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Endoscopic Monitoring of Postoperative Sinonasal Mucosa Wounds Healing

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1. Introduction

Nasal epithelium lies on the basement membrane, situated on the lamina propria. Pseudostratified columnar (respiratory) epithelium is composed of four major types of cells: ciliated cells, nonciliate cells, goblet cells and basal cells, ensuring mucus production and transport, resorption of surface materials, and formation of new epithelial cells. Lamina propria consists of two layers of seromucous glands, i.e. superficial and deep layers. Just beneath the basement membrane, lymphocytes and plasma cells form a lymphoid layer.

Maintenance of normal ventilation/aeration of sinus spaces is necessary for normal functioning of paranasal sinuses. The sinus labyrinth spaces and ostia of various sinus areas can be visualized by use of endoscopic techniques, e.g., in functional endoscopic sinus surgery (FESS). Ventilation and normal sinus function can be maintained by this minimally invasive method. Endoscopic sinus surgery (ESS) is the superior surgical method of treatment for recurrent acute sinusitis, chronic sinusitis, obstructive nasal polyposis, extramucous fungal sinusitis, periorbital abscess, rhinoliquorrhea, antrochoanal polyp, foreign body extraction, mucocele, dacryocystorhinostomy, excision of various tumors of the sinuses, nose, anterior, middle and posterior cranial fossa, epistaxis control, optic nerve decompression, choanal atresia, and orbit decompression. . Functional endoscopic sinus surgery (FESS), a minimally invasive technique, remains the most widely accepted therapy for chronic rhinosinusitis (CRS) and nasal polyposis (NP) after failure of medical treatment. FESS aims to remove inflammatory mucosa and to restore both ventilation and drainage of the sinus cavities. However, healing quality significantly influences the functional outcome. The exact mechanism of mucosal healing after sinus operation remains unclear. Postoperative wound healing is a highly coordinated process that includes coagulation, i.e. clot formation, inflammatory stage, and tissue formation and remodeling. During the process of healing, the extracellular matrix of nasal mucosa may be directly influenced by the growth factor (GF), while the expression of GF receptors may influence the cell phenotype and its adhesion. Endoscopic observation of the nasal and sinus mucosa healing after FESS revealed four clinical stages: stage 1 characterized by the formation of abundant crusts, lasting for 1-10 days; stage 2 characterized by obstructive lymphedema, with pronounced swelling of residual mucosa, lasting for up to 30 days; stage 3 characterized by mesenchymal growth, when pale, edematous mucosa is transformed to red mucosa, lasting for up to 3 months; and stage 4 characterized by cicatrix formation, lasting for 3-6 months.

The duration of particular stages can be reduced or prolonged by postoperative treatment. Any derangement in the process of healing may result in the formation of hypertrophic scar or impaired tissue differentiation, thus reducing functioning capacity of the organ involved. Healing defects of the respiratory mucosa regularly lead to development of infection or obstruction scar formation, making revision surgery necessary. Iatrogenic complication after FESS appears in 5% to 30% of patients, and recurrence is reported in about 18% of patients (Tan BK. 2010). Proper treatment of postoperative cavity is a significant segment in the process of mucosal healing, and thus part of the FESS. Due knowledge of the healing stages can help recognize a mucosal healing impairment and introduce appropriate therapy depending on the stage of the healing process. The healing stages and planning of postoperative therapy after endoscopic sinus surgery are presented.

1.1 Structure of sinonasl cavity

The nasal cavity and sinusies are covered with respiratory epithelium which is composed of ciliated pseudostratified columnar epithelium (respiratory epithelium) composed of four major types of cells: ciliated cells, nonciliated cells, goblet cells and basal cells assuring mucus production and transports, absorbtion of surface materials and formation of new epithelial cells. The lamina propria consists of two layers of seromucous glands: the superficial layer is situated just underneath the epithelium and the deep layer is under the vascular layer. Just beneath the basement membrane, lymphocytes and plasma cells form a lymphoid layer. The basal cells are intermediate stem cells capable of differentiation into ciliated columnar or goblet cells. Occasional cuboidal and squamous cells are also found the epithelium. The columnar cells are 25μm long and 7μm wide, tapering to 2-4μm at the base. They are separated from each other by tight junctions. Each cell is always covered by 300-400 microvilli, and may or may not have cilia. Microvillies increase the surface area, thereby preventing drying. The number of cilia on each cell and size of the cilia varies between different species. The goblet cells produce mucus. The size and staining characteristics of the cell will depend on the phase of the secretory cycle of each individual cell. The number of cells varies throughout the nose and sinuses. On the septum, there is gradual increase in numbers passing from anterior to posterior and increase from superior to inferior. The seromucinous glands are found in the submucosa of the respiratory epithelium. They are relatively few in number and are more numerous in the mucosa near the choanae. The mucosa of the nasal cavity is much thicker than that of the sinuses. Mucosa tends to be thin and dry over bony excrescences and outcroppings that are characteristically notable over the nasal septum and in nasal valve area. Sinus mucosa is much thinner than that lining the rest of the nasal cavity. Epithelium tends to be lower; there are generally few goblet cells; and seromucinous glands are extremely scarce. The basement membrane is attenuated or not readily discernible and the lamina propria is often absent. The basic cells are columnar ciliated epithelial cells. They average 5μm long and 0.2μm thick and carry between 100 and 150 cilia on each luminal cell surface. Microvilli are much smaller, averaging around 1.5μm long and 0.08μm in diameter. Goblet cells are shorter except during the active phase of secretion. The maxillary sinus is lined with ciliated columnar respiratory epithelium containing goblet cells and glands. The mucous membrane is relatively thin, less vascular and more loosely adherent to the bony walls than in the nasal cavity. Density of goblet cells in the maxillary sinus is the highest of any in the paranasal sinuses, and similar to that on the inferior turbinate. There is no obvious increase in goblet cell density around the ostium. The seromucinous glands, though few in number compared with the goblet cells, are again

