgery reported average LM scores of 9.5 and 7.4-10.1 respectively. This contrasts with an average LM score of 15.1 in our group of patients with an average LM score

of 1.2 for the right and left frontal sinus respectively. This suggests that good technical results can be achieved despite more severe radiological disease.

Hosemann[164] showed a link between frontal ostium size and stenosis. We confirmed this finding. Intuitively this is not unexpected, as smaller frontal ostia increase the chance of mucosal trauma. Additionally recurrence of polyposis and mucosal oedema would more easily lead to complete closure of small frontal ostia.

The risk of requiring a salvage frontal drillout procedure is increased with a stenosed frontal ostium. 4/11 patients with a stenosed frontal ostium required a FDO, whereas only 5/98 with a patent frontal ostium required FDO ($p=0.0066$). Patients undergoing FDO had residual endoscopic and radiological evidence of frontal sinus disease despite appropriate medical treatment. Following the FDO, these patients had complete resolution of their symptoms. We hypothesize that the FDO allows complete eradication of inflammatory mediators intraoperatively, and facilitates topical therapy postoperatively.

EMCRS, asthma, polyposis and smoking have all been considered potential risk factors for poorer outcomes in ESS[32,142]. In this study, no significant correlation could be found between these risk factors and frontal ostium patency or resolution of symptoms.

There were only 2 patients with Samter's triad of Asthma, Nasal Polyposis

and Aspirin sensitivity in this series. This is a lower rate than reported elsewhere in the CRS literature. The incidence of aspirin hypersensitivity in the general population ranges from 0.6 % to 2.5%[199] and in adult asthmatics from 4.3 % to 11% for mild asthmatics, and up to 24% in severely asthmatic patients[200]. It is conceivable that not all patients with this triad are being identified. Aspirin and salicylate intolerance is dose related, and therefore without a formal diagnosis with an aspirin challenge, patient reported sensitivity might be lower than the true incidence[199 200,201].

Although this is the largest series of primary frontal sinus surgery in the literature, it is still only 109 cases over a 7-year period. This reflects the tertiary referral nature of senior author's practice, where the vast majority of the operative case- load is revision sinus surgery and endoscopic skull base surgery. The strength of the results lie in the fact that there are no confounding surgical or medical factors and that this series is made up of consecutive unselected patients operated upon over the study period. None of the patients had undergone prior sinus surgery and therefore each patient had exactly the same medical and surgical treatment.

Symptom improvement after ESS might be attributable to resolution of pathological changes involving any of the paranasal sinuses. What this study shows, however, is that post surgical stenosis of the frontal sinus ostium correlates significantly with persistence of symptoms, infection and polyp recurrence and increases the risk of salvage frontal sinus surgery in the form of a Frontal Drillout Procedure (Draf 3). This suggests that residual disease in

the frontal sinus contributes to ongoing sinus symptoms.

We advocate a philosophy in which the frontal sinus should be treated no differently to any of the other sinuses. Persistent mucosal inflammation in the frontal sinus confirmed endoscopically and radiologically despite adequate medical treatment should be addressed surgically. Frontal pain or headaches should not be thought of as the only surgical indication for endoscopic frontal sinusotomy. Mucosal disease in the frontal sinus without symptoms of headache can still contribute to the other symptoms of CRS such as NAO, PND, rhinorrhea and anosmia. None of the other sinuses require symptoms specific to it as a pre-requisite for surgical intervention. Therefore the philosophy that a diseased frontal sinus should not be treated without specific frontal sinus symptoms being present is not supported by our data and secondly has no scientific basis in the literature. In this study, a patent frontal ostium was associated with both symptom resolution and endoscopic normalization of the mucosa. Furthermore, no patients in this study experienced worsening of their facial pain or headaches as a result of their frontal sinusotomies. Not one patient with absence of facial pain on presentation developed facial pain after surgery. There was only one patient in this study who had persistent symptoms of facial pain post-operatively. This patient presented with symptoms of NAO, PND and facial pain and all these symptoms except the facial pain resolved with surgery.

Other evidence which supports our view that the clinically diseased frontal sinus should be addressed surgically is corroborated by the National Audit of

Sinonasal Surgery [202,203]. This showed that patients who did not have the frontal recess cleared had a surgical revision rate of 19% at 5 years, which fell to 14.1% when the frontal sinus disease was treated surgically.

However, given the technically demanding nature of performing a Draf2A frontal sinusotomy, we caution that frontal sinus surgery is probably best not performed by the occasional sinus surgeon. This study shows significantly poorer outcomes with a stenosed frontal ostium postoperatively. Although this might be the result of the disease process, it might also be the result of iatrogenic injury from mucosal stripping during frontal sinusotomy or remnant cells. Particular care must also be taken in cases with naturally narrow frontal ostia.

3.6 CONCLUSION

To our knowledge, this is the largest study of primary endoscopic frontal sinus surgery in the literature. Endoscopic frontal sinus surgery for frontal sinus disease is successful when performed by an experienced sinus surgeon. The technical and subjective measures of success are high, with a patency rate of 92%, revision surgery rate of less than 9% and improvement of symptoms noted in 78% of patients.

It should therefore be offered to medically refractory, symptomatic patients with endoscopic and/or radiographic evidence of disease affecting the frontal sinus.

Risk Factors and Outcomes for Primary, Revision and Modified Lothrop (Draf 3) Frontal Sinus Surgery

chapter 4

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Naidoo, Y., Bassiouni, A., Keen, M. & Wormald, P.J. (2013) Risk factors and outcomes for primary, revision, and modified Lothrop (Draf III) frontal sinus surgery.
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Data collection, manuscript editing.

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Data collection, manuscript editing.

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Principal project supervision, manuscript editing.

4.1 ABSTRACT

Objectives/Hypothesis: To detail the outcomes of primary, revision and endoscopic modified Lothrop (EMLP) (Draf 3) frontal sinus surgery and evaluate whether risk factors would help determine which patients would benefit from which procedures

Study Design: Retrospective Cohort study

Level of Evidence: Level 4

Methods: Retrospective chart review. Endoscopic assessment of frontal ostium patency and patient reported symptoms were prospectively collected on patients who underwent frontal sinusotomy between January 2003 and December 2009. High risk cohorts were studied to assess their response to standard ESS compared with EMLP.

Results: 339 patients underwent either primary or revision endoscopic frontal sinus surgery who met the inclusion and exclusion criteria. The average length of follow up was 20.8 months (95% CI 18. -22.9 months, SD 18.7 months). Post surgical recurrence of disease with persistence of symptoms requiring an EMLP occurred in 9 patients in the primary group and 38 in the revision group. The highest risk groups for failure of standard frontal sinusotomy were patients with nasal polyps, asthma, Lund Mackay score >16 and frontal ostium size <4mm. (Relative risk 9.9, P<0.0001).

Conclusions: Patients with underlying asthma and polyposis as well as narrow frontal ostia and extensive radiological disease have a high failure rate from standard endoscopic frontal sinusotomy. In this patient group

consideration should be given to offering the patient a primary EMLP procedure, which has excellent success rates with low risks and morbidity.

Key Words: Endoscopic Modified Lothrop Procedure, Frontal sinusotomy, endoscopic sinus surgery, patency, outcomes, risk factors

4.2 INTRODUCTION

Endoscopic sinus surgery (ESS) is accepted as the treatment of choice for chronic rhinosinusitis (CRS) refractory to medical treatment. However, the most appropriate extent of surgical treatment is not well understood at this time and recommendations are largely based on anecdotal observations[204].

Currently, there are two differing philosophies[205 206]to the surgical treatment of frontal sinus disease. The first is based on the notion of "functional" ESS, which postulates that the frontal sinus is "dependent" on the anterior ethmoid sinus (bulla ethmoidalis)[2]. Removing disease in this sinus alone (Draf I) is sufficient because it allows resolution of frontal sinus mucosal disease by re-establishing ventilation and mucociliary function.

The alternative view is that the frontal sinus should be treated no differently than any other sinus, and hence an endoscopic frontal sinusotomy (Draf 2A) is indicated where there is radiological or endoscopic evidence of disease in the frontal sinus after maximal medical treatment[3].

The short and long term outcomes after endoscopic frontal sinus surgery have previously been reported in the literature [164,169,170,206], and confirm both objective and subjective improvement in symptoms in the majority of patients. However, there is a subset of patients, who relapse with persistent frontal sinus disease despite excellent surgery.

The Endoscopic Modified Lothrop Procedure (EMLP), (otherwise known as a Draf III frontal sinusotomy or Frontal Drillout (FDO)) has been used as a salvage procedure for failed frontal sinusotomy and its success is now well documented[184,207]. Presently in our department, it is ***never*** used as a primary surgical option for CRS involving the frontal sinuses, largely due to a lack of evidence supporting this course of action.

The objective of this study is to evaluate whether a particular subset of patients are at increased risk of failing standard endoscopic frontal sinusotomy and would benefit from an EMLP as the first surgical intervention.

We hypothesized that this group would have poor anatomy (ie. small frontal ostium size) and/or disease factors (such as nasal polyps, eosinophilic mucin, osteitis with new bone formation, asthma and aspirin intolerance (ASA)), which would increase the risk of primary ESS failure with subsequent EMLP. The ability to identify, pre-operatively, patients who are more likely to fail primary or revision ESS may allow these patients to be offered an EMLP procedure as their primary surgical therapy.

4.3 MATERIALS AND METHODS

4.3.1 Study Design

Retrospective cohort study. This retrospective review of prospectively collected data was undertaken in the tertiary referral rhinology practice of the senior author (PJW) based in Adelaide, South Australia, Australia. Enrolment occurred between January 2003 and December 2009. The institution's Human Ethics Committee approved the study (Application Number 2011021).

