State of the Art: Evidence-Based Decision-Making in Rhinology

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Introduction – Evidence Based Medicine

On any given day, as rhinologists we interact with patients who ask us questions that deserve answers. Those questions can be, “What is causing my symptoms?” or “How can I best get rid of my symptoms?” Sometimes we answer, “Chronic rhinosinusitis,” or, “Reduce inflammation,” but these responses don’t get to the heart of etiology or effective treatment, much less a personalized treatment for a particular patient’s pathophysiologic manifestations. In a sense, our patients’ questions become our own questions: “What does cause chronic rhinosinusitis?” and, “What are the most effective treatment options?”

Evidence-based medicine (EBM) has played an increasingly prominent role in our clinical decision-making, especially in the last 10–15 years. As medical expenditures rise, it’s natural to take a hard look at the effectiveness of a particular intervention and often understanding the underlying etiology guides those interventions. There are varying views on what constitutes EBM and some consider it “cookbook medicine”, where pathways and algorithms are laid out in simplicity, based on various published research. This simplistic view of EBM fails to take into account the variations in pathophysiology, environmental conditions, comorbidities, socioeconomic issues, and a host of other patient factors which significantly impact the effectiveness and applicability of any therapeutic option.

EBM is, therefore, best seen as a combination of three important factors: best external evidence published in peer-reviewed literature, individual clinician expertise based on experience and local practice factors, and patient values and expectations. Figure 1 shows the EBM “sweet spot” where these three elements overlap. We must explore our patients’ concerns and their priorities as we consider treatment for their conditions and we must as objectively as possible consider our own clinical expertise and experience. We certainly rely on the wisdom of our teachers and we continually learn about new developments in the scientific meetings of our societies and associations. We must also know the published literature well in order to apply it to our patients’ situation.

Staying abreast of an increasingly large body of rhinologic “best available evidence” can be a significant challenge. While rhinosinusitis accounts for only 0.1% of articles pub-

Figure 1  Evidence based medicine is a combination of three important factors. Adapted from: Armstrong EC. Harnessing new technologies while preserving basic values. Fam Syst Health 2003; 21: 351–355. EBM = evidence-based medicine.
lished annually, the number of rhinologic journal articles published annually has increased significantly, to over 1200 annually\(^a\). Moreover, the quality of these thousands of articles varies substantially, from high level meta-analyses of multiple randomized controlled trials (level 1 evidence) to small case series (level 4 evidence) or even case reports. The literature in rhinosinusitis, unfortunately, while large in volume tends toward the lower levels of evidence overall, presenting an opportunity to improve the quality of our “best available evidence.”

In an effort to condense and sift through this large volume of literature, panels of experts have produced consensus statements that summarize this evidence. Two of the most prominent and rigorous consensus documents are the European Position Paper on Rhinosinusitis and Nasal Polyps (EPOS), published in 2012\(^b\),\(^c\), and the International Consensus Statement on Rhinology and Allergy: Rhinosinusitis (ICAR-RS), published in 2016\(^d\). The EPOS document built upon previous editions and followed a more traditional pattern of a panel of experts reviewing the literature, writing a portion of the manuscript, and then meeting to discuss and resolve any differences. In contrast, the ICAR-RS process adapted an electronic and partially blinded methodology initially developed by Rudnik and Smith\(^e\). Briefly, experts are invited to create a structured evidence-based review with recommendations, and this is then sent to additional experts who are blinded to the original author’s identity. Recommended changes are then resolved between the original author and reviewer, after the blinded review is completed. Two or three additional blinded review steps are completed in order to maximize the effectiveness of the critical review. With blinding in place, bias due to expert opinion is minimized. For the ICAR-RS, over 140 topics were submitted to this process, following which the entire document was assembled and reviewed by all authors. The result is a condensed, easily accessible, evidence-based review of scores of topics relating to rhinosinusitis etiology and treatment with nearly 1500 references. This same process has recently been used to generate a comprehensive analysis of allergic rhinitis\(^f\).

With our expert colleagues condensing the available evidence to a consumable size, we can examine three different areas where our patients—and we as rhinologists—may have some questions:

(I) What is the best frontal sinus surgery procedure?