more numerous in the maxillary sinus compared with the other sinuses, and are more concentrated around the ostium. Ethmoid sinuses are also lined with ciliated columnar respiratory epithelium. The density of goblet cells is lower then in the maxillary sinus. Tubuloalveolar seromucinous glands are found trough out the mucosa and are actually more numerous in the ethmoid than in the other sinuses. In sphenoid sinuses the respiratory epithelium contains goblet cells and glands, as in the other sinuses. Goblet cells are of similar density as in the ethmoids, though the glands are last numerous in these sinuses and are therefore not found on all walls. The frontal sinus respiratory epithelium has the fewest number of goblet cells and very few glands. Mucus has a gel and sol layer with the narrow sol layer covering the cilia, facilitating their movement, and the gel layer on top to which foreign material will stick. Mucus blanket sweeps from the nares to the choanae and in the sinus cavities toward their ostia. The only exception to this is the frontal sinus in which the mucus blanket sweeps from the ostium, arcs over the roof of the sinus, and progresses along the floor to empty into the lateral aspect of the frontal sinus ostium. Vasculature of the nose is characterized by capacitance vessels. With these vascular specificities, nasal mucosa can regulate the airflow, adapt the nasal resistance, filter and condition the inspired air, and organize the first line of immune defense. Ethmoid bloc is the most complex of the sinuses. It often appears to be pivotal sinus in pathophysiology of sinus inflammatory disease (Donald PJ.1995).

1.2 Cytokines and GFs in nasal repair

The transforming growth factor-beta (TGF-β) is the most relevant growth factor in wound healing, affecting nearly all the phases of the process. Besides its immunosuppressive effects, TGF-β1 influences cell proliferation and myofibroblast differentiation. GFs are mediators produced by cells, tissue or blood products that activate target cells to proliferate by binding to their high-affinity surface membrane receptors. Transforming GF (TGF) β is released by major cell types participating in the repair process (epithelial cells, inflammatory cells, fibroblast, etc.) and nearly all cells express TGF-β receptors. More than 85% of TGF-β in adult wound fluid is of the type 1 isoform. TGF-β had important activities such as an adverse effect in vitro on reepithelization, immunosuppression, or stimulation of ECM deposition. PDGF isoforms have potent mitogenic and chemotactic activities on dermal fibroblasts, endothelial cells, smooth muscle cells, neutrophils, and macrophages and stimulates collagen synthesis and collagenase acitivity. PDGF isoforms have potent mitogenic and cemotactic activities on fibroblasts, endothelial cells, smooth muscle cells.

Epidermal GF (EGF) family, including aphiregulin and TGF-α has been shown to induce epithelial development and differentiation, to promote angiogenesis, and, in vivo, to accelerate wound healing. Cells associated with wound healing such as inflammatory cells (macrophages and T lymphocytes), vascular endothelial cells, and fibroblasts can produce fibroblast GF (FGF), which are mitogens for a wide variety cell types. Insulin-like GF (IGF) I and II have an amino acid sequence homologous to proinsulin and are secreted by a wide range of adult tissues. IGF-I (known as Somatomedin-C) stimulates, in vitro mitosis of fibroblasts, osteocytes and chondrocytes. Because its combination with other growth hormones is more effective than either peptide alone, it frequently acts in synergy with PDGF to enhance epidermal regeneration. GFs enhance the deposition of extracellular matrix (ECM). Extracellular matrix provides nutrients support, and adhesion for the inflammatory on structural cells participating in repair (Watelet JB. 2002).

1.3 Neutrophils in wound healing

Neutrophils play an important role in tissue remodeling occurring after tissue damage. The particular inverse relationship between eosinophils and fibrosis found at baseline persists during the healing process. On the other hand, macrophages and eosinophil cells are highly associated not only with the tissue remodeling characteristic of chronic sinus disease but also with the neutrophilic inflammation occurring during wound repair. Macrophages and eosinophil cells were highly associated not only with the tissue remodeling characteristic of chronic sinus diseases but also with the neutrophilic inflammation occurring during wound repair. The selective recruitment of eosinophils into sinonasal inflamed tissue involves priming, activation, and recruitment mediated by chemoattractants, cell adhesion molecules, and cytokines. Activated eosinphils contribute to the production of cytokines and inflammatory molecules, which damage nasal mucosa, leading to edema and inflammation. The differentiation of mast cells occurs by the effects of released cytokines from inflammatory cells. Histamine, prostaglandine E2, and leukotriens are released from degranulate mast cells. Sensory nerve stimulation by these mediators attracts eosinophils to the inflammatory areas. Substance P released by mast cells causes increased vasodilatation, increased vascular permeability, mucous secretion, and eosinophil chemotaxis; increase mast cells degranulation; and enhances the response to allergens in atopics patients (Watelet JB. 2006).