4.3.2 Inclusion and Exclusion Criteria

Inclusion Criteria and Selection of Patients

All patients who underwent surgery had previously failed at least a 2 month course of maximal medical treatment for chronic rhinosinusitis (CRS) that included culture directed antibiotics, saline douches, topical nasal steroids and a 3 week course of oral steroids. All patients had persistent symptoms of nasal blockage (NAO), facial pain/headache (FP), rhinorrhea, postnasal drip (PND), and/or anosmia .

Selection of Patients for Draf 2A/Revision Draf2A or EMLP

A patient was selected for primary Draf 2A frontal sinusotomy only if there was objective evidence of persistent post-treatment mucosal thickening in the frontal recess or frontal sinus on paranasal CT scans, and endoscopic evidence of ongoing disease such as polyposis, mucosal edema and/or muco-purulence.

Patients were offered an EMLP after primary standard functional endoscopic sinus surgery if there was persistence of symptoms, together with endoscopic and CT evidence of disease in the frontal sinuses despite previous ESS and continued maximal medical therapy. This included a further minimum two month course of culture directed antibiotics, topical and oral steroids, and nasal douching.

Patients who had their primary surgery performed by the senior author were offered EMLP if symptoms and signs returned. Patients who had their primary surgery performed elsewhere were offered revision Draf 2a if this was not performed adequately by the previous surgeon (for example, remnant cells with incomplete clearance of the frontal recess). They were offered an EMLP if previous frontal surgery had been properly performed and failed. The EMLP included addressing of all the other diseased sinuses at the same time with complete clearance of all disease.

Exclusion Criteria

Patients without objective radiological evidence of post-treatment mucosal thickening in the frontal recess or frontal sinus were given ongoing medical treatment and not offered further surgery. Patients undergoing endoscopic sinus surgery for reasons other then chronic sinusitis were excluded. This included patients undergoing surgery for benign and malignant paranasal sinus tumors, mucoceles, trauma, cystic fibrosis, Kartagener's syndrome or other primary mucociliary abnormalities. Finally, any patient not available for long term follow up was excluded from this analysis. This includes interstate and overseas patients referred to the senior author for primary surgical intervention but who received post-operative care from the referring physician in a different geographical location.

4.3.3 Recording of Data

Demographic and clinical information was compiled by reviewing each patient's chart. Potential prognostic factors for CRS such as asthma, aspirin sensitivity, allergies, and history of smoking was collected.

Allergy status was determined using an immunocap allergen test or skin prick test, for common environmental allergens, and total serum IgE level. No patient had taken antibiotics, antifungals or steroids in the three weeks prior to their surgery.

Patient symptoms that were recorded on a scale of 1 to 5 (Table 4.1: Patient Reported, Surgeon Recorded Symptom Scores) included nasal obstruction, rhinorrhoea, post-nasal drip, headache or facial pain and sense of smell. These scores were added to give a total out of 25.

Table 4.1: Patient Reported, Surgeon Recorded Symptom Scores

Score	Description
1	Absence of symptoms
2	Mild
3	Moderate
4	Severe
5	Extreme

Intraoperative findings of fungus, mucous, polyps and mucopurulence were documented. Patients were classified into CRS with nasal polyposis (CRSwNP), CRS without nasal polyposis (CRSsNP) and the presence or absence of eosinophilic mucus documented (EMCRS). This was based on the results of intraoperative tissue samples, which were sent for histological analysis. When clinically indicated, patients had microbiology swabs sent for bacterial and fungal cultures.

The dimension of each frontal sinus ostium was documented intraoperatively using a standardized 4mm olive tipped probe or measuring tool designed specifically to record ostium dimensions. This measurement system had

been previously validated in our department. [208]

Postoperatively, persistence of symptoms was noted and endoscopy performed on each visit. Postoperative endoscopic evaluation involved assessment of the maxillary sinus, ethmoid cavity, frontal ostium and sphenoid sinus, for evidence of stenosis, crusting, scarring, edema, polyposis or purulent discharge. The frontal sinus was defined as being patent if the ostium could be visualized endoscopically, and stenosed if there was scarring, edema or polyposis occluding the frontal ostium. A sinus was deemed to be infected if there was evidence of mucopurulence on endoscopy, regardless of whether there was a positive culture result.

Cohort Selection for Analysis

Our hypothesis was tested by calculating the risk of requiring an EMLP for "high risk" groups with the worst anatomical, radiological and disease factors based on current literature.[32,142,164,206]

Finally the success of the EMLP in relieving symptoms for this high-risk group was analyzed. These high risk patients who underwent a EMLP were contacted by post and asked to record their *current* symptoms on a scale of 1 to 5 and their overall quality of life on a scale of 0-10 using a visual analogue scale (Figure 4.1).

Figure 4.1 Patient Questionnaire

Figure 1: Patient Questionnaire

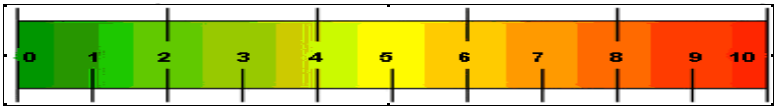
Dear _____ ,

Thank you once again for participating in this study.
To provide us with information about your symptoms following sinus surgery, please circle one number on the scales below using the scale as follows:

1: Symptom Free; 2: mild symptoms; 3: moderate; 4: severe; 5: unbearable

Symptom	**Score**
Facial pain	1 2 3 4 5
Nasal obstruction (blocked nose)	1 2 3 4 5
Anosmia (decreased or loss of smell)	1 2 3 4 5
Anterior rhinorrhoea (runny nose)	1 2 3 4 5
Post nasal drip (mucous back of throat)	1 2 3 4 5

Additionally, please rate your **overall** discomfort by marking an X on the scale below
(0: no symptoms – 10: unbearable symptoms):



4.3.4 Surgical Technique

The extent of sinus surgery was determined by reference to preoperative CT scans and intraoperative findings. All sinuses with evidence of mucosal inflammation, infection, or polyposis were opened surgically and any diseased mucosa debrided carefully without stripping or exposing underlying bone. The sinuses were irrigated meticulously with saline to remove inflammatory mediators. The size of the maxillary antrostomy was determined by the degree of inflammation within the sinus and canine fossa trephination[125,194] performed when necessary to completely clear severely diseased maxillary sinuses. The sphenoid sinuses were opened from the skull base to the floor of the sinus in cranio-caudal extent and from septum medially to the junction with the orbit laterally. The ethmoid cells were completely removed in every case with clearance of the skull base and lamina papyracea in all cases. All frontal sinusotomies were performed using the axillary flap technique and 3-D building block model of the frontal recess[195,196].

The surgical technique for Draf 2A frontal sinusotomy focuses on two key aspects: ostium size maximization and mucosal preservation. The frontal ostium is maximized by complete clearance of all cells in the frontal recess and removal of cells migrating through the ostium. The bone forming the natural frontal ostium is not removed/drilled – only the cells below and in the ostium are removed.

Routine postoperative medical therapy was used. This consisted of oral antibiotic therapy for 7-10 days, and in nasal polyp patients a tapering dose of oral prednisolone was given. Saline douches and a debridement at 2 weeks was performed. Maintenance topical nasal steroids were given and, if required, antibiotics and 3-week courses of oral prednisolone were prescribed. Regular 3-6 monthly follow up was performed thereafter.

The technique for performing the EMLP has been previously well described by the senior author.[128]

4.3.5 Statistical Analysis

Statistical analysis was performed using GraphPad Prism 5.0 software (San Diego, CA). Continuous data are displayed as mean ± SD. Characteristics of the two groups were compared using chi-square, Fisher exact, and t tests where appropriate. Statistical significance was accepted when $P < .05$.

4.4 RESULTS

339 patients who met the inclusion and exclusion criteria underwent endoscopic frontal sinus surgery. The average length of follow up was 20.8 months (95% CI 18. -22.9 months, SD 18.7 months). Primary endoscopic frontal sinus surgery was performed on 118 patients. Revision frontal sinus surgery was performed in 221 patients who had undergone a mean of 2.3

(95% CI 2.1- 2.5, range 1-12) prior ESS procedures. Post-surgical recurrence of disease with persistence of symptoms requiring an EMLP occurred in 9 patients in the primary (standard functional FESS performed by PJW) group and 38 in the revision (patients who had undergone primary FESS at another institution) group. Demographic and clinical data for the primary and revision ESS group is shown in Table 4.2.

Table 4.2: Demographic and clinical data-Primary and Revision ESS group

	Primary ESS		Revision ESS	
	No FDO	FDO	No FDO	FDO
N	109	9	183	38
Male(N)	68	7	100	21
Female(N)	41	2	83	17
Age(N)	47.2	54.1	50.0	47.4
Asthma (N)	29	5	67	23
ASA(N)	1	2	14	6
Smoker (N)	11	0	18	0
Total Symptom Score	15.1	17	16.1	16.8
Allergy(N)	79	7	109	16
LM(Mean)	14.9	19	14.3	18.2
CRSwNP(N)	70	8	122	30
EMCRS(N)	43	4	87	24
Number of Prior Surgeries	0	0	2.2	2.8

Cohort Analysis

The risk of failing standard ESS and requiring EMLP was analyzed on the basis of presence of the nasal polyps, asthma, Lund Mackay score and anatomical size of the frontal ostium. With the addition of each risk factor, the relative risk of requiring an EMLP increased. The highest risk group was found to be patients with nasal polyposis and asthma, LM score greater than 16 and frontal ostium size of less than 4mm. None of these risk factors on its own were significant. However, the cumulative impact of each additional factor led to an increasing probability of requiring an EMLP and was statistically significant (Table 4.3).