(2) How should we be caring for patients after endoscopic sinus surgery?

(3) What are the best methods for diagnosing and treating a cerebrospinal fluid leak?

Applying Evidence Based Medicine

– Decision-Making in Frontal Sinus Surgery

In typical cases of rhinosinusitis, we pursue medical therapy prior to considering surgical options and we know that endoscopic sinus surgery is superior to continued medical therapy that incompletely addresses patients’ symptoms\(^g\).\(^h\). We assume, but don’t truly know, if this is the case for frontal sinusitis specifically. Complicating matters in frontal sinus surgery decision-making, there are a multiple approach options ranging from a simple anterior ethmoidectomy to an extensive “drill-out” of both frontal sinuses. How does one choose the appropriate procedure?

Moreover, we must consider what the goals of the surgery are, literally how we are defining a successful outcome. Some of the evidence uses patency of the sinus ostia, others use an absence of mucosal thickening on imaging, and still others employ patient symptoms. And we must determine what an appropriate length of follow-up is necessary. In a now classic analysis, Neel examined patients following frontal surgery at 13 years and at 20 years following the procedure and found the success rate declined over the intervening 7 years\(^i\). Most of the frontal sinus surgery literature follows patients for 6–12 months, which will likely not be long enough for us to know the true durability of our outcomes.

Frontal sinus surgery approaches were classically categorized into four levels of extent (I, IIa, IIb, and III) by Draf\(^j\). More recently, this classification has been expanded into seven levels (0–6)\(^k\). The range of options, therefore, for frontal sinus surgery ranges from anterior ethmoidectomy alone through balloon dilation and simple frontal sinus ostium enlargement to bilateral drilling procedures. The following is a summary of what we can learn from the best available peer-reviewed evidence for each one of these procedures:

- Anterior ethmoidectomy is up to 89% effective in resolving symptoms of frontal sinusitis without instrumentation of the frontal sinus ostium\(^l\).\(^m\).
- Balloon dilation of the frontal sinus demonstrates 94%–100% patency for up to one year\(^n\).\(^o\). Whether this effectiveness is an improvement over anterior ethmoidectomy
alone, which is often performed with frontal balloon dilation, is yet to be determined.
- Frontal sinusotomy results in symptomatic improvement in 69–92% of patients, with narrower ostia at the time of surgery (<4.5mm diameter) having a higher tendency to close. Overall, frontal ostia narrow about 30–40% postoperatively and polyps, asthma, and allergy do not appear to have an effect on stenosis.
- Unilateral drilling frontal procedures have a more limited amount of evidence. Initially, patency was reported as 42% but more recently is reported at greater than 90%.
- Bilateral drilling frontal procedures that include resection of the intersinus septum and the superior nasal septum have shown variable patency, ranging from 55–96%. Ostium size appears to decrease in size for up to two years and irrigation penetration has been shown to be better than in simple frontal sinusotomy approaches.

In summary, there are only a few studies looking at outcomes in frontal sinus surgery and almost no head-to-head comparisons. Less aggressive procedures show effectiveness, including anterior ethmoidectomy alone. More aggressive drilling procedures don’t have superior results compared to less aggressive ones, but are probably differentially applied to more difficult cases (e.g., revision surgery, polyps, new bone growth). Much more research needs to be done in this area to better define the best approach for a particular patient’s condition.

**Applying Evidence Based Medicine**

**– Care Following Endoscopic Sinus Surgery**

Postoperative care following endoscopic sinus surgery (ESS) is felt by many to be important for the eventual outcome of the patient. A number of interventions have been studied following ESS. Rudmik et al. performed an evidence based review with recommendations in 2011. This analysis was recently updated for the ICAR-RS. The following is a summary of the best available evidence on postoperative care following ESS and the reader is referred to Rudmik et al. and Orlandi et al. pages S165–S167 for details and references. It must be remembered that the recommendations apply to routine situations and that the patient’s individual circumstances must always be taken into consideration:

- Saline irrigation appears to improve outcomes with minimal harm, according to multiple studies. It is recommended following ESS.
- Endoscopy and debridement allow for inspection and documentation of the patency and status of each sinus operated on and identify early complications of healing. They provide an opportunity to correct areas of early stenosis and scarring and fibrinous exudate can be removed. The published evidence demonstrates improved outcomes with endoscopy and debridement and there is moderate cost and discomfort. Based on the published evidence, postoperative endoscopy and debridement are therefore recommended following ESS.
- Systemic steroids have been examined following ESS in only one study. This study did show improved outcomes but there are significant risks and side effects associated with systemic steroid use. For this reason systemic steroids following ESS are considered optional.
- Topical corticosteroids have been shown in multiple studies to improve outcomes, with these studies typically involving sprays and drops. There is minimal harm and the costs are moderate. For these reasons topical corticosteroids in the form of sprays or drops are recommended following ESS. There are no studies regarding non-standard delivery methods such as high volume steroid irrigations in the immediate postoperative period. For this reason these are considered optional and may be beneficial in patients with higher risks of polyp recurrence and other forms of inflammation immediately following ESS.
- Oral antibiotics are commonly given following endoscopic sinus surgery. Interestingly there are very few studies examining this practice. Only cefuroxime and amoxicillin/clavulanate have been examined. The evidence does show some improved outcomes but there is significant potential harm both to the individual due to resistance emergence and gastrointestinal problems. The societal costs of using antibiotics unnecessarily are also high. Because the amount of evidence is so small, it is hard to fully weigh the risks and benefits and therefore the evidence supports oral antibiotics as an option. Hopefully more studies in the future will delineate this balance better.
- Topical decongestants have been examined in one study, which showed no evidence of improved outcomes but did show increased pain. For this reason topical decon-
gestants are not recommended following ESS.

- Leukotriene receptor antagonists have also been examined in only one study in the immediate postoperative period. Minimal improved outcomes were seen and there is significant potential harm and cost. For these reasons they are not recommended in the immediate postoperative period.

- Drug eluting spacers and stents have garnered much attention recently. There is early evidence for improved outcomes. There is also, however, significant cost associated with this intervention. Evidence continues to be produced examining the long-term value, change in outcome compared to cost, and this evidence will continue to guide our practices. For now drug-eluting spacers and stents are considered optional in the immediate postoperative period following ESS.

In summary, we have some evidence to guide our postoperative care following ESS, but much more is needed. Many of our practices rely on tradition, what we were taught by our professors, and what makes sense to us based on our knowledge of CRS and our experience caring for our patients. Which types of CRS benefit from which interventions is not known (for example, whether leukotriene inhibitors or oral steroids are more beneficial for patients with aspirin exacerbated respiratory disease). Clearly much more research and evidence is needed to better guide our treatment of our patients in the immediate postoperative period.

**Applying Evidence Based Medicine**

-- *Diagnosis and Management of Cerebrospinal Fluid Leaks*

Rhinologists not infrequently encounter patients with clear fluid coming from the nose, suggestive of a cerebrospinal fluid (CSF) leak. Two recent papers have analyzed the evidence regarding the diagnosis of CSF rhinorrhea and its management. Oakley et al. performed an extensive systematic review and produced two evidence-based reviews and recommendations\(^{21, 22}\). For details and references, the reader is referred to these two sources.

The first step in addressing a possible CSF leak is making an accurate diagnosis\(^{20}\). Patients can have profuse watery rhinorrhea which may be vasomotor in origin. Definitive diagnosis is therefore very important:

- Glucose testing of rhinorrhea is sometimes used as an indicator of CSF leakage. There is, however, a high false-negative and false positive risk with this test. For this reason the evidence suggests that it not be used as a definitive diagnostic marker for CSF.

- Beta-2 transferrin testing is very reliable, based on the evidence, with a nearly 100% positive and negative predictive value. Moreover the evidence shows that the protein is stable at room temperature for 7 days. Beta–trace protein is similarly highly reliable.

- Radionuclide cisternography, where pledgets are placed in the nose to capture radioactive fluid injected intrathecally is not as reliable and is invasive. Its routine use is therefore discouraged.