1.3.1 Neutrophil-derived Metalloproteinase-9

Metalloproteinase-9 (MM-9) expression in ECM was also significantly correlated with healing quality. MM-9 is actively expressed by eosinophils, monocytes-macrophages, epithelial-derived cells and is stored by neutrophils. It degrades collagen fibres, basement membrane, fibronectin and elastin. MM-9 activity is controlled at different levels: transcription of the gene under control of cytokines or cellular interaction, activation of the proenzyme by serin proteases or other MMPs, and finally, activity regulation by natural tissue inhibitors (TIMPs). The amounts of MMP-9 in nasal fluid are linked to ECM expression of MMP-9. The MMP-9 deposition inside ECM correlates with inflammatory cells. The number of neutrophils and lesser extent, macrophages could predict MMP-9 release in nasal fluid. There is close relationship between MMP-9 and neutrophils and they establish a direct link between the severity of the inflammatory reaction and the consequent tissue damage. MMP-9 is considered as effector but also as a regulator of leukocyte function. It is stored in granules of mature neutrophils and has been shown to be a specific marker of neutrophils and has been shown to be a specific marker of neutrophils maturation. Transcription of the gelatinase-B gene is stimulated in leukocytes by cytokines, viral or bacterial products, or cellular interactions. In response to lipopolysaccharide, the neutrophil is responsible for the rapid secretion of MMP-9 as a result of release of preformed enzymes stored in granules. The level of MMPs parallels the severity of clinical condition. Release of gelatinase-B by degranulation of neutrophils occurs within the first hour when these cells are stimulated by chemotactic factors. During wound healing, the association beween neutrophils and macrophages observed in tissue suggests that the amounts of MMP-9 requested are high and that a conjunction of rapid release and continuous production is needed. MMP-9 has been shown to clip many cytokines or chemokines such as interleukin (IL) -1β or IL-8. On the other hand, the binding of MMP-9 to the plasma membrane of neutrophils enables it to be inhibited by TIMPs and thereby may alter the pericellular

proteolytic balance in favor of ECM degradation. The MMP-9 production by neutrophils participates actively in airway remodeling (Watelet JB. 2005)

2. General principles of wound healing

Wound healing of the mucosa lining consists a few phases such as: inflammation, cell proliferation, matrix deposition and remodeling (Watelet JB.2002).

2.1 Coagulation

Injury to the nasal epithelium causes hemorrhage with exposure of platelets to the connective tissue, which activates the platelets and results in an almost immediate release of numerous vasoactive substances (serotonin, bradykinin and histamine). The subsequent transient (5-10 minutes) vasoconstriction helps to control bleading and is followed by the formation of a primary hemostatic plug with aggregation of platelets in the mucosal effect. Platelets are critical elements during this early response, not only because of their concurrent release of numerous cytokines. Damaged nasal cells release PDGF, TGF-α and TGF- β and mast cells represent another source of biologically active substance or GFs that regulate the early repair sequences. Fibrin, in conjunction with fibronectin, acts as a provisional matrix for the influx of monocytes and fibroblasts. Fibrin also stimulates the α-granules within the aggregated platelets to release PDGF, EGF, IGF-I, TGF-β and FGF.

2.2 Inflamation

In the nasal lamina propria, an intense inflammatory reaction starts simultaneously with the coagulation phase. This inflammation is marked by an infiltration of leukocytes, which migrate through vessel walls by a process known as diapedesis. Polymorphonuclear neutrophils predominate during the first 24-48 hours and stimulate release of elastase and collagenase molecules, which facilitate cell penetration into the ECM. Three to five days after injury, the neutrophilic population in the wound is replaced by monocyte predominance. Unlike neutrophils, the influx of macrophages is essential for the continuation of nasal wound repair. Macrophages contribute to cellular debridement and secret a number of GFs: TGF-β, basic FGF (b FGF), EGF, TGF-α and PDGF. They amplify and sustain the wound healing process. Lymphocytes and their products, TGF-β, interleukin, tumor necrosis factor and interferons also interact with the macrophages during the inflammatory process, linking the immune response to wound healing. In a typically clean surgical wound, this inflammatory reaction subsides over a period of several days.

2.3 Tissue formation

New stroma or granulation tissue consisting of fibroblasts, macrophages and neovasculature can be observed 4 days after injury within a loose connective tissue matrix of collagen, hyaluronic acid and fibronectin. Macrophages of the nasal lamina propria provide a continuing source of cytokines necessary to stimulate proliferation of fibroblast and angiogenesis.

2.3.1 Fibroplasia

This term reflects fibroblast cell migration or proliferation and ECM deposition. Through a variety of cytokines from platelets and macrophages or through an autocrine regulation,

fibroblasts are attracted to the nasal wound. Structural molecules of the early ECM also contribute to tissue formation by providing a network for cell mobility and guidance (fibronectin, collagen and hyaluronic acid) and by acting as a cytokine reservoir. Once the nasal fibroblasts have migrated into the wound, they gradually switch their major function to protein synthesis and GF release. The composition and structure of granulation tissue depends both on the time course since tissue injury and on the distance from the wound margin.

2.3.2 Angiogenesis

Nasal endothelial cells start to proliferate through fragmented basement membranes. They migrate into the perivascular space, and other endothelial cells follow. Angiogenic GFs: FGF, TGF-β, EGF, TGF -α and PDGF, released from injured nasal cells, platelets and ECM, induced vascularization, resulting in delivering oxygen to the wound bed. Endothelial cell migration depends on continuous collagen secretion and is accompanied by proteoglycan synthesis.

2.3.3 Reepithelization

Migration of new respiratory cells from the undamaged areas starts within a few hours, with an estimated velocity of 4μm/hour in the sinuses. The nasal epithelial cells at the wound edge lose their apical-basal polarity and develop cytoplasmic extensions into the wound. Four different processes are operative during regeneration: migration from adjacent epithelium, multiplication of undifferentiated cells, reorientation and differentiation. Undifferentiated respiratory basal cells from adjacent non-traumatized areas seem to serve as the main source of new cells. Different hypotheses are proposed to explain the initiation of reepithelialization: absence of neighbor cells at the wound margin, local release of GFs (TGF-α and EGF) or increase of GF receptors.

2.4 Tissue remodeling

Nasal ECM remodeling, cell maturation and cell apoptosis overlapping with tissue formation and wound remodeling may continue up to 6 month after surgery. Most cells produce proteinases able to degrade the ECM. These enzymes can be subdivided into three groups: the serine proteinase, the matrix metalloproteinases ad the cysteine proteinase (cathepsins). The matrix metalloproteinases need an active Zn+ site for their catalytic mechanism and they can be categorized in function of their degradation abilities in the ECM: interstitial collagenases 1-3, stromelysins 1-3, gelatinases A and B, matrilysin, macrophage metalloelastase and transmembrane metalloproteinase. Their proteolytic activity is controlled by tissue-erived metalloproteinase inhibitors 1-3.