Table 4.3: Primary ESS: Risk of requiring FDO by Cohort

PRIMARY FESS COHORT					
	All Primary ESS patients	**CRSwNP**	**Asthma & CRSwNP**	**Asthma, &CRSwNP &LM>16**	**Asthma &CRSwNP, &LM>16 , &FO<4mm**
N	118	78	23	6	4
Risk of FDO	7.6%	10%	22%	67%	75%
P value	n/a	0.16	0.014	0.0002	0.0012
Relative Risk	n/a	n/a	3.4	24	36

The analysis was then extended to assess whether this relationship was maintained for the revision surgery group and for the entire ESS group (Table 4.4 and Table 4.5)

Table 4.4: Revision FESS-Risk of requiring FDO by cohort

REVISION ESS COHORT					
	All Revision ESS Patients	**CRSwNP**	**Asthma & CRSwNP**	**Asthma, &CRSwNP & LM>16**	**Asthma, & CRSwNP, & LM>16 & FO<4mm**
N	221	152	74	26	9
Number of Prior ESS	2.3	2.15	2.46	2.77	3.10
Risk of FDO	17%	20%	30%	46%	56%
P value	n/a	0.18	0.0011	0.0002	0.0087
Relative Risk	n/a	n/a	2.04	4.12	6.02

Table 4.5: Overall risk of FDO by cohort

ALL FRONTAL SINUS PATIENTS					
	All patients	**CRSwNP**	**Asthma and CRSwNP**	**Asthma, & CRSwNP & LM>16**	**Asthma, & CRSwNP, LM>16 & FO<4mm**
N	339	230	97	32	13
Risk of FDO	14%	17%	28%	50%	62%
P value	n/a	0.0437	<0.0001	<0.0001	<0.0001
Relative Risk	n/a	1.2	2.4	6.2	9.9

Symptom Resolution

Eight (8) patients in the highest risk group underwent EMLP , three (3) who were from primary ESS cohort, five (5) from the revision ESS cohort. Six out of these eight patients had a complete resolution of their symptoms. The other 2 patients reported persistent rhinorrhea as their only remaining symptom.

The mean follow up time for this cohort was 35.3 months (95%CI 16.6-53.9 months, SD 22.3).

All 8/8 patients (100%) returned their post treatment questionnaires. The total

symptom score fell from 19.0 preoperatively to 9.0 postoperatively (p=0.0003). The overall post EMLP quality of life VAS score was 3.0 (95%CI 1.9 to 4.1, SD 1.15)

4.5 DISCUSSION

This study reviewed the likelihood of failure of standard frontal sinus surgery on a large cohort of 339 patients who underwent either primary or revision ESS. The overall success rate of standard endoscopic frontal sinus surgery is high with only 47/339 (<15%) requiring an EMLP for persistence of symptoms. Within this small group of patients requiring an EMLP, a subset of patients with a combination of poor anatomical and inflammatory risk factors, and a high disease burden, were identified as having an increased risk for failing standard primary or revision ESS. If the risk factors for all patients undergoing EMLP are assessed, these factors (asthma, CRSwP, LM >16, narrow FO) provide a reasonable basis for considering an EMLP in patients who otherwise would undergo revision ESS. This particular subset may well benefit from a primary EMLP.

EMCRS, asthma, polyposis, allergy and smoking have all been considered potential risk factors for poorer outcomes in ESS. In this study, no significant correlation could be found between each of these risk factors individually and failure of frontal sinusotomy. However, when these prognostic factors are combined, each adds to the relative risk of the patient eventually requiring an

EMLP, suggesting patients with multiple risk factors for failure warrant more extensive surgery to improve their ultimate outcomes.

Symptom improvement after ESS might be attributable to resolution of pathological changes involving any of the paranasal sinuses. However, recently published work by this department showed that persistent disease in the frontal sinus is an **independent** risk factor for persistence of CRS symptoms, despite the presence or absence of disease in other sinuses.[206]

Frontal ostium size has previously been noted as a risk factor for failure of frontal sinusotomy[164] and persistence of symptoms[206]. The smaller the ostium, the greater the risk that scarring, adhesion formation or polyp recurrence, will lead to complete stenosis. Narrow frontal ostia, also increases the risk of cicatricial mucosal injury by instrumentation in the intraoperative and postoperative period. Finally, smaller ostia are less likely to be penetrated by saline douching and other topical therapies[134]

The EMLP overcomes these anatomical limitations by creating a maximally enlarged single neo-ostium draining into the nasal cavity via a superior septal window. The success of the EMLP in resolving persistent symptoms of CRS is supported by two recently published literature reviews into the failure of ESS[209,210] which dealt with the concept of “inflammatory load”[210] and “mucosal remodelling”[209].

Intraoperatively, the EMLP allows the majority of the frontal sinus to be

accessed, with removal of polypoid mucosa and eosinophilic mucous. Osteitic bone is also more readily removed. In a standard frontal sinusotomy, narrow ostia prevents instrumenting the entire frontal sinus to achieve a similar surgical end point. It is important to note that all other diseased sinuses were also addressed at the time of performing the EMLP so that all of the paranasal sinuses had maximal ventilation and removal of inflammatory mediators.

Postoperative management is also facilitated by the EMLP. The creation of a large neo-ostium enhances topical delivery of saline and topical therapy to the frontal sinus[134]. Postoperative debridement and ongoing long-term instrumentation of the frontal neo-ostium is also substantially enhanced and capable of being performed without causing mucosal trauma. The EMLP has been shown to enhance frontal ostium patency rates over the long term, and this is strongly correlated to mucosal appearance and symptom scores[187].

4.6 CONCLUSION

This study raises the possibility that patients that have multiple risk factors fall into a particular poor outcome group. These patients should be counselled on the higher risk of failure and the potential for requiring an EMLP. Under the care of a tertiary rhinologist, consideration should be given to performing a primary EMLP in this patient group. Further research is needed to confirm these findings and a randomized clinical trial of standard frontal sinusotomy vs EMLP is recommended.

Long-term Outcomes for the Endoscopic Modified Lothrop/Draf III Procedure – a 10-year review

Conducted in the Department of Otolaryngology Head and Neck Surgery,

University of Adelaide, Adelaide, Australia

Naidoo, Y., Bassiouni, A., Keen, M. & Wormald, P.J. (2014) Long-term outcomes for the endoscopic modified Lothrop/Draf III procedure: a ten year review.
Laryngoscope, v. 124(1), pp. 43-49

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5.1 ABSTRACT

Objectives/Hypothesis: To detail the long term outcomes of the Endoscopic Modified Lothrop Procedure (EMLP), (a.k.a Draf III/Frontal Drillout) and identify key risk factors for failure

Study Design: Retrospective Cohort study

Level of Evidence: Level 4

Methods: Retrospective chart review. Endoscopic assessment of frontal ostium patency and patient reported symptoms were prospectively collected on patients who underwent EMLP between January 2001 and December 2011 for chronic rhinosinusitis (CRS). Risk factors for failing EMLP were identified

Results: 229 patients met the inclusion and exclusion criteria and underwent an EMLP. The average number of standard endoscopic sinus surgery (ESS) procedures prior to an EMLP was 3.8 (95% CI 3.4 -4.2, SD 3.3). The average length of follow up was 45.0 months (95% CI 41.2 -48.9 months, SD 22.3 months). The EMLP was successful in 95% (217/229) with no further surgery being required. Post-surgical recurrence of disease with persistence of symptoms requiring revision EMLP occurred in 12 patients. No complications were identified. Allergic Fungal Sinusitis (AFS) and recurrent Staphylococcus Aureus infections were identified as potential risk factors for failure.

Conclusions: This is the single largest study of EMLP in the literature with a long follow up period. It illustrates the benefit of the EMLP for patients with chronic rhinosinusitis (CRS) recalcitrant to medical and standard endoscopic

sinus surgery.

Key Words: Draf III frontal sinus surgery, Frontal Drillout, Endoscopic Modified Lothrop Procedure, Frontal sinusotomy, endoscopic sinus surgery, patency, outcomes, risk factors

5.2 INTRODUCTION

Endoscopic sinus surgery (ESS) is accepted as the treatment of choice for chronic rhinosinusitis (CRS) refractory to medical treatment. However, the most appropriate extent of surgical treatment is not well understood at this time and recommendations are largely based on anecdotal observations[204].

The short and long-term outcomes after endoscopic frontal sinus surgery (Draf 2A) have previously been reported in the literature [164,169,170,206], and confirm both objective and subjective improvement in symptoms in the majority of patients. However, there is a subset of patients, who relapse with persistent frontal sinus disease despite excellent primary surgery.

The Endoscopic Modified Lothrop Procedure (EMLP), (otherwise known as a Draf III frontal sinusotomy or Frontal Drillout (FDO)) has been used as a salvage procedure for failed frontal sinusotomy (Draf 2a) and its short term outcome has been reported in the literature[184,207].

The primary objective of this study is to evaluate the long-term success of the EMLP in treating patients who have failed standard endoscopic frontal sinus surgery. Technical and qualitative measures of surgical success were measured. The secondary objective was to identify the risk factors for failure of the EMLP in those patients recalcitrant to surgical intervention. To our

knowledge, this is the largest series with the longest follow up in the literature.

5.3 MATERIALS AND METHODS

5.3.1 Study Design

Retrospective cohort study. This retrospective review of prospectively collected data was undertaken in the tertiary referral rhinology practice of the senior author (PJW) based in Adelaide, South Australia, Australia. Enrolment occurred between January 2001 and December 2011. The institution's Human Ethics Committee approved the study (Application Number 2011021).

