

Examination of resorbable nasal dressings and their effects on the healing processes of the nasal cavity, after endoscopic sinus surgeries

Thesis

Zalán Piski MD

University of Pécs – Clinical Centre, Otorhinolaryngology – Head and Neck Surgery

Topic leaders: Prof. Dr. Gerlinger Imre PhD, Dsc, Dr. Lujber László PhD

Clinical Medical Sciences, Doctoral School (D94)

Leader: Prof. Lajos Bogár MD

Program: A-327/1995 The investigation of pathological conditions of the circulation in in vivo surgical models and in patients

Leader: Gábor Jancsó MD

Pécs

2020

1. Introduction

Since the introduction of endoscopic technics in sinus surgery 30 years ago, there are still several aspects which have remained debated and unclear, especially the issue of the postoperative nasal packing. Although, this surgical step seems to be a marginal problem, but as a part of postoperative care, it is a crucial factor which effects the entire healing process, the final result and the long-term outcome of the procedure as well. Although, nowadays a large variety of packing materials are available, including dozens of absorbable devices, the majority of ENT departments favours the old- fashioned non-absorbable nasal packings, resulting in the lack of significant experience with the new materials. In endoscopic sinus surgery (ESS) due to technical and anatomical reasons, the conventional wound closure cannot be carried out. Although percutaneous approach is not performed, the integrity of the nasal mucosa is effected by the surgery, leading to a bleeding surgical field, which is exposed to the infections via the nostrils. Inadequately treated bleedings might be significant complications even in the first postoperative days, which may lead to reoperation in certain cases. The aim of the surgeries is to restore the nasal airflow, which should be preserved in the course of the postoperative healing period. This aspect carries more difficulties than it seems to. A non resorbable, nasal package stuck in the operated middle meatus, must be removed in a while, which is a painful manoeuvre resulting the removal of healing mucosa as well, leaving fresh injured surfaces in the nasal cavity. In this narrow area, the mucosa has excellent perfusion and venous plexus, furthermore excessive postoperative crusting and discharge are also the main causes of the adhesion formation. Due to adhesions one of the most important achievement, the restored nasal airflow can be impaired.

There are artificial and natural products on the market in gel, foam or solid forms, but until now, the lack of strong evidence has necessitated randomized, double-blind placebo control studies on this issue. Nevertheless, some authors suppose that the nasal packing itself, is a completely unnecessary step. If the decision is made to pack the nose, an absorbable material seems to be the better solution, since the physical tamponade removal is not necessary when using these materials. This way, plenty of discomfort, and pain, which could remain one of the worst memories of the treatment, together with bleeding, mucosal injuries and longer hospitalization due to the removal of the nasal package, can also be spared for the patients and the staff as well. Beyond the abovementioned advantages, absorbable nasal packings may have further favourable prosperities, which should be scientifically assessed, in order to prove if these materials are superior to the conventional nasal dressings. If so, it is also important to

determine an optimal material among numerous absorbable dressings. Further factors which may be influenced by the type of the dressing are the postoperative crusting, mucosal edema, adhesion formation, discharge, the patency of the ostiomeatal complex and the frequency and severity of bleeding. With the examination of these phenomena, the condition of the mucosal healing process and ciliary epithelium can be observed, which is probably significantly affected by nasal packing. The scientific assessment can be performed with clinical studies or animal models in case of methods requiring invasive approach.

The characteristics of an optimal nasal package:

- Fast intraoperative haemostasis
- Long lasting postoperative haemostasis
- Prevention of adhesion formation
- Prevention of crusting, and discharge
- Reepithelization
- Microbiologic safety
- Hypoallergenicity
- Keeping the patency of the ostiomeatal complex
- Barrier function against infective agents
- Drainage of the surgical field
- Comfort

Dressing type*	Resorbability	Consistency	Origin	Advantages	Disadvantages
cotton gauze	no	Solid	artificial	cheap	removal necessary
latex covered tampons	no	Solid	artificial	cheap	removal necessary
polivynil-alcohol (Merocel®)	no	Solid	artificial	cheap	removal necessary
silicone tube	no	Solid	artificial	nasal breeding possible	fixation, removal necessary
Hyaluronic acid (Merogel®)	yes	Gel	animal derived	prevent adhesions	expensive
Bovine gelatine +human thrombin (FloSeal®)	yes	Foam	animal derived +human	haemostatic effect	crusting
fibrin glue (Tisseel®)	yes	Gel	human	haemostatic effect	expensive
porcine gelatine (Surgiflo®)	yes	Foam	animal derived	haemostatic effect	expensive
denaturised porcine gelatine (Gelfilm®)	yes	Solid	animal derived	-	crusting, adhesions
oxidised-regenerated cellulose (Surgicel®)	yes	Solid	plant derived	haemostatic effect	-
CMC (Sinu-Knit®)	yes	Foam	plant derived	-	-
Microporous polysaccharide hemispheres (MPH®)	yes	Solid	plant derived	haemostatic effect	-
polyurethane (Nasopore®)	yes	Solid	artificial	prevent adhesions, discharge, haemostatic effect	-
Chitosan (Posisep®)	yes	Solid	animal derived	prevent adhesions, haemostatic effect, mucosal regeneration	-

Table 1. Different types of nasal packings (*Material of the packing, product name in parenthesis)

2. Aims

A large variety of packing materials is now available, including dozens of absorbable materials. The broad spectrum of these nasal dressings consist of hugely different products regarding features, the origin of the material, shape and even financial issues. Nowadays prospective, randomized, double-blinded and controlled studies are necessary to compare surgical techniques and materials.

1. The aim of our first study was to assess the characteristics of a porcine gelatine matrix used as a middle meatal dressing in clinical patients after FESS. We designed our examination to observe if the porcine gelatine matrix shows any advantage compared to a polivynil-alcohol nasal package, regarding the healing process of the nasal mucosa.

2. Our second study was an examination of a new packing material, which seemed superior to the porcine gelatine matrix in regard of physical and financial prosperities. We assessed the effects of a polyurethane dressing to the mucosal healing process, compared to a non tamponated nasal cavity with clinical patients after FESS.

3. In our third study we examined a new Chitosan based nasal dressing. Data available in the literature that this material may provide better mucosal reepithelization than other solutions. Our question was if there are any advantages with the application of the Chitosan based package in comparison with a non tamponated nasal cavity after standard mucosal damage in rabbit model, examining the mucosal healing with endoscopic and scanning electron microscopic methods.

3. Clinical and experimental studies

3.1 Human study with porcine gelatine matrix and polyvinyl alcohol

3.1.1. Materials and methods

A prospective, randomized, double-blind, placebo-controlled study was performed with the enrolment of 18 patients (13 males, 5 females). The mean age was 47.5 years (range: 17-84).