In the remodeling or maturation phase, the inflammators response and angiogenesis diminish, whereas the intense fibroblast proliferation starts to attenuate. The composition of ECM changes as the wound matures. Initially, The ECM is composed mainly of hyaluronic acid, fibronectin and collagen types I, III and V. During remodeling, the ratio of collagen type I to III changes until type I is the dominant form; elastin fibers or proteglycans are actively produced within the matrix. This dynamic balance between collagen synthesis and lysis is responsible for the maturation of the wound. This phase increases wound tensile strength and resilience to deformation.

3. Endoscopic observations of wound healing

Endoscopic observation of normal wound healing revealed four different phases (Hosemann W. 1991, Xu G.2008):

3.1 I Phase of blood crusting (day 1-10)

During the first stage / peak the operative cavity is clean or dry, which is called "*stage of clean cavity*". In the 3-5 days after the filled nasal material was taken away, oozed blood clotted and formed a dry and hard black crust. During the first 10 days the endoscopic picture was dominated by blood crusts. After 12th days the whole wound was covered by blood crusts. There was no change of the residual mucosa underneath these crusts within the first 2-3 days. Due to shortage of mucosa clearance, viscous secretion was gathered in the bottom of the sinus, and mucosa gap and fibrous pseudomembrane was observed on the surface of mucosa with responsive edema. The edematous swelling became more marked after detachment of the crusts in the second phase. On days 7-10, the edema was relieved and secretion was reduced, and clots and crusts decreased or disappeared after cleaning. After 10 days, the operative cavity became clean.

3.2 II Phase of obstructive lymphedema (up t 30 days)

During this period, the residual mucosa showed edematous swelling. This is secondary peak which occurs in the third to tenth weeks. Edema reoccurred in the operative cavity mainly due to lymphatic obstruction. Vesicles, mini-polyps and granulation tissue began to grow in the mucosa gap, which is called "*reaction to mucosa removal*". Hyperplasia and adhesion of connective tissue were also observed in this stage. In the meantime, regeneration and epithelialization were also happening, competing against mucosa diseases. After the vesicles, granulation tissue, mini-polyps and fibrous adhesion had been cleaned and mucosa regeneration and epithelialization expanded little by little, the scope of disease got smaller and smaller, and complete epithelialization was attained in the end. This secondary edema regresses spontaneously. If this phase is not handled carefully, the diseases would expande gradually and hamper epithelialization, resulting in deferred inflammation, leading to adhesion, constriction and blockage of the operative cavity and sinus ostium. In view of stage characterized by coexistence and rivalry of mucosa regeneration and disease, it is called "*stage of mucosal transitional competition*". The generation of vesicles or polyps during this stage was simply regarded as "recurrence of disease" instead of an inevitable mucosal transitional process. When the local reaction to mucosal removal was under control, mucosa restored well.

3.3 III Phase of mesenchymal growth (up to 3 months)

After the 30th day, mucosal reorganization took place preferably below the regenerated epithelial covering. This is the third stage/ peak. After 10 weeks, implying finished epithelialization of the operative cavity, which was called "stage of complete epithelialization". Though epithelialization started in the first 2 weeks and extended to the second stage, only a small number of cases finished epithelialization within 5 weeks, the majority was after 10 weeks and had a benign outcome. The color of the mucosa changed from a yellowish-pale edema to a more reddish color.

Infection with additional destruction of the mucosa or excessive granulation allergic factors, hyperplasia of connective tissue and lack of control of regenerated polyps could slow down this epithelialization.

3.4 IV Phase of scarification (after 3 months)

At this time reorganization of tissue in the operated area had nearly finished. Subepithelial changes are noted after 6 months.

During these four phases in operative field can be seen:

1. *Clean cavity*: no oozing, fibrous pseudomembrane nearly disappeared, secretion decreased, clots and brown-yellow crusts diminished or disappeared
2. *Mucosal edema*: the whole inflammatory cavity and mucosa swelled, with smooth surface and indistinct boundary
3. *Edematous vesicle*: single or multiple or patches of polyp-like edematous vesicle appeared, with a grey, smooth and thin wall.
4. *Polyp*: it exists singly and locally
5. *Granulation tissue*: local or scattered hyperplasia occurred, with unsmooth papillary-like surface, fragile and easy to bleed
6. *Polyp-like mucosal edema*: extensive polyp-like changes and severe mucosal edema with plenty of purulent secretion were found
7. *Cicatricial tissue hyperplasia*: extensive connective tissue was yielded, mostly connected to patches, which was thick, tough and easy bleeding
8. *Adhesion*: fibrous membranous or cicatricial bridges resulted, mostly lying between the anterior verge of the middle turbinate and the lateral wall of the nasal cavity
9. *Empyema*: mostly was a viscous purulent secretion difficult to exudate
10. *Narrow or blocked sinus ostium*: fibrous cicatricial bridges occurred around the sinus ostium or connective tissue hyperplasia appeared
11. *Constriction and blockage of sinus cavity*: caused by adhesion of the laterally moved middle turbinate or connective tissue hyperplasia of the sinus wall
12. *Epithellization*: thin and smooth mucosa was found, which was closely linked with the preserved sinus bone wall and anatomical processes, and well-opened sinus ostia were clearly observed.
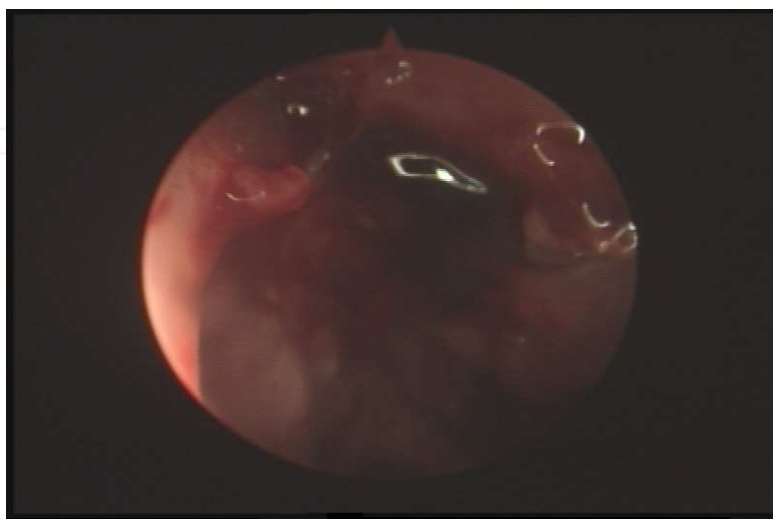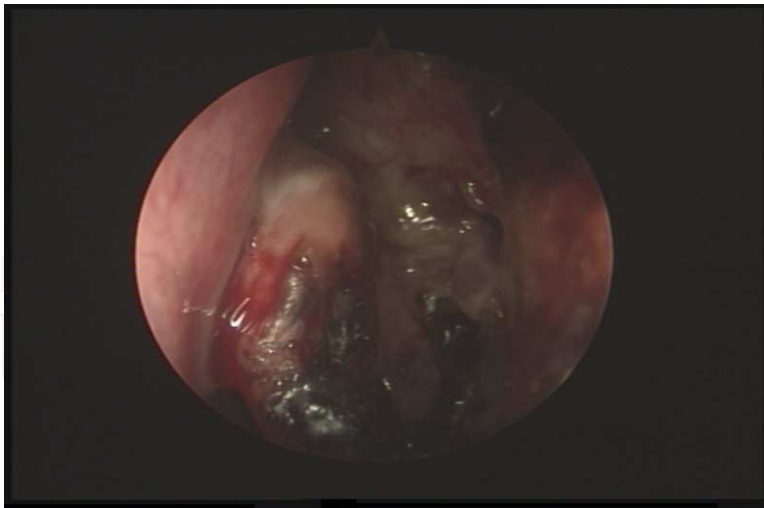

Fig. 1. Clean cavity (blood clot)

Fig. 2. Clean cavity (hard black crusts)