5.3.2 Inclusion and Exclusion Criteria

Inclusion Criteria and Selection of Patients

All patients who underwent surgery had previously failed at least a 2 month course of maximal medical treatment for chronic rhinosinusitis (CRS) that included culture directed antibiotics when pus was seen, saline douches, topical nasal steroids and a 3 week course of oral steroids

All patients had persistent symptoms of nasal blockage (NAO), facial pain/headache (FP), rhinorrhea, postnasal drip (PND), and/or hyposmia .

Selection of Patients for EMLP

Patients were selected for frontal sinus surgery (Draf 2a) if, and only if, there was objective evidence of persistent post-treatment mucosal thickening in the frontal recess or frontal sinus on paranasal CT scans, and endoscopic evidence of ongoing disease such as polyposis, mucosal edema and/or muco-purulence.

Patients were offered an EMLP only *after* standard functional endoscopic sinus surgery had failed. Each of these patients had persistence of symptoms together with endoscopic and CT evidence of continuing disease in the frontal sinuses despite previous ESS and continued maximal medical therapy. This included a further minimum two week course of culture directed antibiotics if pus was present, topical and oral steroids, and nasal douching. No patient had an EMLP performed as primary surgery.

Patients who had their primary frontal surgery performed by the senior author (PJW) were offered the EMLP if symptoms and signs returned. Patients who had their primary ESS surgery performed elsewhere were offered revision Draf 2a if there were residual remnant cells obstructing the frontal recess. They were offered an EMLP if previous frontal surgery had been adequately performed but failed. The EMLP included opening of all the other diseased sinuses at the same time with complete clearance of all disease within those

sinuses.

Revision EMLP was offered where there was objective evidence of disease in the frontal sinus despite prior EMLP. Patients in this group were persistently symptomatic despite ongoing medical treatment and prior EMLP. Medical treatment in this group included mupirocin nasal washes[105] (10 mls of 0.05% mupirocin twice daily for 3 months) for recalcitrant Staphylococcus Aureus infections, itraconazole (100mg twice daily for 6 months[211]) for persistent fungal infection, and daily budesonide nasal washes (1mg of budesonide in 200mls of normal saline).

Exclusion Criteria

Patients without objective radiological or endoscopic evidence of post-treatment mucosal thickening in the frontal recess or frontal sinus were given ongoing medical treatment and not offered further surgery. Patients undergoing endoscopic sinus surgery for reasons other then chronic sinusitis were excluded. This included patients undergoing surgery for benign and malignant paranasal sinus tumors, trauma, cystic fibrosis, Kartagener's syndrome or other primary mucociliary abnormalities. No other patients were excluded and this cohort is unselected and consists of consecutive patients undergoing EMLP.

5.3.3 Recording of Data

Demographic and clinical information was compiled by reviewing each patient's chart. Potential prognostic factors for CRS such as asthma, aspirin sensitivity, allergies, and history of smoking was collected.

Allergy status was determined using an immunocap allergen test or skin prick test, for common environmental allergens, and total serum IgE level. No patient had taken antibiotics, antifungals or steroids in the three weeks prior to their surgery.

A standard validated patient reported outcome measure (PROM) scoring system was used [212]with symptoms recorded on a scale of 1 to 5 (1 = absent and 5 = extreme). The severity of five key symptoms were reported by the patient: nasal obstruction, rhinorrhoea, post-nasal drip, headache or facial pain and sense of smell (Table 5.1). These were added to give a total out of 25. (Note, on this scale a total score of 5 is symptom free, a score between 5-10 is mild, 10-15 mild to moderate, 15-20 is moderate to severe and 20-25 severe to extreme).

Table 5.1: Patient Reported, Surgeon Recorded Symptom Scores

Score	Description
1	Absence of symptoms
2	Mild
3	Moderate
4	Severe
5	Extreme

Intraoperative findings of fungus, mucous, polyps and mucopurulence were documented. The presence or absence of eosinophilic mucous was documented. This was based on the results of intraoperative tissue samples, which were sent for histological analysis. When clinically indicated, patients had microbiology swabs sent for bacterial and fungal cultures.

The dimension of the frontal sinus neo-ostium was documented intraoperatively using a standardized 4mm olive tipped probe or a measuring tool designed specifically to record ostium dimensions. This measurement system has been previously validated in this department. [208] The lateral extent was determined by the distance at the level of the frontal "T" from side to side in the coronal plane. The anterior-posterior dimension was measured from the frontal T posteriorly to the anterior limit (see Figure 5.1 and Figure 5.2)

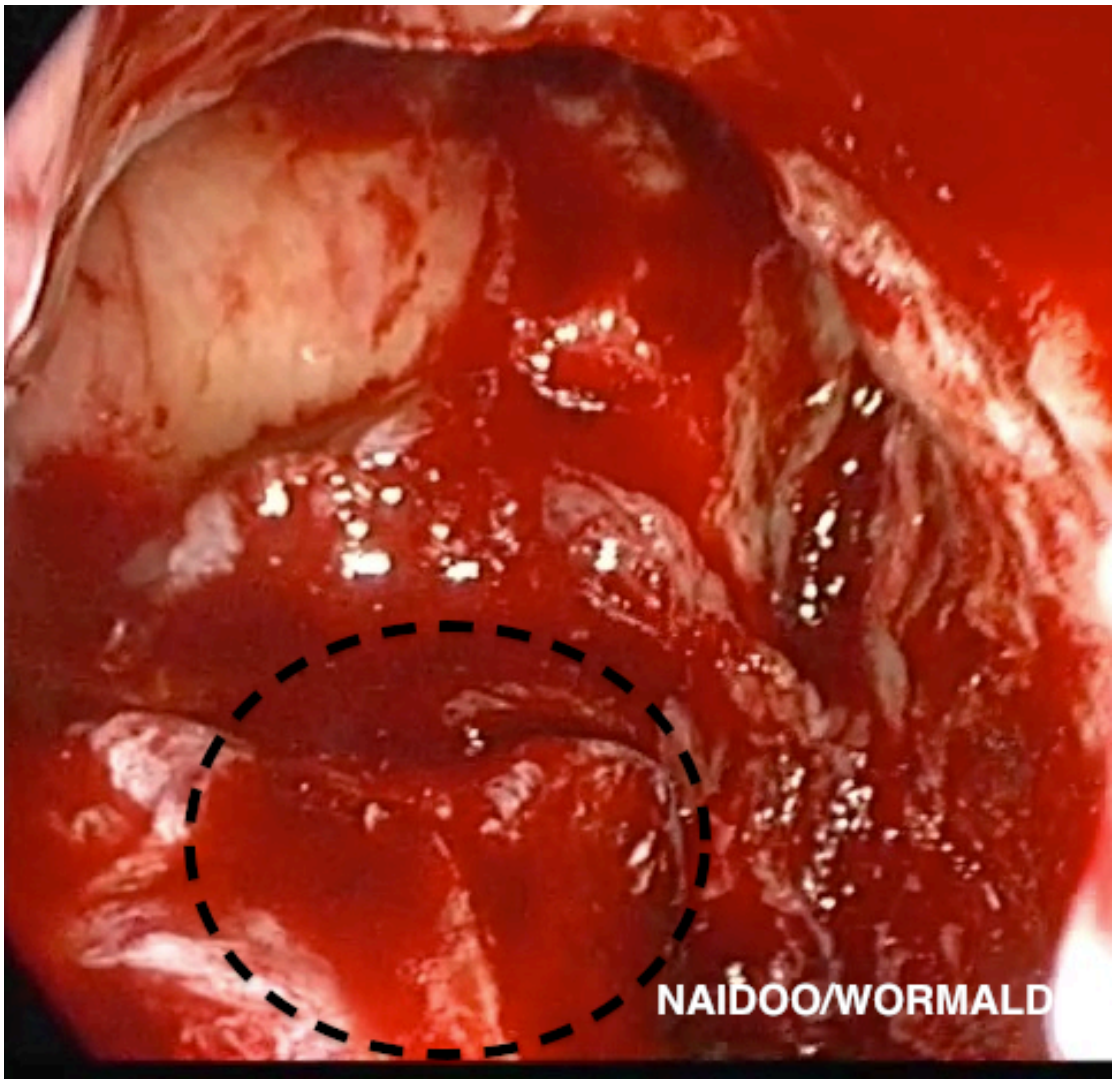
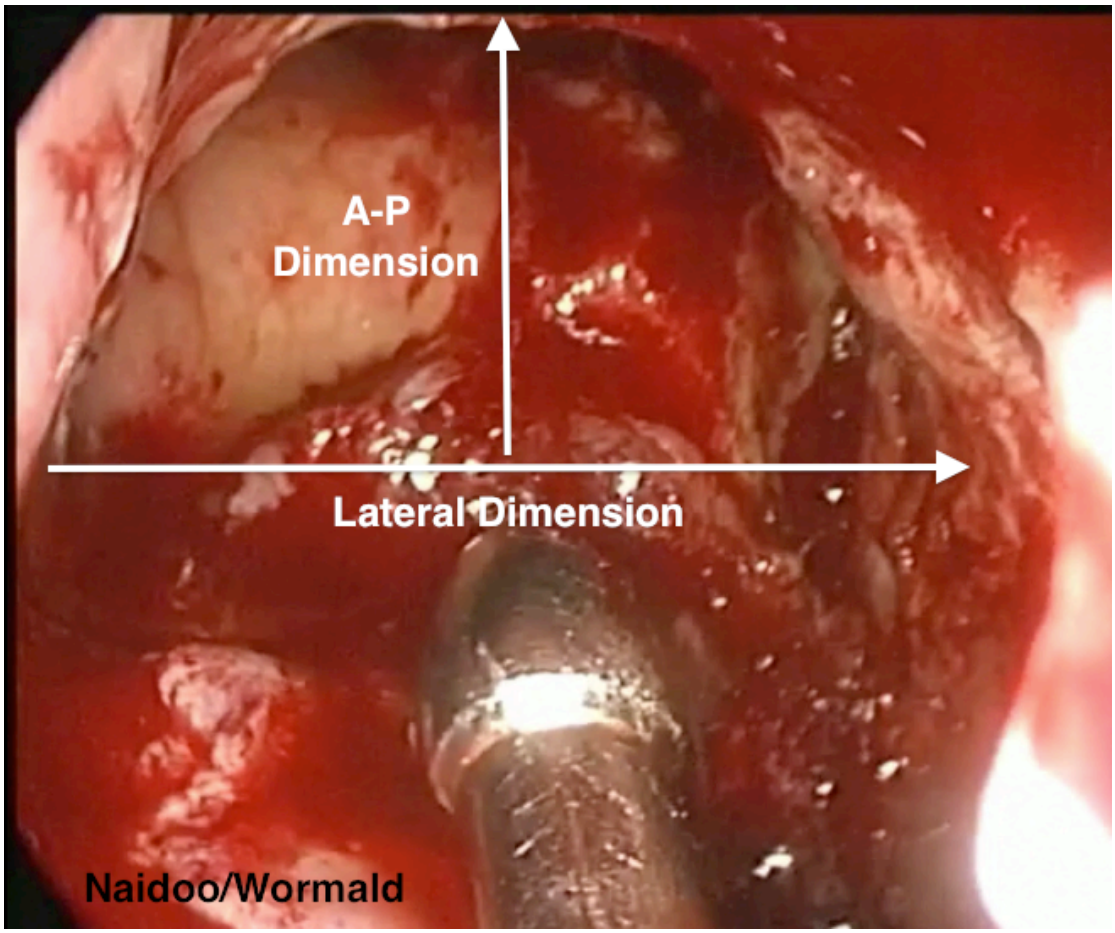