Our inclusion criteria were as follows:

1. Chronic rhinosinusitis with nasal polyps (CRSwNP) with failed conservative therapy
2. Age higher than 18

Our exclusion criteria were as follows:

1. previous FESS
2. haemostatic disorders
3. diabetes mellitus (type I or II)
4. immunosuppression
5. systemic disorder with nasal mucosa manifestation
6. septal deviation

A bilateral functional endoscopic sinus surgery (FESS) was carried out. The extension of the surgeries depended on the severity of the illness, but a middle meatal antrostomy and anterior-posterior ethmoidectomy were performed in every case. By the end of the intervention on one side the middle meatus was tamponated with Merocel and the other was treated with Surgiflo foam, which was prepared from the components right before the insertion. The side was chosen in advance prior to the surgery by an OR staff member, who was not a member of the operating team. The patients were not informed about the type of nasal package used in their nasal cavities.

All patients underwent three follow-up visits postoperatively at the 1st, the 4th and the 12th weeks. On each visit an endoscopic examination was carried out and the patients were asked to filled in a visual analogue scale (VAS) with which the CRS symptoms such as nasal obstruction, nasal discharge, facial pain, smelling disorders and their overall condition could be assessed. The condition of the ostiomeatal complex was also recorded, using our institutional

classification (Lujber et al.) to measure the patency of that area. The grading system classifies the ostiomeatal complex as follows:

0 point: wide OMC (≥ 4 mm, the standard rigid endoscope can pass)

1 point: open OMC with narrowing (2 mm - 4 mm, no adhesions)

2 point: narrow OMC (≤ 2 mm, presence of adhesions)

3 point: completely closed OMC

The results of the VAS questionnaires and the objective examinations were evaluated statistically by two sample t-test, using SPSS software. The level of statistical significance was determined as $p=0.05$.

Assessment of endoscopic examination					
mucosal edema	none	mild	severe	atrophy	/
crusting	none	spots	moderate	obstruction	/
scarring	none	mild	moderate	obstruction	/
OMC	wide (≥ 4 mm)	open (2-4mm)	narrow (≤ 2 mm)	closed	/
reepithelization	>90%	50-90%	0-50%	/	/
discharge	normal	serous	seromucous	purulent	/
bleeding	none	blood-stained	on-off bleeding	treatment needed	surgery needed
scores:	0	1	2	3	4

Table 2. Assessment of endoscopic examination

3.1.2. Results

Seven days after surgery, lower amount of crusting, bleeding and adhesion formation, less severe nasal blockage and discharge were observed at the nasal cavity treated with Surgiflo. Although there were higher grade of edema and smelling disorder, with lower patency of OMC at the same visit. At the second and third control the symptom scores were dropped on the side of the Surgiflo. At the last visit (12th week) there were no remarkable differences regarding the vast majority of symptoms, hence the mucosa had already been healed.

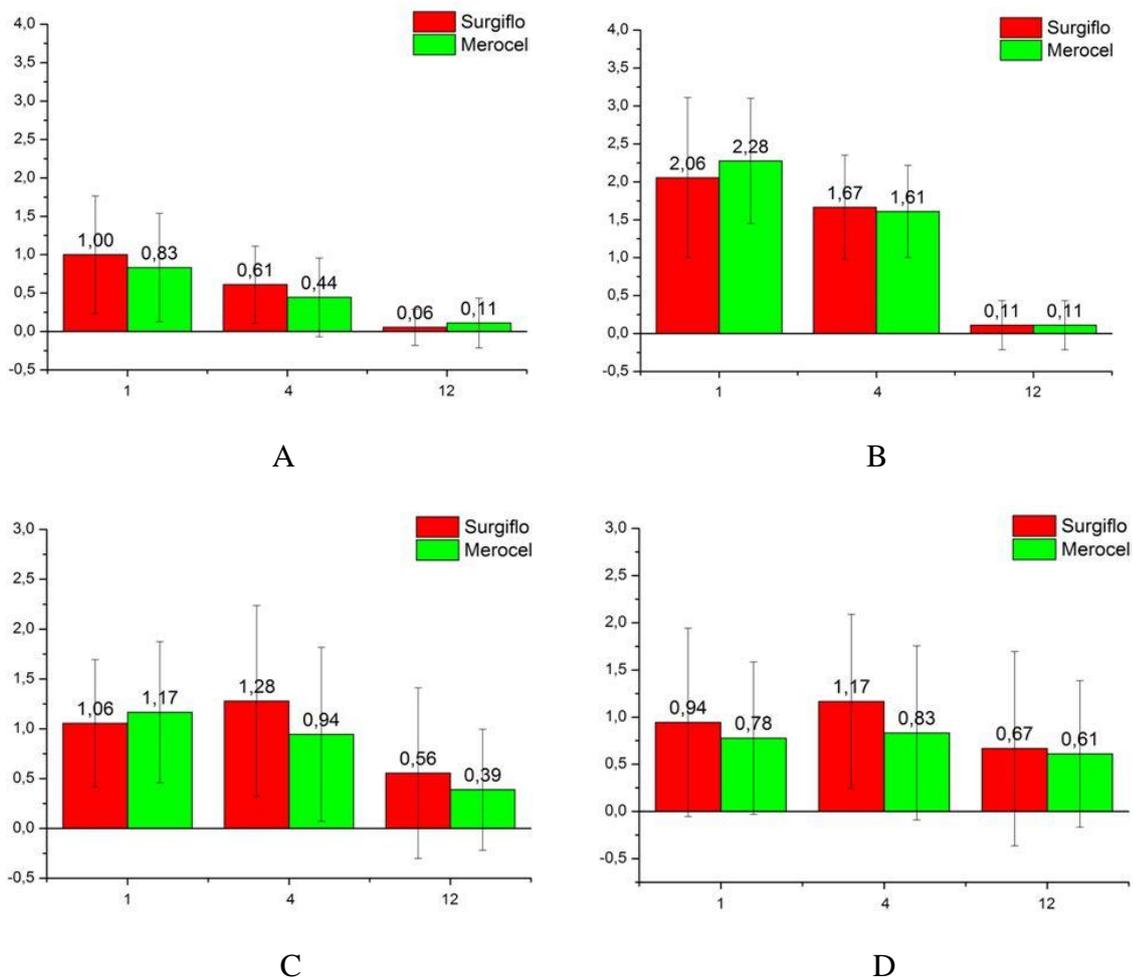
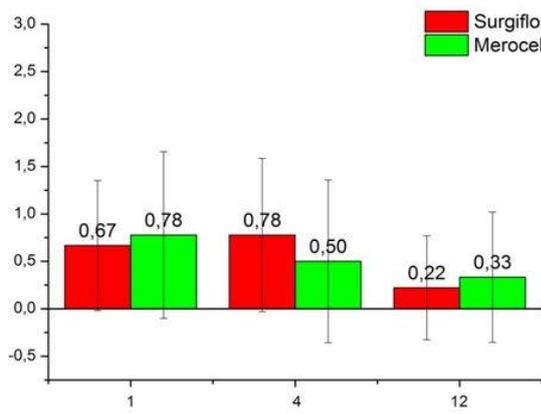
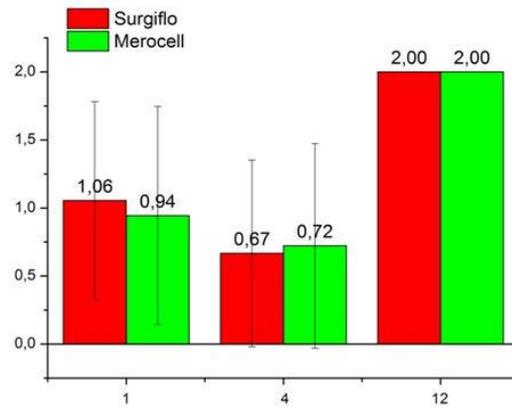