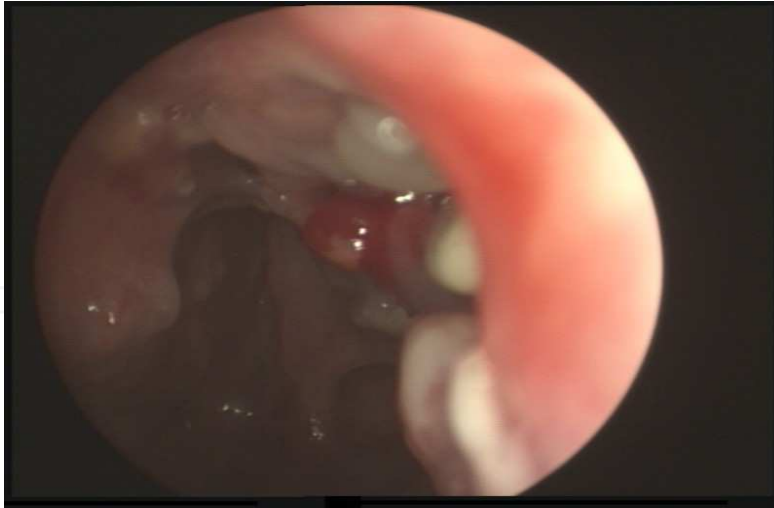Fig. 3. Mucosal edema

Fig. 4. Edematous vesicle

Fig. 5. Polyp formation

Fig. 6. Granulation tissue
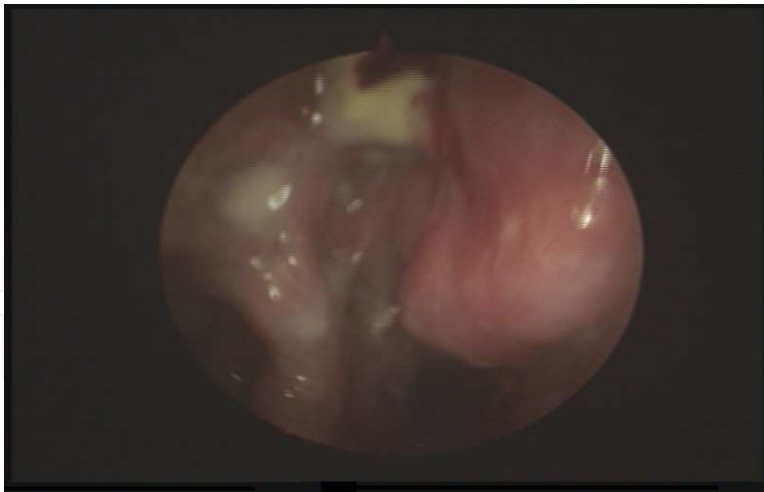

Fig. 7. Polyp like mucosal edema

Fig. 8. Cicatrical tissue

Fig. 9. Adhesion

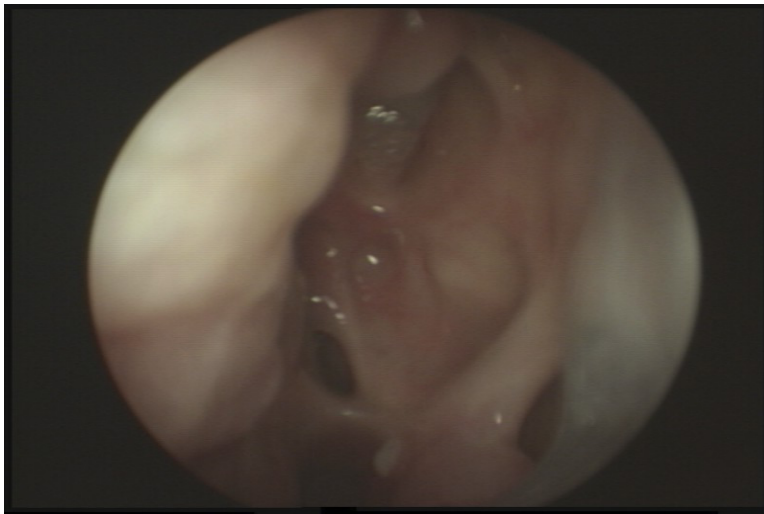Fig. 10. Empyema

Fig. 11. Narrow or blocked sinus cavity

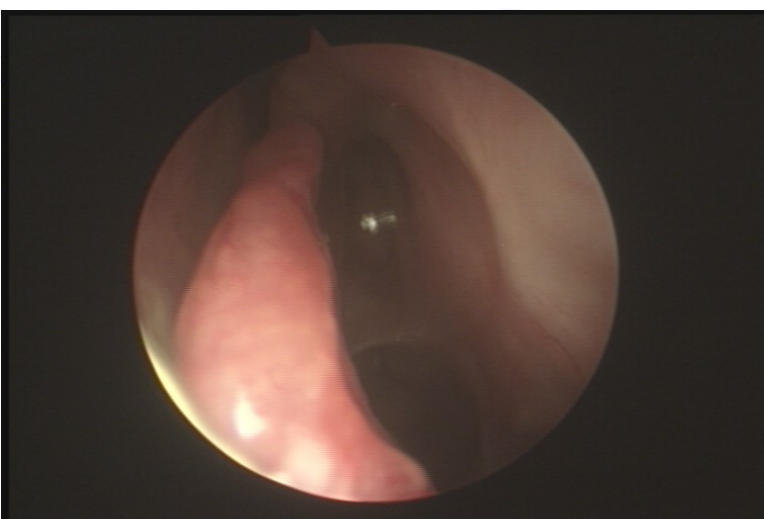Fig. 12. Constriction and blockage of sinus cavity

Fig. 13. Epithelization

Clinical observations of wound healing in human beings have shown predisposed areas of reduced healing, suggesting that local microanatomical factors may play a decisive role in the reparation process. The closure of a defined wound of the respiratory mucous membrane is independent of the direction of blood, lymph or mucociliary flow. The management of the operative cavity especially in the first and second stages was essential to the whole curative effect, making up an important part of ESS.

Functional postoperative results are directly dependent on the healing quality of the nasal or sinusal mucosa and it can end differently. If the healing is dominant it can end with completed epithelial metaplasia, but if there is dominance of regenerative phase, epithelial metaplasia will be incomplete with adhesion, partial or total obstruction of the ostium and sinus cavity. Despite advances in instrumentation and surgical technique, postoperative synechia formation continues to occur in between 1-27% of patients. When sinechia occur in the middle meatus, the maxillary, ethmoid and frontal sinuses may become obstructed resulting in recurrent problems. The reported complications following ESS can be classified broadly into immediate postoperative complications such as bleeding and crusting; short-term complications such as infection, synechiae formation, and turbinate lateralization; and long-term complications such as ostial stenosis, refractory disease, and disease recurrence.

Mucosal sparing techniques, middle turbinate resection or medialization and frequent postoperative debridement have been used to varying degrees and with varying success to prevent postoperative synechia.

4. Principles of management in different stages after operation

Different author suggests different time of postoperative observation and care after extensive paranasal surgery. It is from 1 to 12 month. The crucial care of postoperative sinonasal mucosa is topical care and it should be:

Nasal packing, whether absorbable or nonabsorbable, has little effect on postoperative bleeding but more importantly, plays a more important role in postoperative healing. Considering the average duration of postoperative bleeding and the infection risk because of the ″ foreign body″ there is no reason to leave a packing for more than 3 days. Blood surrounding the packing may (re)organize and the fibrin deposits around the packing could lead to scar tissue and adhesions. Packing moreover may obstruct evacuation of blood and secretions from the paranasal sinuses (Jorissen M. 2004.). Gelatin antibiotic and glucocorticosteroid can accelerate mucosa regeneration.

Rinse with enzymes contributes to the dissolution of fibrous pseudo membrane, clots and crusts, thus promoting the cleaning and healing of the sinus mucosa. Irrigation with saline solution is conductive to improve local nasal blood circulation and ciliary clearance. Using small volume (up to 1ml) only dampens the nasal mucosa, and the paranasal sinuses can not be reached. Only with large volume (300ml for a nose can) can the paranasal sinuses be reached, rinsed and washed. In addition to the pure mechanical rinsing, the saline will mix with secretions and decrease viscosity, propagating evacuation by mucociliary transport. High volume-low pressure rinsing of the nose and paranasal sinuses is the preferred technique for cleaning the surgical cavity and improving wound healing (Jorissen 2004). Welch recently published a study of the irrigation bottles used by patients after ESS and found that bacteria could be cultured from the irrigation bottles in 29% of studied patients including *Pseudomonas aerugionosa, Acinetobacter baumanni,* and *Klebsiella pneumoniae*