Figure 5.1: The Frontal "T"

The frontal "T" is the bony projection formed by the superior attachment of the middle turbinates to septum and skull base

Figure 5.2: Intraoperative measurement of Frontal neo-ostium.



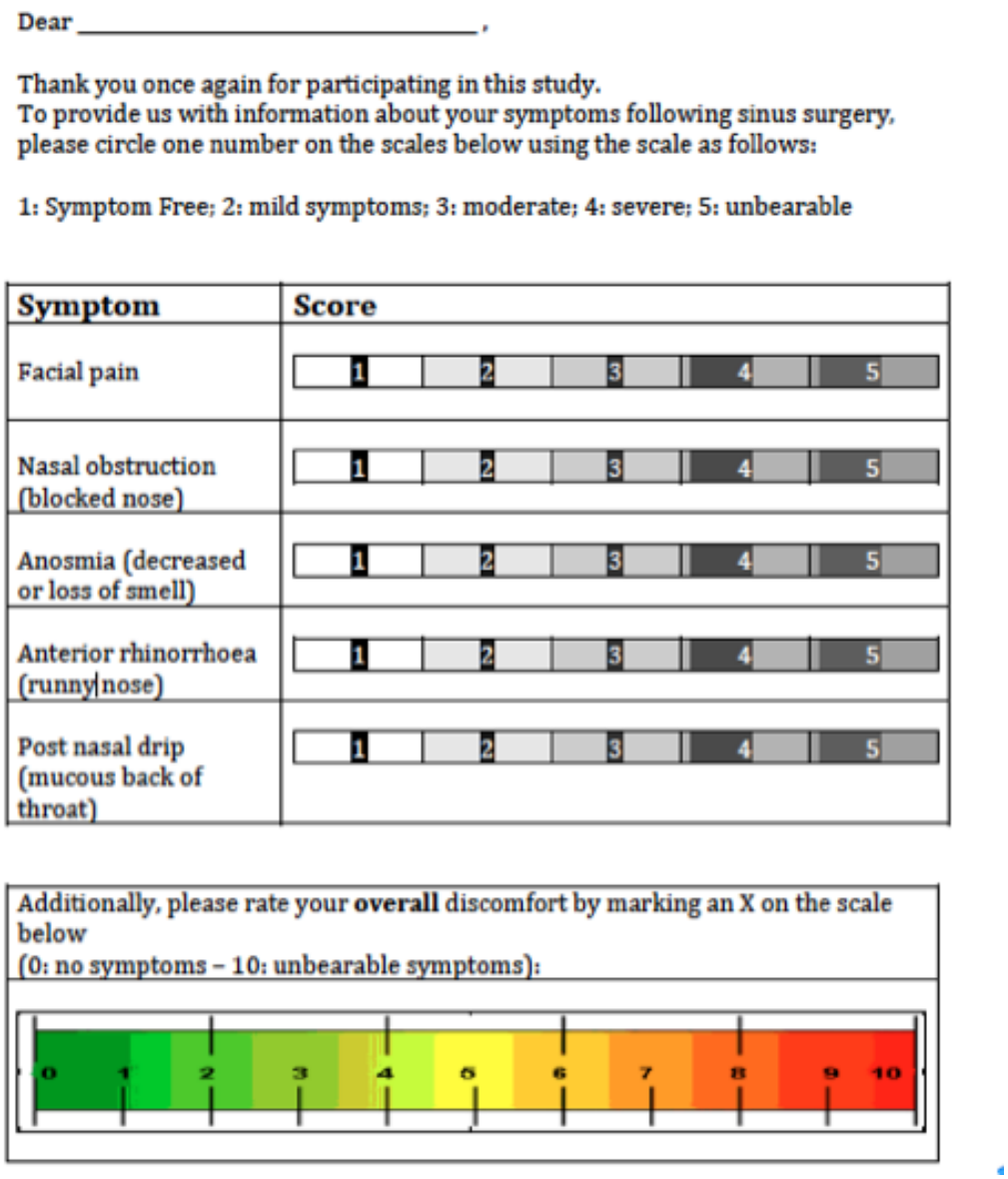
Measurement is made of the lateral extent at the frontal T in the coronal plane, and of the anterior-posterior dimension from the frontal T posteriorly to the anterior limit.

Postoperatively, persistence of symptoms was noted and endoscopy performed on each visit. Postoperative endoscopic evaluation involved assessment of the maxillary sinus, ethmoid cavity, frontal neo-ostium and sphenoid sinus, for evidence of stenosis, crusting, scarring, edema, polyposis

or purulent discharge. The frontal sinus neo-ostium dimension was documented at each postoperative visit. A sinus was defined to be infected if there was evidence of mucopurulence on endoscopy, regardless of whether there was a positive culture result.

Finally, the success of the EMLP in relieving symptoms was recorded with the same scale as described earlier. Patients were also contacted by post and asked to record their current symptoms on a scale of 1 to 5 and their overall quality of life on a scale of 0-10 using a visual analogue scale (Figure 5.3).

Patients were classified into asymptomatic (total symptom score <6), mildly symptomatic (total symptom score 6-10), moderately symptomatic (total symptom score 11-15), and severely symptomatic (total symptom score >15).



Dear _____,

Thank you once again for participating in this study.
To provide us with information about your symptoms following sinus surgery, please circle one number on the scales below using the scale as follows:

1: Symptom Free; 2: mild symptoms; 3: moderate; 4: severe; 5: unbearable

Symptom	Score
Facial pain	1 2 3 4 5
Nasal obstruction (blocked nose)	1 2 3 4 5
Anosmia (decreased or loss of smell)	1 2 3 4 5
Anterior rhinorrhoea (runny nose)	1 2 3 4 5
Post nasal drip (mucous back of throat)	1 2 3 4 5

Additionally, please rate your **overall** discomfort by marking an X on the scale below
(0: no symptoms – 10: unbearable symptoms):

0 1 2 3 4 5 6 7 8 9 10

Figure 5.3: Post operative Symptom and Quality of Life Survey proforma

5.3.4 Surgical Technique

The extent of sinus surgery was determined by reference to preoperative CT scans and intraoperative findings. All sinuses with evidence of mucosal inflammation, infection, or polyposis were opened surgically and any diseased mucosa debrided carefully without stripping or exposing underlying bone.

Submucosal abscesses were removed. The sinuses were irrigated meticulously with saline to remove inflammatory mediators. The size of the maxillary antrostomy was determined by the degree of inflammation within the sinus and canine fossa trephination[125,194] performed when necessary to completely clear severely diseased maxillary sinuses. The sphenoid sinuses were opened from the skull base to the floor of the sinus in cranio-caudal extent and from septum medially to the junction with the orbit laterally. The ethmoid cells were completely removed in every case with clearance of the skull base and lamina papyracea in all cases. No stents were used.

The technique for performing the EMLP has been previously described by the senior author.[128] Routine postoperative medical therapy was used. This consisted of oral antibiotic therapy for 21 days and, in nasal polyposis, a tapering dose of oral prednisolone was given over 3 weeks (25mg prednisolone daily for 7 days, 12.5 mg daily for 7 days, 12.5mg every second day for 7 days), and saline douches. Endoscopic debridement of the sinuses was performed 2 weeks postoperatively. Regular 3-6 monthly follow up was performed thereafter for most patients, although some interstate patients had their follow up performed by the referring ENT surgeon. At each visit, symptom scores were noted and the sinuses endoscopically evaluated as described above. The sinuses were debrided if there was evidence of crusting or purulence. No polyps were removed in the office setting. When polyps were noted, topical intransal corticosteroids were initiated.

5.3.5 Statistical Analysis

Statistical analysis was performed using GraphPad Prism 5.0 software (San Diego, CA). Continuous data are displayed as mean ± SD. Characteristics of the two groups were compared using chi-square, Fisher exact, and t tests where appropriate. Statistical significance was accepted when $P < .05$.