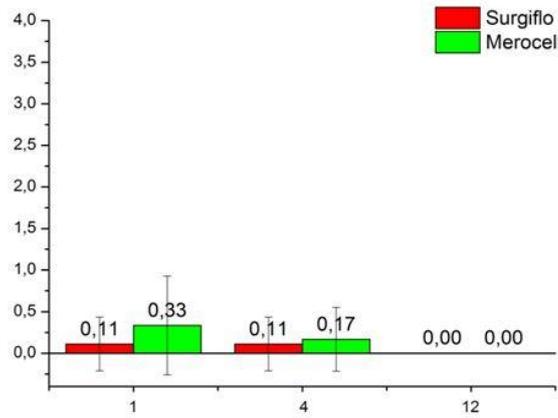
Figure 1. Mean scores of mucosal edema (A), crusting (B), scarring (C) and the patency of OMC (D)



A

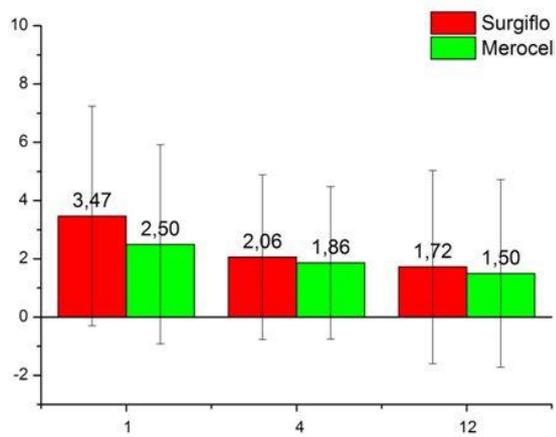


B

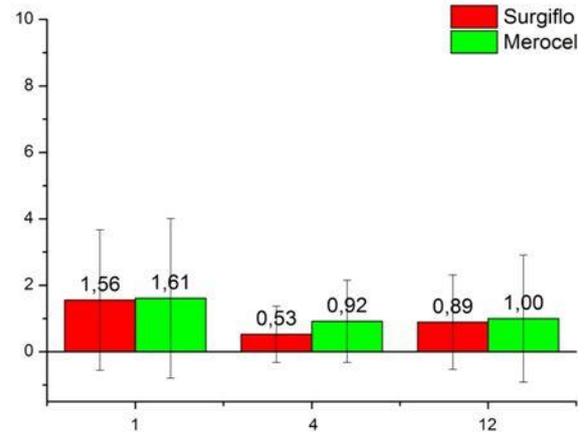


C

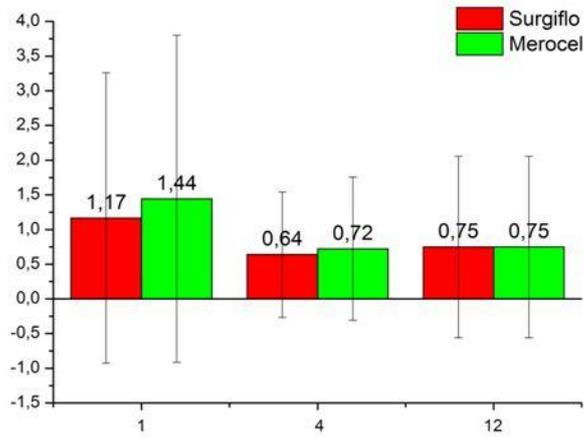
Figure 2. Mean scores of reepithelization (A), nasal discharge (B) and postoperative bleeding(C)



A



B



C

Figure 3. Mean scores of smelling disorder by VAS (A), nasal blockage by VAS (B), and nasal discharge by VAS (C)

3.2 Human study with polyurethane nasal packing

Our second study was carried out with a solid resorbable nasal dressing. The new polyurethane sponge, an artificial material, seemed to be a promising method for nasal packing.

- Its solid frame is supposed to maintain the OMC better than other resorbable packings.
- An artificial material probably not induces significant crusting and tissue reaction.
- It is notably cheaper than the porcine gelatine matrix.

3.2.1. Materials and methods

A prospective, randomized, double-blind, placebo-controlled study was performed with the enrolment of 53 patients (16 males, 17 females). The mean age was 53.87 years (range: 33-75). Our inclusion criteria were as follows:

3. Chronic rhinosinusitis with nasal polyps (CRSwNP) with failed conservative therapy
4. Age higher than 18

Our exclusion criteria were as follows:

1. previous FESS
2. haemostatic disorders
3. diabetes mellitus (type I or II)
4. immunosuppression
5. systemic disorder with nasal mucosa manifestation
6. septal deviation

Bilateral FESS (10) was carried out under general anaesthesia for all patients. The extent of surgery depended on the severity of the disease, but middle meatal antrostomy and anterior/posterior ethmoidectomy were performed in both nasal cavities in every case. After these procedures the selected nasal cavity was packed with Nasopore Standard 4 cm sponge under the middle meatus, while the contralateral nasal cavity was left unpacked. The side to be packed was selected prior to surgery by an OR staff member who was not affiliated with the surgical team or study team in any way. Patients were not informed which nasal cavity had been packed.

Every patient received three follow-up appointments at the first, fourth and 12th postoperative weeks. At each visit they underwent a detailed endoscopic nasal examination. Bleeding, synechia formation, nasal discharge, mucosal edema, and crusting were observed and analysed

according to the grading system of Berlucchi et al. The edema, crusting, and nasal discharge were given scores from 0 to 3 according to the severity of the findings; bleeding tendency was given scores from 0 to 4. The patency of the ostiomeatal complex was also recorded using our institutional classification (Lujber et al).

0 point: OMC wide (≥ 4 mm)

1 point: OMC patent (2 mm - 4 mm, no adhesions)

2 points: OMC narrow (≤ 2 mm, adhesions)

3 points: OMC completely closed

Higher scores represent worse findings and symptoms.