although fortunately no clinically significant postoperative infections were noted. Frequent changing and sterilization of nasal irrigation bottles is advocated (Welch2009). Nasal irrigation with sulfurous-arsenical-ferruginous solution locally reduce the eosinophil number and may limit eosinophil-mediated production of cytokines and inflammatory molecules, which damage nasal mucosa, leading to edema and sinonasl inflammation. As eosinophils play an important role in allergic response through the release of mediators as eosinophilic cationic protein, major basic protein, and leukotrien C4, which causes extracellular matrix deposition, epithelial denudation, and basement membrane disruption. Sulfurous-arsenical ferruginous solution nasal irrigation significantly reducing the local eosinophil count should be suggested for allergic patients (Staffieri A. 2008). Local steroid spray has potent regional anti-allergy anti-inflammatory and anti-edema effects, which can control the generation of vesicles and mini polyps. The incidence of morphological changes in the nasal mucosa of patients with perennial rhinitis following treatment for 1 year with MFNS (mometasone furoate nasal spray) 100-200µg b.i.d. has demonstrated that this agent did not lead to any significant adverse tissue changes including increase in epithelial thickness or tissue atrophy, although the numbers of inflammatory cells in the epithelium and lamina propria were significantly decreased, compared to baseline (Minshall E. 1998). Subjects with an initial diagnosis of nasal polyps (CRSwNP) were more likely to experience MFNS-mediated improvements in wound healing than subjects with an initial diagnosis of chronic rhinosinusitis without polyposis (CRSsNP). At a subcellular level, corticosteroids have an antiinflammatory effect by activating glucocorticoid receptors,which interact with inflammatory transcription factors resulting in suppression of proinflammatorymolecules. At a cellular level, corticosteroids reduce the quantity of inflammatory cells (eosinophils, T lymphocytes,mast cells, and dendritic cells), the degree of inflammatory suppression correlates with the tissue concentration of steroid (Jorissen M. 2009). Oral steroids used preoperatively in patients undergoing endoscopic sinus surgery for nasal polyposis have been shown to reduce vascularity and improve surgical nasal field conditions resulting in shorter operating time. Postoperative administration of intranasal corticosteroids has also been demonstrated to reduce nasal polyp recurrence after endoscopic sinus surgery. The effect of oral steroids was investigated in the UZ Leuven in prospective, randomized comparative study: 1 tablet of betamethasone 0,25mg during 20 days versus a reducing regimen (4co/d d1-d5, 3co/d d5-d10, 2co/d d11-d15 and finally 1 co/d d16-d20). For all groups of patients beneficial effects of a higher dose of steroids during the first 3 weeks after ESS were found and the systemic and local side effects of the higher dose oral regimen were minor (Jorissen 2004). Gelomyrtol forte capsules are conductive to loosen viscous mucus secretion, dissolve fibrous adhesion and increase mucociliary clearance. Inhibitor of proton pump once / at night or twice a day is recommended to reduce gastric fluid acidity. Gastroesophageal reflux may play a significant role in wound healing. This is illness that includes the most of population. In GERB the lower esophageal sphincter doesn't work well, but in LPR (laryngopharyngeal reflux) the problem is in upper esophageal sphincter. Laryngopharyngeal reflux is defined as the retrograde movement of gastric contents into the larynx, pharynx, and upper aerodigestive tract. Mucosa of the respiratory tract is more sensitive on acid and pepsin instead of esophageal mucosa. Acids can locally harm the mucosa and increase mucosal reaction that leads to prolonged inflammation with granulation. Night reflux phases are much longer than day phases and they can lead to mucosal damages. The nasal symptoms aggravate during nights and in the mornings which can be connected with LPR. So, LPR can aggravate healing of sinonasal mucosa (Kleemann 2005).

Crusting or cloting may trap mucus, resulting in reinfection of the sinuses, and the old blood itself may serve as a culture medium for bacteria. The crusts may act as bridges in which scar formation may occur, leading to an obstructed postoperative cavity and synechia formation in the middle meatus. Retained bone fragments that are denuded of mucosa may act as base for reinfection. Removing the crust, suctioning the retained secretion, and preventing lateral synechia formation and the obstruction of ostia and air cells are essential for healing and successful surgical outcome. Blood crusts cover the mucosal wound in the first 2 to 3 weeks and mucosal edema continues about 4 to 6 weeks after the operation. Although frequent postoperative debridement may remove the loose crusts and small devitalized bone fragments. Hard or fixed crusts cannot be cleaned because of bleeding from the underlying mucosal surface, discomfort and pain, and reformation of blood crusts. Loose, removable crusts were observed 2 weeks after the operation, indicating that mucosal re-epithelization requires at least 2 weeks. Mucosal edema was increased and sustained for 4 to 6 weeks. Mechanical wound care and the removal of blood crusts was avoided for at least 10 days. Gentle suction cleaning for several mounts. Violent tearing and too much cutting, which may cause injury to the epithelium, should be avoided. Sharp curette, electric cutter (debrider) and laser are recommended to lean the regenerated lesions. During the process of epithelization, the sinus was managed once at week, and any invalid surgery should be avoided unless the above-mentioned diseases occur because newly formed epithelium is loosely connected to bone, which is easy to tear away (Lee JY. 2008). The postoperative cleaning should continue until the operative site is mucosally covered. Presence of cultured bacteria from post-ESS patient cavities remains unclear. Several investigators have described the presence of biofilms in post-ESS cavities, and a retrospective pathologic study by Psaltis found that bacterial biofilms were found in 20 (50%) of the 40 CRS patients. Patients with biofilms also had significantly worse preoperative radiological scores and, postoperatively, had statistically worse postoperative symptoms and mucosal outcomes (Psaltis AJ. 2008). The use of an antibiotic (amoxicillin/clavulanate) in the postoperative period is able to improve the outcome in the early blood crust healing phase: nasal obstruction and drainage are reduced and the endoscopic score objectively showed a faster recovery (Albu S. 2010). Patients recover in 9 to 10 days after ESS when provided with appropriate pain management. Postoperative pain after ESS can be controlled effectively with acetaminophen 665mg modified-release tablets three times a day during the first five postoperative days (Kempainen TP. 2007). Postoperative treatment after endoscopic surgery of frontal sinus or frontal recess is a little bite different of others sinuses. No nasal packing needs to be used. The frontal sinus cannulae are left in place for up to 5 days if there has been inadvertent trauma to the frontal ostium mucosa, if the natural frontal sinus ostium is very narrow (<3mm), if there was evidence of osteitis with new bone formation in the frontal recess or ostium, and if there was extensive polyposis resulting in significant traumatized mucosa after the polyp removal. Frontal sinus saline douches are started through the frontal cannulae within 2 hours of completion of the operation. This will wash any blood clot out of the frontal ostium. The frontal cannulae are flushed with 5mL normal saline every 2 hours starting immediately after surgery. If prednisolone drops are to be used 0, 5 to 1mL is instilled with a syringe into the frontal sinus after every second douche. The aim of the prednisolone is to dampen the inflammatory response of the mucosa. Immediately prior to removal of the frontal sinus cannulae, 5mL of steroid and antibiotic cream (not ointment) is injected through each cannulae. This coats the newly created frontal sinus ostium and tends to decrease the amount of adherent crusts (Wormald PJ2008). Every operation, no matter how minor, is accompanied by swelling of the surrounding tissues. The