5.4 RESULTS

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229 patients (136 male, 93 female) with an average age of 49 years met the inclusion and exclusion criteria. The average patient had undergone 3.8 (95% CI 3.4 -4.2, SD 3.3) standard endoscopic sinus surgery (ESS) procedures prior to the EMLP, with one patient having had 21 prior sinus procedures .The average length of follow up was 45.0 months (95% CI 41.2 -48.9 months, SD 22.3 months).

12 patients required at least one revision EMLP, and 2 patients underwent 2 revision EMLPs for a total of 14 revision EMLPs. Demographic and clinical data for the original and revision group is shown in Table 5.2

Table 5.2: Demographic and clinical data-EMLP and Revision EMLP group.

(CRSwNP – Chronic sinusitis with polyposis, EMCRS-Eosinophilic Mucin Chronic Rhinosinusitis, LM-Lund –Mackay, ASA- aspirin and salicylate intolerance.*2 patients had the EMLP revised twice)

	EMLP	Revision EMLP
N	229	14*
Male(N)	136	8
Female(N)	93	6
Age(N)	48.6	45.3
Asthma (N)	129	9
ASA(N)	35	2
Smoker (N)	12	0
Total Symptom Score	17.6	18.3
LM(Mean)	15.5	14.7
CRSwNP(N)	135	9
EMCRS(N)	106	7
Number of Prior Surgeries	3.8	4.1

Symptom Resolution

All patients noted an improvement in their postoperative symptoms. No patients complained of a worsening in their symptoms following surgery.

There was a statistically significant improvement in each of the five key symptoms postoperatively (Figure 5.4). Even in the group requiring revision EMLP there was an improvement in the total symptom score, although no statistically significant improvement was found for post-nasal drip or sense of smell (Figure 5.5).

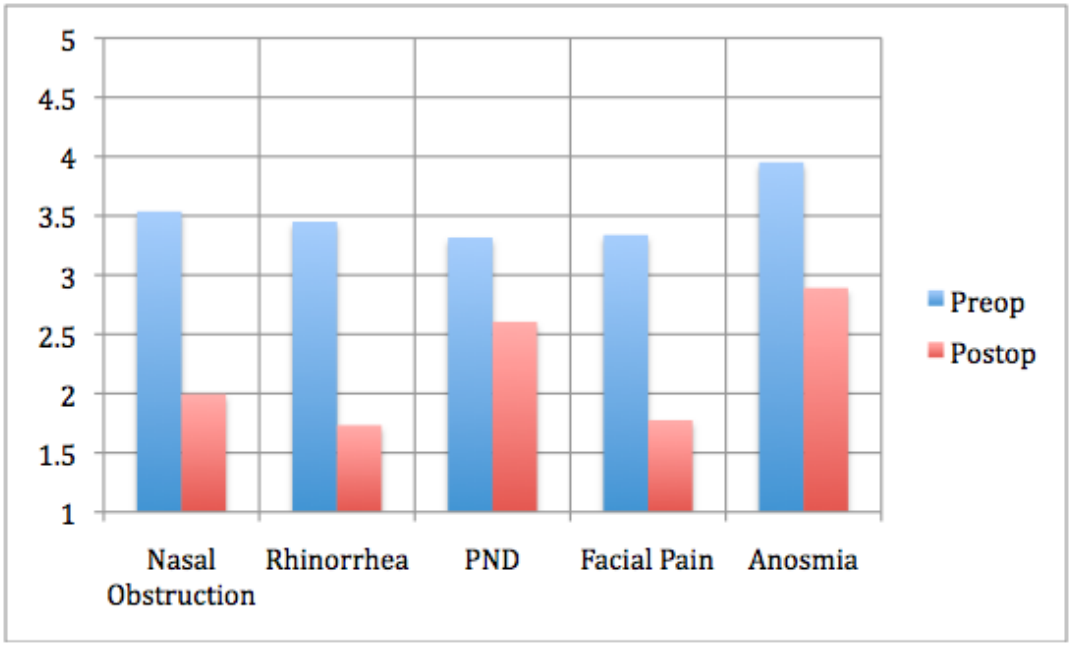

Figure 5.4: Overall symptom improvement post EMLP .

(PND-post-nasal drip. The symptom scale from 1 to 5 is as defined in Table 5.1. P values for change in symptom scores are Nasal Obstruction P<0.0001, Rhinorrhea P<0.0001,PND P<0.0001, Facial Pain P<0.0039,Anosmia p<0.0001)

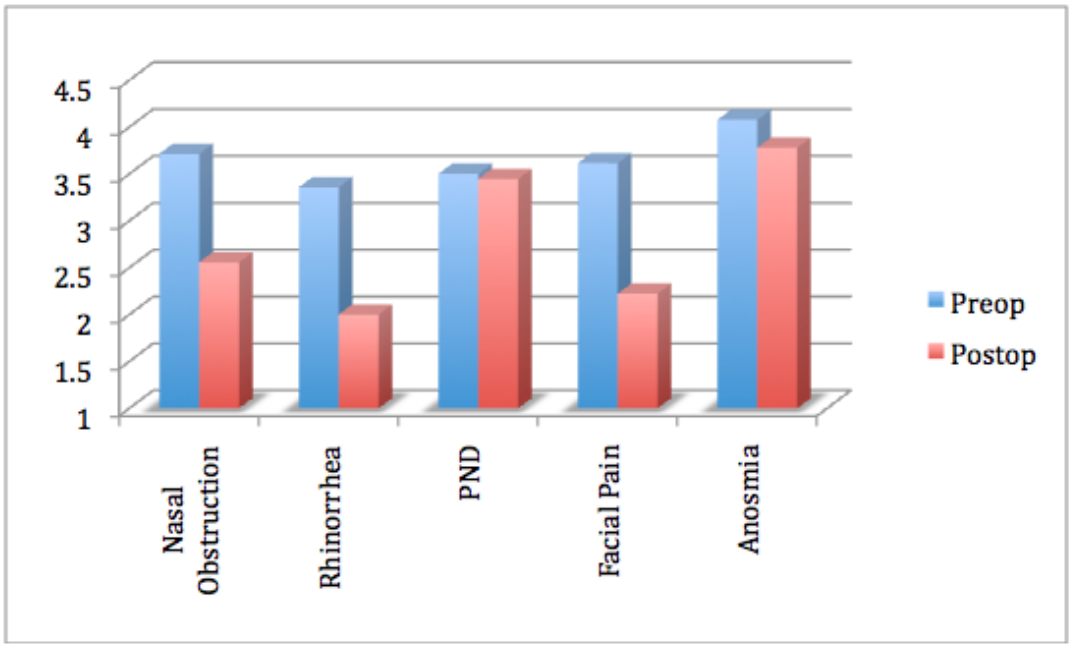

Figure 5.5: Symptom improvement post EMLP in the revision group.
(PND-post- nasal drip. The symptom scale from 1 to 5 is as defined in Table 1. (P values for change in symptom scores are Nasal Obstruction P<0.0025, Rhinorrhea P<0.0021,PND P<0.85, Facial Pain P<0.006, Anosmia p<0.61))

When classified into degree of symptom resolution, a small but significant percentage remain persistently symptomatic (Figure 5.6). 27% of patients are mildly troubled by their symptoms, 18% have moderate symptoms, and 8% have severe symptoms. However, all patients reported an improvement in their symptoms after surgical intervention, and no patient reported a worsening of their symptoms.

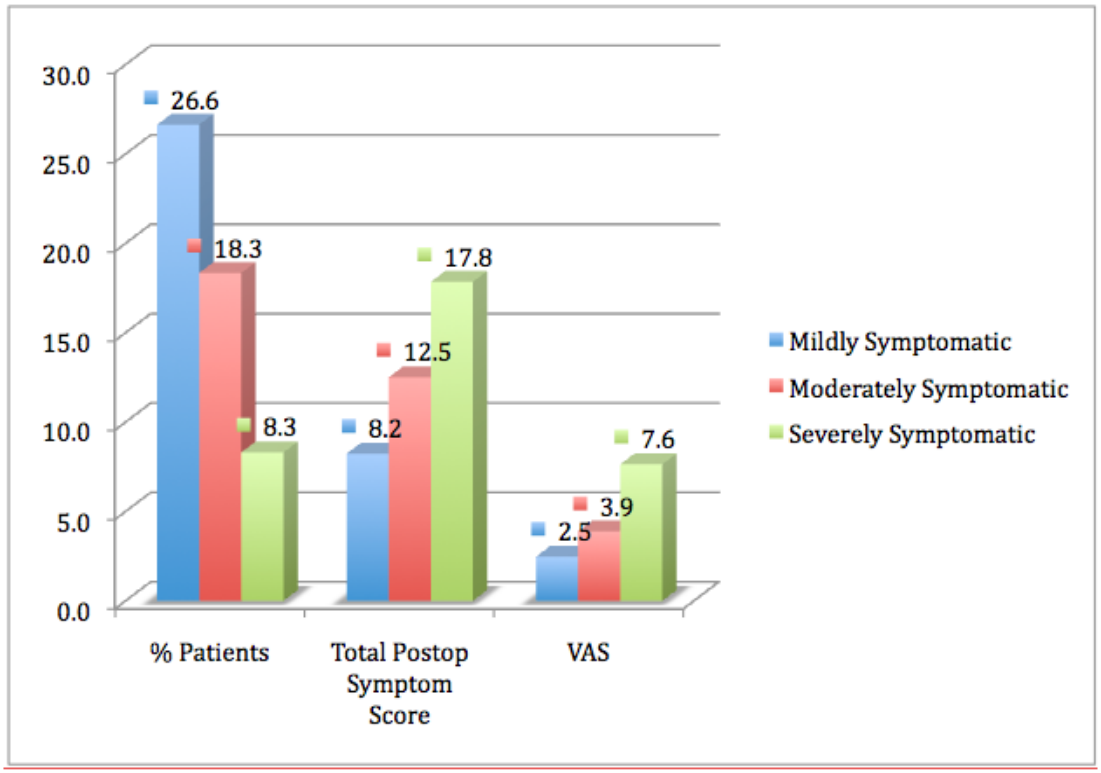

Figure 5.6: Classification of Patients by Symptom Severity Post EMLP.
(Maximum Total Symptom score = 25, Maximum VAS =10)

Frontal sinus patency

The frontal neo-ostium remained patent in 221/229 cases. This reflects a 97% patency rate. The frontal neo-ostium was occluded by polyps in 6 cases and became stenosed in 2 cases.