Mucosal edema	none	mild	severe	atrophic	/
Crusting	none	spots	moderate	obstructing	/
Synechia	none	mild	moderate	obstructing	/
OMC	wide (≥ 4 mm)	open (2-4mm)	narrow (≤ 2 mm)	closed	/
Nasal discharge	normal	serous	seromucous	purulent	/
Bleeding	none	bloodstained discharge	on-off bleeding	need for treatment	need for surgery
Scores:	0	1	2	3	4

Table 3. Assessment of endoscopic examination

Statistics: Data analysis was performed with the SPSS Statistics software package (Version 20.0, IBM, 35 Armonk, NY, USA). To analyse differences between the two sides in the extent of bleeding, synechia formation, nasal discharge, mucosal edema, crusting and the patency of the ostiomeatal complex, we used the Chi-square, Fisher, Wilcoxon, Kendall's W and Cochran tests. Wilcoxon and Friedman tests were carried out in order to analyse the patient's subjective symptoms (nasal blockage, nasal discharge, and loss of sense of smell) because in these cases the visual analogue scores were not normally distributed. Differences were considered significant at $p < 0.05$.

3.2.2. Results

Six important parameters were recorded for the condition of the healing mucosa at follow-up endoscopy examinations. At the end of the first postoperative week there were no marked differences between the Nasopore-packed and non-packed nasal cavities regarding bleeding tendency, synechia formation, mucosal edema or crusting. The patency of the OMC showed better results for the Nasopore-packed cavity at the first follow-up, and nasal discharge was less intense on the unpacked side, but the differences were not statistically significant. At the second follow-up examination (four weeks after surgery) nasal endoscopy revealed significant improvement ($p=0.002$) in the patency of the OMC on the Nasopore-packed side: total points 17 (mean 0.6 standard deviation (SD):0.6), unpacked side: total points 43 (mean 1.6 SD: 1.2). No bleeding was observed on either side, apart from a single case, in which a blood-stained discharge was noted from the non-packed nasal cavity. Synechia formation and nasal discharge were greater on the unpacked sides, but the difference was not statistically significant. Although crust formation occurred in a higher number of patients on the side previously packed with Nasopore, the degree of crust build-up was greater on the unpacked side. Scores for mucosal edema were almost equal in both nasal fossae at this stage of postoperative follow-up.

At the time of the third follow-up visit at 12 weeks, the scores for OMC were significantly better (lower) on the side initially packed with Nasopore than on the unpacked side ($p=0.001$). (Total points on packed side: 13, on unpacked side: 48, mean value on packed side: 0.5 on unpacked side: 1.8).

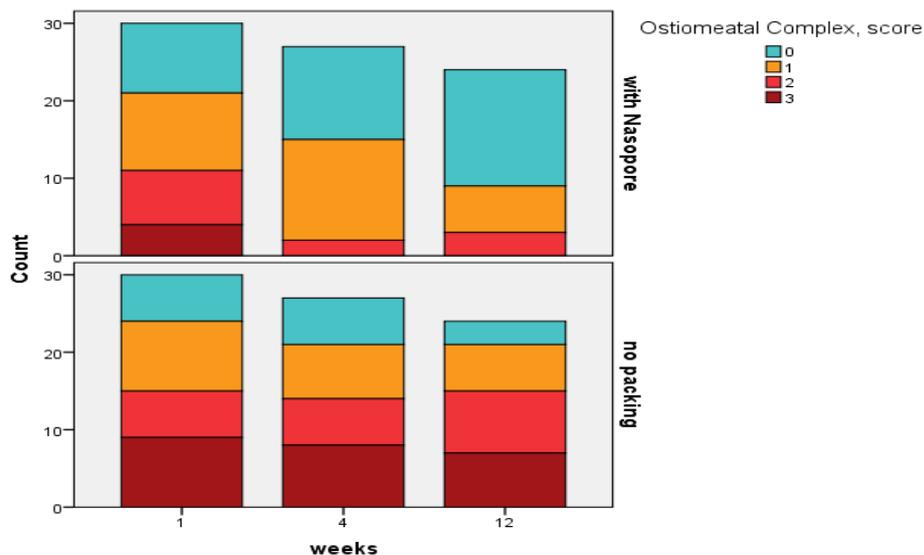


Figure 4. The patency of the OMC

The same tendency was observed also regarding synechia formation ($p=0.018$) (Total points on packed side: 8, on unpacked side: 19, mean value on packed side: 0.3 SD:0.6 on unpacked side: 0.8 SD: 1.0)

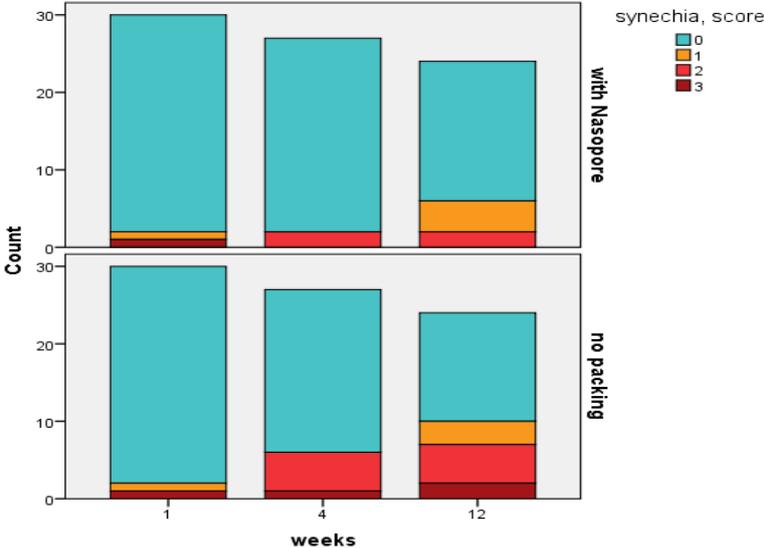


Figure 5. The level of adhesion formation

The results of nasal discharge were also significantly better on the packed side ($p=0.041$). (Total points on packed side: 2, on unpacked side: 13, mean value on packed side: 0.08 SD:0.3 on unpacked side: 0.5 SD: 1.0).

