SELLAR RECONSTRUCTION AFTER ENDOSCOPIC TRANSSPHENOID PITUITARY SURGERY: SYSTEMATIC REVIEW AND META-ANALYSIS

ABDELHMAN YOUNES BADAWY*
AHMED ELFAROUK ABDELFATTAH**
HESHAM NABIL LASHEEN***

*Lecturer of Otorhinolaryngology, Faculty of Medicine, Cairo University, Egypt
**Professor of Otorhinolaryngology, Faculty of Medicine, Cairo University, Egypt
***Lecturer of Otorhinolaryngology, Faculty of Medicine, Cairo University, Egypt

Abstract
During the past decade, the popularity of the endoscopic approach for the treatment of sphenoid sinus & the related skull base lesions has been increased because its minimal invasiveness & improvement patient’s comfort. Following the endoscopic transnasal pituitary surgery, the resultant sellar defect requires reconstruction to form a watertight barrier separating the intracranial compartment and sinonasal tract. Failure to achieve adequate separation can lead to complications, including cerebrospinal fluid (CSF) leak, pneumocephalus and meningitis. The current options available for reconstruction have expanded and the decision to reconstruct must take into account the anticipated location, size, and shape of the defect. But, the most reconstructive techniques used for the sellar region are the FAT, the MIDDLE TURBINATE FLAP, and the NASOSEPTAL FLAP.

We decided to do our best trying to reach the most appropriate method for sellar reconstruction after endoscopic surgeries, so we chose the most powerful and evident type of search studies which is known as Metanalysis and systematic review.

Our study shows that all of them (fat, middle turbinate flap and nasoseptal flap) are reliable methods of sellar reconstruction after endoscopic transsphenoidal pituitary surgery and the best one of them is the nasoseptal flap.

But, in fact we can’t depend on these results as an evidence for the usage of the nasoseptal flap as the best method of sellar reconstruction after endoscopic transsphenoidal pituitary surgery because of the previously reported causes. So, we recommend that Future studies with more effort should concentrate on developing well designed controlled human trials to provide more statistically valuable results.

Keywords: Pituitary, Trans-Nasal, Sellar Reconstruction, CSF Leak
Introduction

During the past decade the endoscopic approach for the treatment of sphenoid sinus & the related skull base lesions has been become the treatment of choice as it is minimal invasive & has less incidence of post-operative complications(1).

Following the endoscopic transnasal pituitary surgery, the resultant sellar defect requires reconstruction to form a watertight barrier separating the intracranial compartment and sinonasal tract and failure to achieve adequate separation can lead to complications, including cerebrospinal fluid (CSF) leak, pneumocephalous and meningitis. So, the need for more robust and reliable reconstructive options has been increased(2).

RECONSTRUCTIVE TECHNIQUES OF THE SELLA

Effective and consistent reconstruction of the dura mater has been a major challenge against the Trans sphenoidal approach to the Sella. So, The great problem which faces the skull base surgeons nowadays is what is the best material to be used in the skull base reconstruction to reach our golden goal (to separate the cranial cavity completely from the sinonasal tract)(3).

Many reconstructive methods can be used in reconstruction of the skull base and they can be categorized into two main categories free tissue grafts as the fat and vascularized pedicled flaps as the inferior turbinate flap, the middle turbinate flap and the nasoseptal flap(4).

Aim of the work

The study aims to analyze and evaluate the studies conducted on the different methods of sellar reconstruction especially fat, middle turbinate flap and nasoseptal flap, and to compare their results in order to reach the best way to reconstruct the Sella in different situations after endoscopic transsphenoidal pituitary surgery.
The systematic review and The Metaanalysis is this will be done by the following steps.

1- Target question and PICO:

Our target question is actually three questions as we have three main methods of sellar reconstruction so our questions are: In patients undergoing endoscopic transsphenoidal pituitary surgery, can sellar reconstruction with (fat graft-middle turbinate flap - nasoseptal flap) form a watertight barrier and prevent the postoperative CSF leak?

Regarding the PICO:

- The (P): patients who underwent endoscopic transsphenoidal pituitary surgery regardless age, sex and the type of the pathology of the Sella.
- The (I):
  - I. (Sellar reconstruction with fat).
  - II. (Sellar reconstruction with middle turbinate flap)
  - III. (Sellar reconstruction with nasoseptal flap).
- The (C): is not available in our study.
- The (O): is postoperative CSF leak.

2- Searching strategy (Identification and location of articles).