The mean operative neo-ostium created was 21.0mm (minimum 11mm, maximum 28mm, 95% CI 20.6 -21.4mm) in lateral dimension and 19.5mm (minimum 10mm, maximum 28mm, 95% CI 19.1-19.9mm) anterior-posterior dimension. There is noticeable narrowing of the frontal neo-ostium over the first 24 months post surgery. Following this initial period, the ostium appears

to stabilize and then increase marginally thought to be due to further stabilization and thinning of the mucosa of the neo-ostium (Figure 5.7)

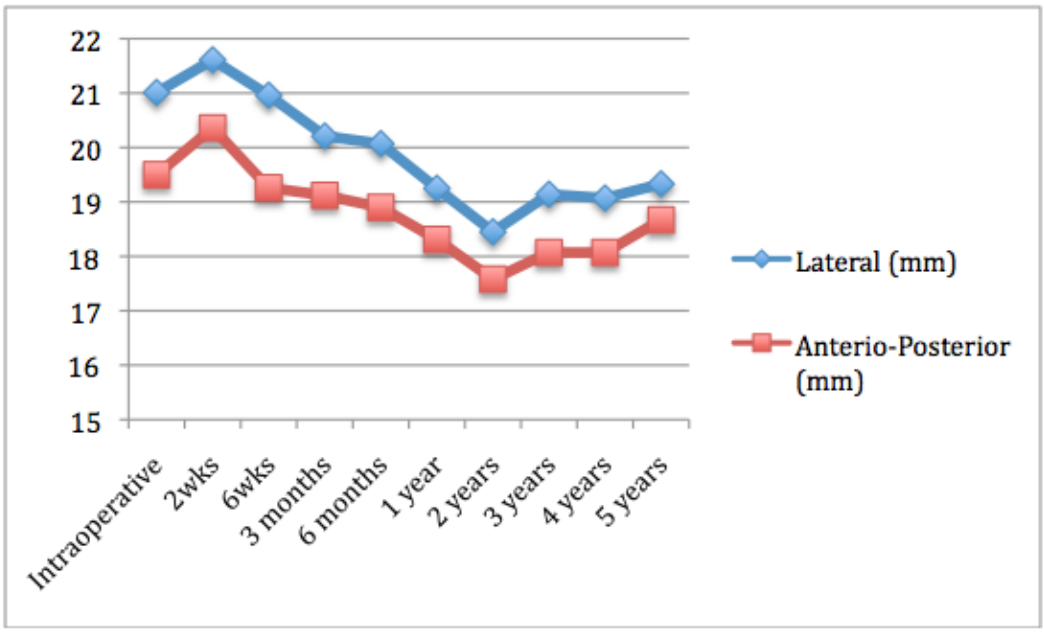

Figure 5.7: Frontal Sinus Patency over a 5 year period.

EMLP Revision

14 revision EMLP procedures were performed in 12 patients, with 2 patients requiring 2 revisions. These were performed for persistent symptoms that were unresponsive to medical treatment and with objective disease within the frontal sinus.

A narrow AP diameter in the failure group (18.1mm vs 19.6mm) was noted but was not statistically significant (p=0.08). In the 12 revision EMLP cases, the frontal sinus was occluded with polyposis in 6, stenosed in 2 cases due to

osteoneogenesis and or scar tissue, and patent in the other 4 cases. AFS was found to be a significant risk for revision (P=0.0455, Odds Ratio 3.58). Recurrent Staphylococcus Aureus infections were noted in the revision group but was not significant (P=0.11).

The 12 failed EMLP cases are shown in Table 5.3: Failed EMLP group.below.

Table 5.3: Failed EMLP group.

(ESS- standard endoscopic sinus surgery, EMLP-Endoscopic Modified Lothrop Procedure, AFS-Allergic Fungal Sinusitis, Samter's Triad- triad of aspirin and salicylate intolerance, asthma and sinonasal polyps, Staph Aureus- Staphylococcus Aureus, Pseudomonas-Pseudomonas Aeruginosa, Haemophilus –Haemophilus Influenzae)

Patient	Sex	Age	Number of Prior ESS	First EMLP	Revised	Frontal Ostium	Reason For Revision	Comment
1	M	33	1	2/05/01	2004/2006	Patent	AFS with polyposis, fungal debris within frontal sinus	Asthmatic
2	F	48	2	27/08/08	2009	Occluded with polyps	AFS with polyposis	Asthmatic
3	M	71	14	27/12/00	2006	Occluded with polyps	AFS/Recurrent infections and polyposis	Asthma/Diabetes, multiple Staph Aureus Infections
4	M	31	2	9/02/09	2010	Occluded with polyps	AFS with polyposis	Pseudomonas, Haemophilus infections
5	F	47	6	29/04/09	2009	Occluded partly with new bone formation	Osteoneogenesis	Staph Aureus Infections
6	F	47	5	5/09/07	2008	Occluded with polyps	AFS with polyposis	Samters Triad
7	M	49	4	11/05/05	2008	Patent	Recurrent Infections	Staph Aureus Infections
8	M	36	4	31/08/07	2010	Occluded with polyps	AFS with polyposis	Allergic mucin,multiple Staph. A and pseudomonas infections
9	M	34	1	28/02/07	2010	Occluded with polyps	AFS with polyposis	Samters Triad
10	F	49	2	17/05/02	2010	Patent	Recurrent Infections	Staph Aureus Infections
11	F	64	4	27/07/07	2009/2010	Patent	Recurrent Infections	Staph Aureus and Pseudomonas Infections
12	M	33	5	19/09/05	2009	Stenosed	Recurrent Infections	Staph Aureus Infections

5.5 DISCUSSION

This study reviewed the outcome of over 10 years of EMLP surgery on a large cohort of 229 patients. The technical (patency of frontal sinus ostium) and qualitative (symptom improvement and overall quality of life) measures of success are high with a 97% patency rate, and only 12/229 (~5%) undergoing revision EMLP for persistence of symptoms. The frontal neo-ostium remains patent in the long term. Similarly symptom scores improve significantly for the vast majority.

Around 26% of patients still have moderate or severe symptoms post-operatively, although these symptoms have not been deemed severe enough, nor uncontrolled enough, by the patients themselves to warrant revision surgery. A small group of patients do have persistence or recurrence of symptoms requiring a revision EMLP. This subset of patients remain partly symptomatic, and fail to respond as well as other patients do to either continued medical or surgical treatment. Allergic Fungal Sinusitis (AFS), and recalcitrant Staphylococcus Aureus infections appear to be significant risk factors. (See Figure 5.8)

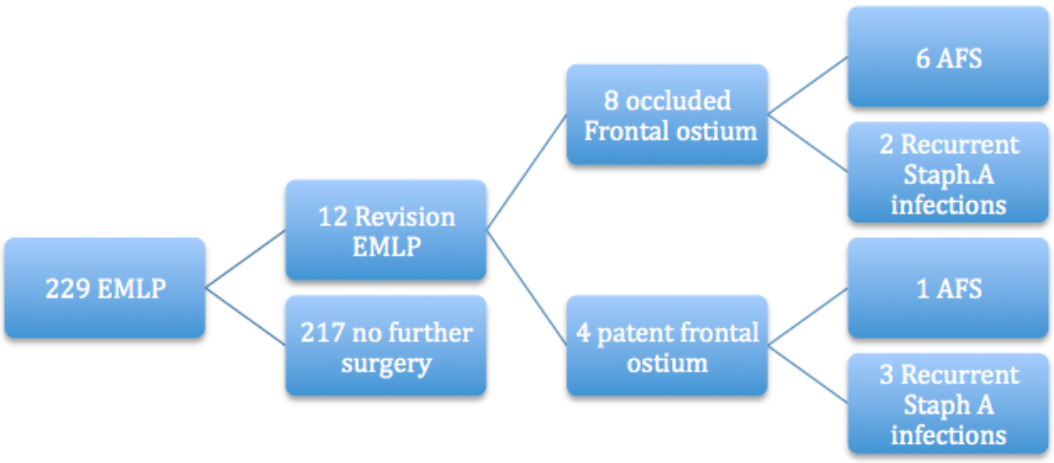

Figure 5.8: Relationship of Revision EMLP to patency of frontal ostium, AFS, and Staph A

(AFS-Allergic Fungal Sinusitis, Staph A- Staphylococcus Aureus)

In this "failure" group, frontal neo-ostium occlusion occurred in 8/12 patients. In 6/8 cases this was due to recurrence of polyposis and the remaining 2/8 cases, stenosis occurred due to osteoneogenesis and or scar tissue. In the remaining 4/12 patients the frontal sinus neoostium remained patent. 3/4 patients had recurrent Staphylococcous Aureus infections. These patients were offered revision surgery due to persistent infection within the frontal sinus despite a patent ostium. The aim of surgery was removal of infected debris, crusting, and submucosal abscesses to remove recalcitrant nidi of infection and to decrease the inflammatory load and thereby regain medical control.