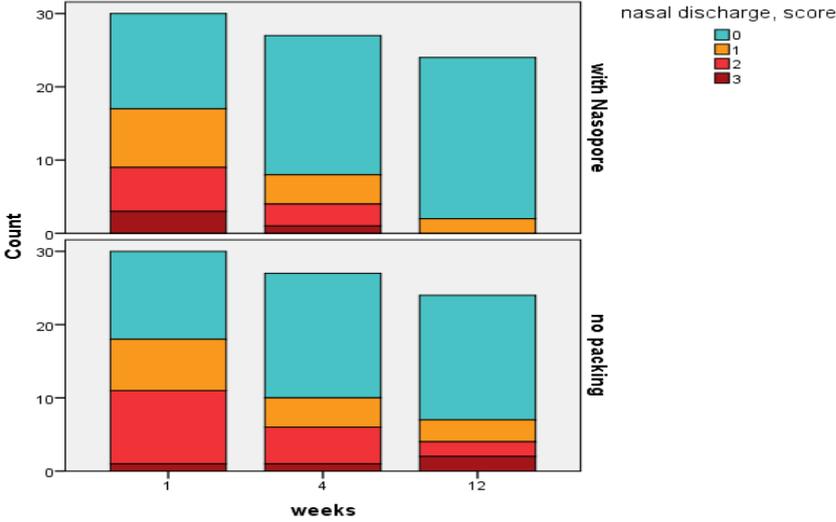


Figure 6. The quality of nasal discharge

Although bleeding did not occur on either side, all other clinical signs showed better results on the side that was originally packed with absorbable nasal dressing. However, these differences were not statistically significant.

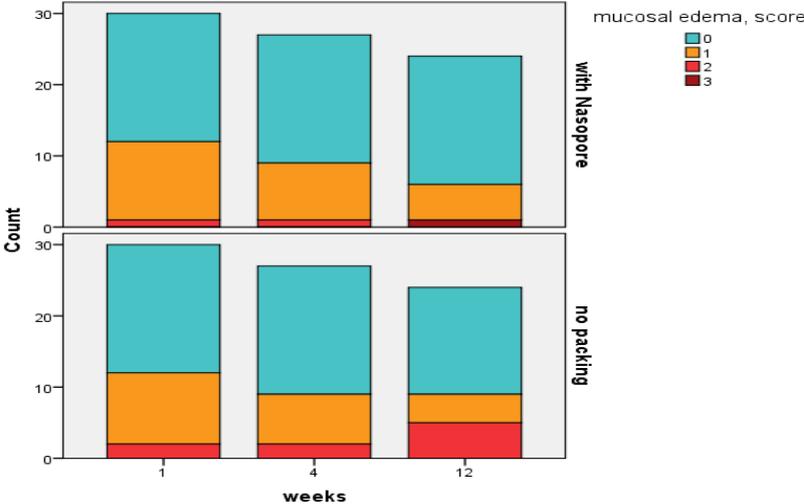


Figure 7. The level of mucosal edema

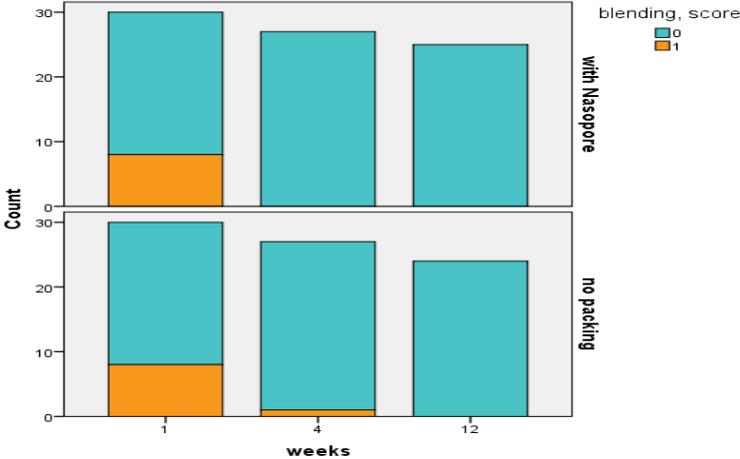


Figure 8. The level of postoperative bleeding

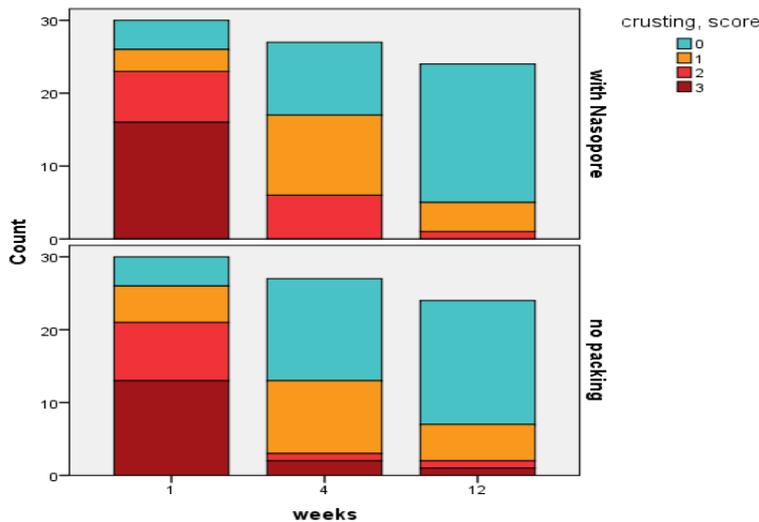


Figure 9. The level of crusting

3.3. Evaluation of Chitosan based nasal dressing in animal model

3.3.1. Materials and methods:

Ten New Zealand rabbit were applied to carry out endoscope assisted procedure after Seduxen seduction and Kalypsol induced general anaesthesia. Middle turbinates were sharply resected as a standard mucosal damage in both nostril. Chitosan nasal packing (Posisep, Hemostasis, Saint Paul, USA) was inserted in a randomly selected nasal fossa of each animal, while the other side was left unpacked. None of the animals got antibiotic or other treatment postoperatively. Symptoms were evaluated during nasal endoscopy on the 12 th postoperative week. The degree of mucosal oedema, crusting, adhesions and the nasal discharge were observed according to the modification of the grading system of Berluchi et al. The higher scores indicated the worse complaints.

From the area of the healed surgical field samples were taken out from both sides for further examinations with scanning electron microscope.

For the assessment of the findings provided by electron microscopy, the following method was used: Focusing on the cilia, which are the most sensitive part of the mucosal surface, the proportion of intact ciliated epithel cells was calculated. An area of 35 square microns was examined under 3000x magnification. This way, at least 50 cells can be observed in every examined area. Scanning these areas for missing or non-ciliated cells, the ratio can be estimated. Three area of 35 square microns were examined in each sample.

Statistical assessment was carried out with the application of Wilcoxon, Fisher and McNemara tests. The level of significance was $p < 0.05$.

3.3.2. Results

The degree of mucosal edema, crusting, adhesions and nasal discharge were observed through nasal endoscopy.

Crusting showed 9 symptom score in the non tamponated cavity (mean: 0.90, SD: 0.74), while in the tamponated side the total score was 10, (mean: 1.00, SD: 0.82)

In respect of adhesions, the non tamponated cavity showed only 1 point (mean: 0.1-es SD: 0.32). The site of Chitosan was free from adhesions in every case. Calculated differences did not reach the level of statistical significance in case of adhesions and crusting ($p=0.806$).