- Once the diagnosis of a CSF leak is made, the next issue is identifying the source. The evidence in the literature indicates that a fine cut CT scan in the coronal plane is the best first localizing test. Common sites of leakage are the lateral lamella of the cribriform plate of the ethmoid especially following ESS, the fovea ethmoidalis of the frontal bone and the posterior wall of the frontal sinus following trauma, and the lateral roof of the sphenoid sinus in a well-pneumatized pterygoid wing, especially for spontaneous leaks. Remember, of course, that the site of leakage may be the ear, with the CSF draining down the Eustachian tube.

- If the CT scan does not clearly delineate the site, MRI is the next best step. The MRI can be performed with or without intrathecal gadolinium. In the United States intrathecal gadolinium is not approved but its safety has been demonstrated over multiple years. The potential benefits and harms must be weighed for each patient.

- Other options for localization include CT cisternography and radionuclide cisternography. The radionuclide study at best can demonstrate what side the leak is coming from. Because of cross contamination of multiple pledgets placed in the nasal cavity and sinuses, precise localization is often not possible with this modality.

- Intrathecal injection of fluorescein is used by some to identify the site of the leak during nasal endoscopy, commonly in the operating room. There is a risk of neurological side effects including seizures and paralysis, seen with undiluted injections, and in the United States this practice is not approved. Extensive use however of diluted solutions has demonstrated safety. Typically 0.1cc of a 10% solution mixed in 10cc of the patient’s...
cerebrospinal fluid or saline can be counted on to be safe. Again the potential risks and benefits must be weighed in each individual patient’s situation.

Many management options have been described for CSF rhinorrhea. Each must be examined in light of the best available evidence. Much of this evidence is unfortunately low level, with case series and retrospective reviews. Nonetheless, assembling all of the available evidence does give us some guidance:

- Lumbar drainage has been used for many years to reduce intracranial pressure and facilitate healing of cerebrospinal fluid leaks, particularly following trauma. It is used by some surgeons to reduce pressure on the repair in the perioperative period as well. In theory, this would lead to a higher success rate, but has never been demonstrated. In fact, one randomized control trial showed no difference. There are significant potential complications with lumbar drainage including meningitis, prolonged leakage of CSF at the drain site after its removal causing persistent spinal headache, and brain herniation and death. Additionally, there are costs with prolonged hospitalization and higher acuity monitoring due to the risk of brain herniation if the patient gets out of bed while the drain is open. A recent review demonstrated that the risk of lumbar drainage complications may be higher than the risk of the repair failure. For these reasons Oakley and colleagues recommended against routine use of lumbar drainage as an adjunct to surgical repair. It may, however, be beneficial in the perioperative period for patients with suspected benign intracranial hypertension and in these cases is an option.
- Other questions surround what type of material should be used to repair the leak. Endoscopic repair of CSF leaks has been shown to be successful in greater than 90% of attempts. Interestingly, it appears from the evidence that the material used for the repair has a little impact. For this reason multiple types of grafts, pedicled or free, as well as exogenous material are all options.
- The use of nasal packing following repair to support the graft and hold it in place makes sense but interestingly there is very little evidence to examine this practice. Packing is therefore an option following CSF leak repair.
- Bedrest is often used following repair to avoid Valsalva maneuver. There is however, no evidence, to indicate how long bedrest must be used and when regular activities may be resumed. Similarly, no studies have examined when it is safe to resume continuous positive airway pressure for patients with obstructive sleep apnea.

Summary and Conclusion

There has been a great deal of evidence published over the last few decades in the field of rhinology. As it increases in quantity, fortunately the evidence also continues to increase in its quality. As rhinologists, it’s incumbent upon us to know this literature as we make evidence-based decisions in the treatment of our patients. Recent systematic reviews, including international consensus statements, have greatly facilitated the dissemination of the best available evidence in rhinology.

This review has examined three areas where the evidence can guide our treatment: decision-making in frontal sinus surgery, immediate postoperative care following ESS, and in the diagnosis and management of CSF leaks. Many more such areas are addressed in consensus documents such as ICAR–RS and EPOS. The reader is strongly encouraged to familiarize himself or herself with these documents in order to provide the best possible care for his or her patients.

Potential Conflicts of Interest

Dr. Orlandi is a consultant for Medtronic ENT, Lyra Therapeutics, and BioInspire Technologies

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