amount of swelling varies from person to person, but it always seems more dramatic when involving the face. We suggest that you keep your head elevated as much as possible. The swelling itself is normal and is not an indication that something is wrong with the healing phase of your operation. Swelling after sinus surgery is not usually seen on the face itself; rather, it manifests itself as a stuffy or blocked nasal passage. Any swelling of the face will be limited to the area around the eyes and will last for only a few days. Symptoms of pain and pressure will be relieved in the very early postoperative period while thick postnasal drainage will continue until the mucosa within the sinuses has returned to normal. This may take weeks to months depending on the severity of the disease and the rapidity of healing. The patients should be warned of this preoperatively.

Proposed therapy

1. The packing, tamponades, should be removed from first till fifth day (as soon as possible)
2. Irrigation with saline solution 3 times a day for 3 weeks, high volume (>100ml), low pressure rinsing
3. Irrigation with sulfurous-arsenical-ferruginous solution for 3 weeks (for patients who has allergy)
4. The frontal cannulae are flushed with 5mL normal saline every 2 hours starting immediately after surgery and Prednisolon drops 0, 5 to 1mL instilled with syringe into the frontal sinus after every second douche (for frontal Sinus surgery)
1. Rinse with enzymes can promote cleaning and healing of sinus mucosa
2. Bloody sediment and the crusts in the nasal cavity should drained with sucker after 10th day
3. Endoscopic treatment once a week in weeks 2-6
4. Topical drugs: glucocorticosteroids nasal spray apply once or twice- daily for 6 months (for patients who has allergy)
5. Topical drugs: glucocorticosteroids can stop once healing has occur (for patients who has no other problems than chronic infection)
6. Oral glucocorticosteroids: Prednison 1mg/kg 5 days before surgery and higher dose of steroids during the first 3 weeks (for patients with nasal polyposis)
7. Mucus eliminator such as Gelomyrtol forte capsules are recommended for 10 weeks
8. Proton pump inhibitors once / at night or twice a day is recommended to reduce gastric fluid acidity for 3 months (for patients who has LPR)
9. Pain killer, Acetaminophen 665mg modified-release tablets three times a day for first 5 days
10. Antibiotics (Amoxicillin/Clavulanate) for 2 weeks

Some tips to shorten the duration of the swelling and improve the ability to breathe through your nose include:

1. Stay vertical. Sit, stand and walk around as much as is comfortable beginning on your second postoperative day. Of course, you should rest when you become tired but keep your upper body as upright as possible.
2. Gentle blowing of the nose is allowed without closing the nasal vestibule.
3. Avoid bending over or lifting heavy things for one week. In addition to aggravating swelling, bending and lifting may elevate blood pressure and start bleeding.
4. Sleep with the head of the bed elevated 45 degrees for 7 – 10 days following your surgery. To accomplish this, place two or three pillows under the head of the mattress and one or two on top of the mattress. It is helpful if you sleep on your back for 30 nights.

5. Avoid straining during elimination. If you need a laxative. Proper diet, plenty of water and walking are strongly recommended to avoid constipation.
6. Avoid sunning of your face for one month. Always use a sunscreen with SPF15 or above.
7. Avoid exercise for one week following surgery.

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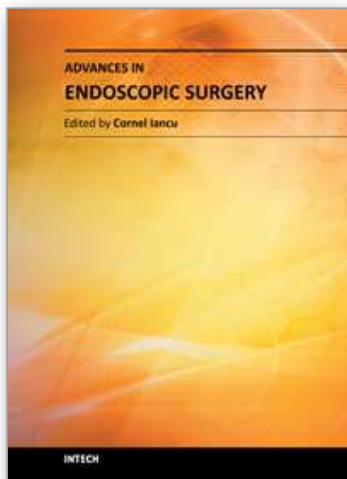
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Edited by Prof. Cornel Iancu

Surgeons from various domains have become fascinated by endoscopy with its very low complications rates, high diagnostic yields and the possibility to perform a large variety of therapeutic procedures. Therefore during the last 30 years, the number and diversity of surgical endoscopic procedures has advanced with many new methods for both diagnoses and treatment, and these achievements are presented in this book. Contributing to the development of endoscopic surgery from all over the world, this is a modern, educational, and engrossing publication precisely presenting the most recent development in the field. New technologies are described in detail and all aspects of both standard and advanced endoscopic maneuvers applied in gastroenterology, urogynecology, otorhinolaryngology, pediatrics and neurology are presented. The intended audience for this book includes surgeons from various specialities, radiologists, internists, and subspecialists.

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