Assessing the findings of the electron microscopy the ratio of cells with damaged surface was given in percentage, regarding the tamponated and the non tamponated nasal cavities. In case of Chitosan package 22.06% (SD: 0.25), while in case of no packing 36.11% (SD: 0.48) of the cells showed damaged surface.

	Chitosan	no package
I	14.86%	7.04%
II	0%	100%
III	uninterpretable	27.69%
IV	58.33%	100%
V	80%	100%
VI	12.67%	0%
VII	0%	4.00%
VIII	8.00%	11.33%
IX	15.33%	10%
X	9.33%	10.67%
mean:	22.06%	36.11%

Table 4. Ratio of cells with damaged surface on scanning electron microscopy

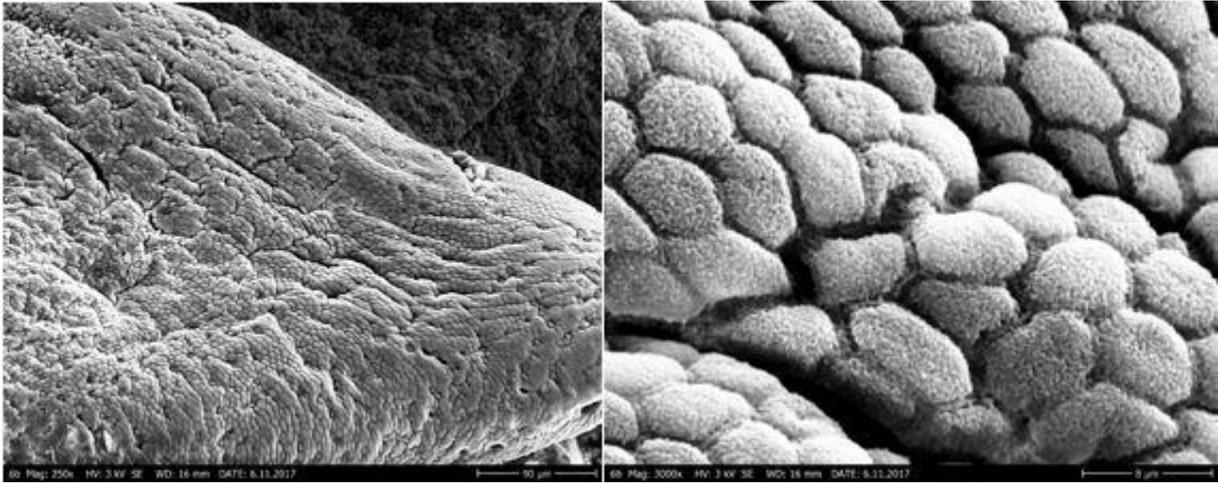


Figure 10. Intact mucosal surface (250x and 3000x magnification, scanning electron microscopy)

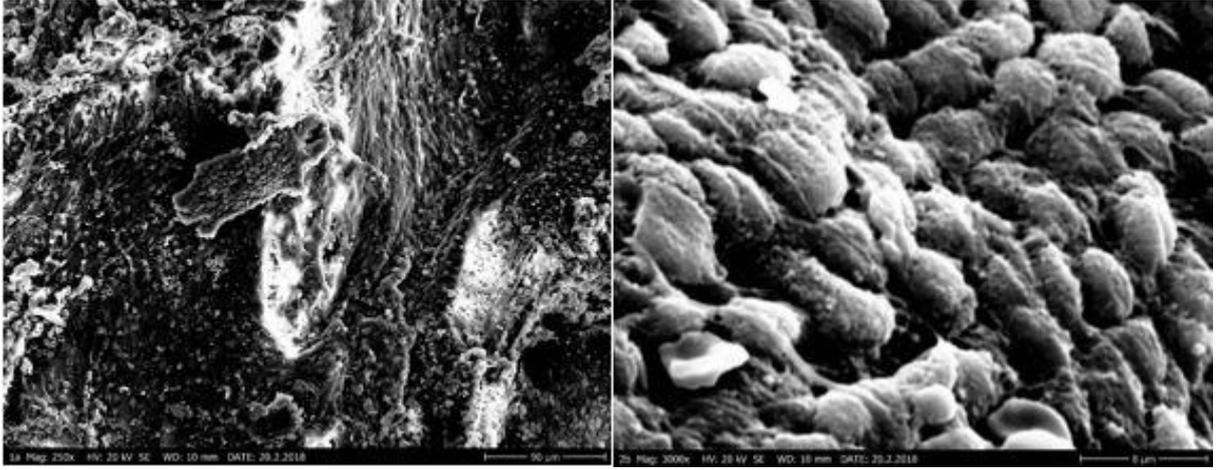


Figure 11. Damaged mucosal surface (250x and 3000x magnification, scanning electron microscopy)

4. Discussion

In our first trial the prosperities of porcine gelatine matrix were assessed in human clinical trial. In a prospective, randomized, double-blind, placebo-controlled study a bilateral functional endoscopic sinus surgery (FESS) was carried out, when on one side the middle meatus was tamponated with PVA packing and the other nasal fossa was treated with Surgiflo foam. All patients underwent three follow-up visits postoperatively at the 1st, the 4th and the 12th weeks. Bleeding, reepithelization, synechia formation, nasal discharge, mucosal edema, the patency of the OMC and crusting were observed and analysed. According to our findings, there was only slight difference between the two types of packages, which did not reach statistical significance. Although the difference is not significant, but in some respect as the OMC and smelling disorders, the PVA showed even better results at every visit.

On each visit the patients were asked to filled in a visual analogue scale (VAS) with which we assessed the CRS symptoms such as nasal obstruction, nasal discharge, facial pain, smelling disorders and their overall condition subjectively. Results did not show significant difference between the two sides.

Regarding our results, the porcine gelatine matrix is equivalent to the PVA package as a nasal dressing after endoscopic sinus surgeries. Data of the 3-month visit showed healed conditions in the operating field, with no remarkable difference between the packing techniques. Advantages of Surgiflo, like easy handling and resorbability, are originated from its consistency, whit which the pain and complications of package removal can be avoided. The cost of this material is undoubtedly high, hence it is inferior to the conventional packings in cost effectiveness.

Because of the disadvantages of Surgiflo, like the high costs and the consistency which is not firm enough to keep OMC open, our team had chosen another resorbable packing solution with the same advantages. The choice was a sponge like, Polyurethane, relatively low cost resorbable nasal dressing, the Nasopore. The characteristics of this synthetic polyurethane sponge were examined in a prospective, double blind, randomized, controlled trial. We compared the nasal fossa packed with Nasopore with the contralateral unpacked nasal fossa of the same patient after functional endoscopic sinus surgery. Our results showed that the nasal cavity in which we used Nasopore sponge had significantly less synechia formation, more favourable nasal discharge and a wider ostiomeatal complex than the unpacked nasal cavity. None of the examined parameters showed significantly better results on the unpacked side at any of the

control visits. As Polyurethane is a synthetic material it might be biologically inert, hence it seems to not induce excessive crusting and fibrosis. Thanks to the solid yet soft consistency of the sponge form and the ideal size, it is an excellent frame of the newly formed areas and the OMC. Comparing the Polyurethane package to the unpacked nasal cavity, results suggest that the Polyurethane package has better influence on the sinonasal regenerating process than leaving the nose unpacked.