Allergic fungal sinusitis with recurrence of fungal infection and polyposis was noted to be a significant risk of failure in the EMLP revision group occurring in 7/12 patients. Polyposis with fungus occluding the frontal neo-ostium was

noted in 5/6 patients, whereas in the remaining patient, the frontal ostium was patent but the frontal sinus filled with fungal debris.

The reason as to why a small group of patients do persistently badly following standard ESS, EMLP and even revision EMLP is the subject of much research in this department and across the world. There appear to be two distinct groups that fail:

- AFS with an occluded frontal sinus neo-ostium due to polyp recurrence
- Recalcitrant Staphylococcus Aureus infections despite a patent frontal sinus neo-ostium

In the occluded frontal ostium group, AFS seems to be the important risk factor. Here it is likely that underlying immune dysfunction leads to polyposis occluding the frontal sinus, inhibiting both ventilation and adequate topical therapy in the form of steroid washes.

In the patent frontal sinus group, recalcitrant infections prevent complete symptom resolution despite adequately ventilated sinuses. It appears that adequately ventilated sinuses are a necessary, but not the only factor, in eradicating disease. These patients appear to be prone to persistent colonization of the sinuses by a wide variety of pathogens, the make-up of which is probably influenced by antibiotic sensitivity, environmental and immune factors. In this group, recalcitrant infections can lead to narrowing of the frontal neo-ostium by scar tissue formation or neo-osteogenesis.

The reasons as to why the EMLP achieves symptomatic control of patients who, on average, have had 3-4 previous sinus procedures are poorly understood. Frontal ostium size has previously been noted as a risk factor for failure of frontal sinusotomy[164] and persistence of symptoms[206]. The smaller the ostium, the greater the risk that scarring, adhesion formation or polyp recurrence, eventually leading to complete occlusion of the frontal sinus ostium. A narrow frontal sinus ostium also increases the risk of cicatricial mucosal injury by instrumentation in the intraoperative and postoperative period. Finally, a smaller ostium is less likely to be penetrated by saline douching and other topical therapies[134]. The EMLP overcomes these anatomical limitations by creating a maximally enlarged single neo-ostium draining into the nasal cavity via a superior septal window. This study shows that the frontal neo-ostium remains widely patent in the long term in the vast majoriy of cases, and this facilitates topical medical therapy.

Another hypothesis as to why the EMLP is successful in resolving persistent symptoms of CRS is supported by two recently published literature reviews into the failure of ESS[209,210] which dealt with the concept of "inflammatory load"[210] and "mucosal remodelling"[209]. Intraoperatively, the EMLP allows the majority of the frontal sinus to be accessed, with removal of polypoid mucosa and eosinophilic mucous. Osteitic bone is also more readily removed. In a standard frontal sinusotomy, a narrow frontal sinus ostium prevents instrumenting the entire frontal sinus to achieve a similar surgical end point. (It is important to note that all other diseased sinuses were also addressed at the

time of performing the EMLP so that all of the paranasal sinuses had maximal ventilation and removal of inflammatory mediators.)

Postoperative management is also facilitated by the EMLP. The creation of a large neo-ostium enhances topical delivery of saline and topical therapy to the frontal sinus[134]. Postoperative debridement and ongoing long-term instrumentation of the frontal neo-ostium is also substantially enhanced and capable of being performed without causing mucosal trauma. The EMLP has been shown to enhance frontal ostium patency rates over the long term, and this is strongly correlated to mucosal appearance and symptom scores[187].

5.6 CONCLUSION

This study is the largest series of EMLP in the literature with a follow up period of up to 10 years. It confirms the long-term efficacy of EMLP for patients with persistent frontal sinus disease. It seems particularly successful in cases where maximizing ventilation and delivery of topical steroid douches can locally control mucosal inflammation. Despite the ongoing adequate ventilation of the sinuses, recurrent infections do seem to continue to occur in a small number of patients. Although this refractory group of patients is symptomatically improved following EMLP surgery, they appear to be prone to frequent exacerbations, despite long-term and ongoing medical treatment. More research is required as to what the underlying reasons are for this, and to identify the most appropriate ongoing treatment for these patients.

Thesis Synopsis

This thesis has examined the surgical treatment of frontal sinusitis following an extensive examination of the literature. CRS is a complex disease, with a number of aetiological factors, which contribute to produce symptomatic disease. CRS is initially treated medically, with surgery reserved for failure of medical treatment to alleviate patient symptoms.

Despite the utilization of surgery to alleviate the symptoms of CRS refractory to medical therapy, there are clear deficiencies in our understanding of what type of surgery to perform, and how extensive this surgery should be so as to maximize long-term symptom alleviation and control. Particular controversy exists regarding addressing the frontal sinus with a wide variety of philosophies employed, but with limited scientific rationale to support such approaches.

We reviewed the outcomes of patients with frontal sinus disease refractory to medical therapy. All of these patients were treated with a common philosophy. That is, the frontal sinus should be treated no differently to any other sinus. Objective and symptomatic disease within any sinus following medical therapy is treated surgically, with the aim of maximally improving patient symptoms. Therefore, medically refractory disease in the frontal sinus was addressed surgically. All patients had their surgery performed by a single surgeon,

utilizing exactly the same surgical technique. In addition, pre and postoperative medical treatment was the same.

The first step in objectively assessing this surgical philosophy was to validate the way we measured symptoms pre and post treatment. This allowed us to quantitatively and qualitatively measure change following intervention. A prospective study was designed and we validated a quality of life tool, the Adelaide Disease Severity Score. Five simple questions directly related to sinus symptoms and a visual analogue quality of life score was found to correlate very highly with other more complex rhinological quality of life tools – the SNOT 20/22. It further correlated with radiological disease burden (Lund Mackay CT score) and endoscopic disease (Lund Kennedy endoscopic score) burden. This study validated our use of this tool to measure quality of life and symptom improvement in patients undergoing surgery.

The next step in investigating the merits of frontal sinus surgery was to look at a cohort of patients with medically refractory frontal sinusitis that had never had surgery before. All of these patients underwent surgery performed by a single surgeon using an extensively published, reproducible technique for frontal sinus recess dissection. This cohort of patients showed demonstrable benefit from having the frontal sinuses addressed surgically. The technical measure of success was high with an overall frontal sinus ostium patency rate of 92% and more importantly, complete resolution of symptoms was noted in 78% of patients.

Some risk factors for persistence of symptoms were identified. In particular, stenosis of the frontal ostium was noted to correlate with persistence of symptoms. This consequently increased the risk for requiring more surgery to alleviate persistent symptoms. The risk of frontal stenosis was strongly related to the intraoperative size of the frontal ostium created. Small frontal sinus ostia were found to be more likely to stenose. However, other risk factors identified in the literature review as associated with failure as such as Asthma, Eosinophilic Mucin Chronic Rhinosinusitis (EMCRS), allergy, and smoking, were not noted to be of significant importance.

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This raised the question as to whether all patients with frontal sinusitis refractory to previous surgery would benefit from this approach. Did patients undergoing revision surgery have a similar outcome to those undergoing primary frontal sinus surgery? Could we identify risk factors for either the primary group or the revision group that predisposed the patient to fail surgical

clearance of the frontal sinus ostium? Was there a cohort of patients that would benefit from more extensive frontal sinus surgery with joining of the frontal sinus ostia such as a EMLP in the first instance?

Analysis of this extended cohort of patients undergoing primary and revision frontal sinus surgery confirmed the overall success of standard frontal sinus surgery as shown in the earlier study. 85% of patients required no further surgery with marked long-term symptom improvement. However, approximately 15% of patients required further surgery in the form of an EMLP for symptom alleviation. Within the small group of patients requiring an EMLP, a subset of patients with a combination of small sinus ostia and inflammatory risk factors, and a high disease burden, were identified as having an increased risk for failing standard primary or revision ESS. These are patients with Asthma, CRS with polyposis, a Lund Mackay score >16 and a frontal sinus ostium less than 4mm in maximum diameter. These risk factors provide a reasonable basis for considering an EMLP in this cohort of patients who otherwise would undergo revision ESS with standard frontal sinus surgery. This particular subset may well benefit from a primary EMLP as 75% of patients with this combination of risk factors fail standard frontal sinus surgery.

The final step in this research was to analyze whether the EMLP was indeed successful in patients with recalcitrant frontal sinusitis. The overall outcomes, as well as risk factors for its success and failure, were investigated. This study found that the EMLP had excellent outcomes in the majority of patients, but

there was a significant minority of patients that had persistence of symptoms. The technical (patency of frontal sinus ostium) and qualitative (symptom improvement and overall quality of life) measures of success were high, with a 97% patency rate. Similarly symptom scores improved significantly. A small group of patients (~5%) did have persistence or recurrence of symptoms requiring a revision EMLP. This subset of patients remained partly symptomatic, and failed to respond as well as other patients did to either continued medical or surgical treatment. AFS and recalcitrant S. aureus infections were found to be significant risk factors

In summary, this thesis supports the hypothesis that the frontal sinus should be treated surgically when medical treatment has failed and there is objective evidence of disease in the frontal sinus. The technical measures of success are high and, more importantly, quality of life is substantially improved. We have also shown that there is a group of patients with multiple risk factors for failure of standard frontal sinusotomy. These patients might benefit from consideration of an EMLP as their primary surgical intervention. However, despite the success of standard frontal sinus surgery for the majority of patients, and the EMLP for those patients with recalcitrant frontal sinus disease, there are patients that remain persistently symptomatic. Clearly surgery itself is not the cure and there is much to discover about how medical and surgical treatment can optimally modify the environmental and host factors in CRS to drive sustained quality of life improvements in our patients.

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