Publications on this topic generally refer the report of *Eliashar et al* and *Orlandi et al*. However, these authors would have proven, that skipping the nasal packing after surgeries is a safe solution, but the latter studies focused exclusively intra-, and postoperative bleedings. Reepithelization, synechia formation, nasal discharge, mucosal edema, the patency of the OMC or crusting were not examined in any of the papers, while these parameters were observed by our team in details.

The packing method probably has an impact on the condition of cilia on the mucosal surface. For the detailed, invasive examination of the postoperative healing process of the mucosal surface, beyond human examinations, additional animal studies are required. In animal model mucosal sampling is also possible to perform electron microscopic examinations. In human trial it would be debated to disturb mucosal integrity at a regenerated state of the surgical field, hence a new chitosan based packing solution which promises better mucosal reepithelization was chosen to perform animal trial. Only a few scientific reports were available on the characteristics of this material.

New Zealand rabbits were applied to carry out endoscope assisted procedure using Chitosan based nasal dressing. The degree of mucosal oedema, crusting, adhesions and the nasal discharge were observed.

From the area of the healed surgical field samples were taken out from both sides for further examinations with scanning electron microscope. Three area of 35 square microns was examined in every sample. According to the results of both method, the conditions were better in the chitosan packed sides, however the difference was not significant. This way it is not proved that the Chitosan provides significantly better cilia regeneration, but it certainly not worsens it. We found more complete cilia regeneration then the available data shows in the literature. It is the consequence of the different animal model and the longer follow up period. Summarizing the data of the literature and our results Chitosan seems to be the only material which helps the reepithelization. It has relatively low costs and excellently maintains the OMC,

avoid bleeding and adhesion formation. In the future it is necessary to carry out controlled, randomized, double-blinded human studies and meta analyses to find the optimal solution for nasal packing.

5. Thesis

- The Surgiflo®, porcine gelatine matrix haemostatic dressing is superior to the PVA package (Merocel®) regarding nasal discharge and postoperative bleeding according to the endoscopic assessment. The difference is not significant.
- The porcine gelatine matrix shows worse results compared to the PVA package regarding the patency of the OMC and the adhesion formation according to the endoscopic assessment. The difference is not significant.
- The porcine gelatine matrix shows worse results on VAS compared to the PVA package regarding the loss of smell. The difference is not significant.
- The porcine gelatine matrix is superior to the PVA package regarding the nasal obstruction, according to VAS. The difference is not significant.

Our study was the first report of a comparison between porcine gelatine matrix as a nasal dressing and PVA package in human study.

- The Nasopore®, polyurethane sponge provides significantly better conditions in the nasal cavity after endoscopic sinus surgery compared with no packing, regarding the patency of the OMC.
- The polyurethane sponge shows significantly better result after endoscopic sinus surgery compared with no packing, regarding the nasal discharge.
- The polyurethane sponge is significantly superior to no packing, regarding the assessment of adhesion formation after endoscopic sinus surgery.

Our study was the first report of a comparison between polyurethane nasal dressing and an unpacked nasal cavity in clinical, human study.

- Chitosan based (Posisep®) nasal package provides lower crusting formation compared to no packing according to endoscopic assessment in animal model. The difference is not significant.
- The Chitosan based package provides better condition in the nasal cavity regarding the adhesion formation, than the unpacked side. The difference is not significant.
- Scanning electron microscopic examination shows higher ratio of intact surface on respiratory epithel cells compared with the unpacked nasal cavity after sinus surgery in animal model. The difference is not significant.

Our study was the first report which represented the characteristics of a chitosan based nasal dressing in rabbit model using endoscopic and electron microscopic assessment.

6. Publications, presentations, posters

6.1. Thesis related articles

1. Piski, Z., Gerlinger, I., Nepp, N., Revesz, P., Burian, A., Farkas, K., Lujber, L. Clinical benefits of polyurethane nasal packing in endoscopic sinus surgery. *Eur Arch Otorhinolaryngol*, 2017;274:1449-1454.
2. Piski, Z., Gerlinger, I., Toth, E., Haromi, I., Nepp, N., Lujber, L. Kitozán hatóanyagú orrtampon tulajdonságainak vizsgálata állatkísérletes modellen. [Evaluation of chitosan-based nasal dressing in animal model]. *Orv Hetil*, 2018;159:1981-1987.
3. Piski Z, G. I., Móricz P, Somogyvári K, Lujber L. Felszívódó orrtampon (Surgiflo™) alkalmazása funkcionális endoszkópos melléküreg-műtétek során. *Fül-, orr-, gégegyógyászat = Otorhinolaringologia Hungarica*, 2014;60:47-53.

6.2. Thesis related presentations and posters

- Dr. Piski Zalán, Dr. Lujber László, Csobó Dávid, Dr. Takács Ildikó, Dr. Burián András, Dr. Révész Péter, Dr. Gerlinger Imre. Felszívódó orrtampon alkalmazása FESS műtétek kapcsán. Magyar Fül-,Orr-,Gége és Fej-Nyaksebész Orvosok 42. Kongresszusa, Pécs, 2012
- Dr. Piski Zalán, Gleta Csilla, Dr. Lujber László, Dr. Gerlinger Imre. Biológiailag lebomló tampon (Nasopore™) alkalmazása endoszkópos melléküreg-műtétek kapcsán. Magyar Fül-,Orr-,Gége és Fej-Nyaksebész Orvosok 43. Kongresszusa, Tapolca, 2014
- Dr. Piski Zalán, Dr. Lujber László, Dr. Gerlinger Imre. Clinical effects of absorbable Polyurethan nasal packing in endoscopic sinus surgery (poszter). 3rd Congress of European ORL-HNS, Prága 2014
- Dr. Piski Zalán, Dr. Lujber László, Dr. Gerlinger Imre. Clinical effects of absorbable Polyurethan nasal packing in endoscopic sinus surgery Congress of European Rhinology Society, Stockholm 2016
- Dr. Piski Zalán, Dr. Lujber László, Dr. Gerlinger Imre. Lebomló orrüregi tamponok tulajdonságainak vizsgálata az endoszkópos melléküreg-sebészetben. Medical Conference for PhD Students and Experts of Clinical Sciences, Pécs, 2018

- Dr. Piski Zalán, Dr. Lujber László, Dr. Nepp Nelli, Dr. Kalinics Péter, Dr. Gerlinger Imre. The evaluation of mucosal healing in animal model, with the application of a Chitosan based nasal dressing, after endoscopic sinus surgery 5rd Congress of European ORL-HNS, Brüssel, 2019

6.3. Additional articles

1. Piski, Z, Gerlinger I, Nepp N, Farkas K, Weber R. TNF-Alpha Inhibitors and Rhinosinusitis—A Systematic Review and Meta-Analysis. *American Journal of Rhinology & Allergy*. doi:10.1177/1945892419898988
2. Orosz, E, Gombos K, Petrevszky N, Piski Z, et al. Visualization of mucosal field in HPV positive and negative oropharyngeal squamous cell carcinomas: combined genomic and radiology based 3D model. *Sci Rep* doi:10.1038/s41598-019-56429-4
3. Gerlinger I, Bakó P, Piski Z et al. KTP laser stapedotomy with a self-crimping, thermal shape memory Nitinol piston: follow-up study reporting intermediate-term hearing. *Eur Arch Otorhinolaryngol* 2014; 271:3171-3177.
4. Révész P, Piski Z, Burián A, Harmat K, Gerlinger I. Delayed Facial Paralysis following Uneventful KTP Laser Stapedotomy: Two Case Reports and a Review of the Literature. *Case Rep Med* 2014; 2014:971362.
5. Révész P, Szanyi I, Ráth G, Bocskai T, Lujber L, Piski Z, Karosi T, Gerlinger I: Comparison of hearing results following the use of NiTiBOND versus Nitinol prostheses in stapes surgery. *EUROPEAN ARCHIVES OF OTO-RHINO-LARYNGOLOGY* online: 6 p. Paper Doi 10.1007/s00405-015-3662-1.
6. Tóth E, Tornóczky T, Kneif J, Perkecz A, Katona K, Piski Z, Kemény Á, Gerlinger I, Szolcsányi J, Kun J, Pintér E. Upregulation of extraneuronal TRPV1 expression in chronic rhinosinusitis with nasal polyps. *Rhinology*. 2018;56:245-254.
7. Lepera D, Volpi L, Facco C, Turri-Zanoni M, Battaglia P, Bernasconi B, Piski Z, Freguia S, Castelnovo P, Bignami M. Endoscopic Treatment of Ewing Sarcoma of the Sinonasal Tract. *J Craniofac Surg*. 2016;4:1001-6

8. Burian A, Gerlinger I, Toth T, Piski Z, Rath G, Bako P. Stapedotomy with incus vibroplasty - A novel surgical solution of advanced otosclerosis and its place among existing therapeutic modalities - Hungarian single institutional experiences. *Auris Nasus Larynx*. doi: 10.1016/j.anl.2019.04.004.
9. Piski, Z., Buki, A., Nepp, N., Burian, A., Revesz, P., & Gerlinger, I. Closure of nasocranial fistulas with „bath plug” technique and multilayer reconstruction. *Ideggyogy Sz*, 2015;69:211-216.
10. Piski Z, Mózes R, Burián A, Révész P, Gerlinger I, Pytel J. Korral járó hallászavarok korai kimutatása. *Fül-, orr-, gégegyógyászat = Otorhinolaringologia Hungarica* 2011; 57:138-144.
11. Piski Z - Tornóczki T - Vida L - Móricz P - Nepp N - Gerlinger I: Idős betegben felfedezett, nagyméretű intrahyodeális ductus thyreoglossus ciszta esete
Fül-, orr-, gégegyógyászat = Otorhinolaringologia Hungarica, 2016;62:22-24.
12. Piski Z, Büki A, Gerlinger I, Tóth I, Nepp N, Lujber L. Minimálisan invazív, endoszkóppal asszisztált, transcribriform reszekció a koponyaalap rosszindulatú daganatainak sebészetében [Minimally invasive endoscopic transcribriform resection of malignant lesions of the skull base]. *Orv Hetil*. 2019;160:1584-1590.
13. Burián A, Piski Z, Bakó P, Török L, Gerlinger I, Lujber L. Orrdeformitást okozó extrém nagy tumorszerű szövetszaporulat sclerosis tuberosa kapcsán. *Fül-, orr-, gégegyógyászat = Otorhinolaringologia Hungarica*, 2010;56.:3.143.
14. Gerlinger I, Molnár Ferenc T, Piski Z, Járai T, Móricz P. Nyaki blokkdisszekciók során eltávolított nyirokcsomók szövettani feldolgozását segítő tálca. *Fül-, orr-, gégegyógyászat = Otorhinolaringologia Hungarica* 2011; 57:26-30.
15. Gerlinger I, Révész P, Piski Z, Burián A, Móricz P. Eseménytelen lézer stapedotomiát követő késői nervus facialis paresis - esetismertetés és irodalmi áttekintés. *Fül-, orr-, gégegyógyászat = Otorhinolaringologia Hungarica* 2011; 57:133-137.
16. Járai T, Piski Z, Lujber L, Gerlinger I. Az arteria sphenopalatina endoszkópos ellátása makacs hátsó orrvérzések eseteiben - technika, buktatók, anatómiai variációk. *Fül-, orr-, gégegyógyászat = Otorhinolaringologia Hungarica* 2013; 59:127-132.

17. Móricz P, Somogyvári K, Burián A, Piski Z, Révész P, Gerlinger I. Hypertonicitás okozta aphonia megoldása myotomiával hangprotézis beültetés után. Fül-, orr-, gégegyógyászat = Otorhinolaringologia Hungarica 2013; 59:45-46.
18. Somogyvári K, Móricz P, Piski Z et al. Rádiófrekvenciás microlaryngealis beavatkozások. Fül-, orr-, gégegyógyászat = Otorhinolaringologia Hungarica 2014; 60:20-22.
19. Gerlinger I - Háromi I - Harmat K- Lujber L - Piski Z. A nervus vidianus endoszkópos neurectomiája Fül-, orr-, gégegyógyászat = Otorhinolaringologia Hungarica, 2015;61:97-102.
20. Gerlinger I - Tóth T - Molnár K - Piski Z - Bölcsföldi T. B - Révész P - Bakó P - Lujber L Tympanomastoidealis paragangliomák (glomus tympanicum tumorok)sebészi kezelésének algoritmus
Fül-, orr-, gégegyógyászat = Otorhinolaringologia Hungarica, 2017;63:55-61.
21. Tóth I, Kaszás B, Horváth G, Piski Z, Bakó P, Lujber L, Gerlinger I, Révész P. Wegener-granulomatosis talaján kialakult krónikus gennyes középfülgyulladás komplex kezelése. Orv Hetil. 2019;160:151-157.
22. Nepp N. Farkas K. Lujber L. Gerlinger I. Piski Z. Tumor nekrosis faktor-alfa-gátló kezelés során észlelt rhinosinusitisek. Rendszerezett áttekintő közlemény. Fül-, orr-, gégegyógyászat = Otorhinolaringologia Hungarica, 2019;65:12-17.