Firstly, we want to be sure that there is no any meta-analyses or systematic reviews concerned with our subject available on the network, so that; we searched on www.google.com and www.cochrane.org by “Metaanalysis of sellar reconstruction after endoscopic transsphenoidal pituitary surgery” and we found that there are no any available meta-analyses on this topic.

The study included published medical articles concerning use of fat, middle turbinate flap or nasoseptal flap in sellar reconstruction after endoscopic transsphenoidal pituitary surgery.

The search was done by two different researchers in 25/1/2015 using the following key words in a search builder manner (usually according to Boolean language [OR, AND, NOT]):

- Endoscopic transsphenoidal
- Endonasal transsphenoidal
- Sellar reconstruction
- Reconstruction of the middle cranial base
- Fat
- Fat graft
- Middle turbinate flap
- Middle turbinate
- Nasoseptal flap
- Haddad bassagasteguy flap

**Inclusion criteria:**

*Participants:*

- Male or female patients at any age underwent endoscopic transsphenoidal pituitary surgery.

*Intervention:*

- Sellar reconstruction with fat, middle turbinate flap or nasoseptal flap.

*Study types:*

- Randomized controlled trials
- Clinical trials

*Outcome:*

- Postoperative CSF leak

**Exclusion criteria:**

*Participants:*

- Patients who underwent pituitary surgery through any approaches other than endoscopic transsphenoidal approach as microscopic pituitary surgery.
- Patients who underwent endoscopic approach to other skull base areas as planum sphenoidale, clivus and olfactory groove.

*Intervention:*

- Sellar reconstruction with any method other than fat, middle turbinate or nasoseptal flap as synthetic dural substances, pericranial flap and temproparietal flap.

*Study types:*

- Cohort studies
- Cross sectional studies
- Unselected case series
- Articles not in English
Outcome:
- Nasal complications
- Meningitis
- Pnuemocephalous

After defining inclusion and exclusion criteria of the articles to be searched for and determination of database sources in which the articles will searched for, the search strategy will follow the following PRISMA flow chart:
The following table summarizes the results of the search:

<table>
<thead>
<tr>
<th>Keywords</th>
<th>Number of articles and their abstracts</th>
<th>Number of articles after removal of duplicates</th>
<th>Excluded articles due to irrelevance</th>
<th>Number of relevant articles</th>
</tr>
</thead>
<tbody>
<tr>
<td>-(fat OR fat graft )AND( endoscopic transsphenoidal OR endonasal transsphenoid) AND (sellar reconstruction OR reconstruction of middle cranial base)</td>
<td>25</td>
<td>16</td>
<td>12</td>
<td>4</td>
</tr>
<tr>
<td>- (middle turbinate flap OR middle turbinate AND endoscopic transsphenoidal OR endonasal transsphenoid AND sellar reconstruction OR reconstruction of middle cranial base).</td>
<td>26</td>
<td>15</td>
<td>10</td>
<td>5</td>
</tr>
<tr>
<td>-(nasoseptal flap OR haddad – bassagasteguy flap AND endoscopic transsphenoidal OR endonasal transsphenoid AND sellar reconstruction OR reconstruction of middle cranial base)</td>
<td>26</td>
<td>15</td>
<td>10</td>
<td>5</td>
</tr>
</tbody>
</table>

N.B: the irrelevance is judged according to the inclusion and exclusion criteria

All articles were 67 and by removing repeated articles (first filter), the total articles are 44. The excluded articles due to irrelevance (the second filter) are 34. So the included relevant articles are 10 articles 4 for the fat, 1 for the middle turbinate flap and 5 for the nasoseptal flap.
3- Screening and evaluation (the third filter):

All articles included were assessed for the validity and quality according to EBL critical appraisal check list.

<table>
<thead>
<tr>
<th>EBL Critical Appraisal Checklist</th>
<th>Yes (Y)</th>
<th>No (N)</th>
<th>Unclear (U)</th>
<th>N/A</th>
</tr>
</thead>
<tbody>
<tr>
<td>Section A: Population</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Is the study population representative of all ones, actual and eligible, who might be included in the study?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Are inclusion and exclusion criteria definitively outlined?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Is the sample size large enough for sufficiently precise estimates?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Is the response rate large enough for sufficiently precise estimates?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Is the choice of population bias-free?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>If a comparative study</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Were participants randomized into groups?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Were the groups comparable at baseline?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>If groups were not comparable at baseline, was incomparability addressed by the authors in the analysis?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Was informed consent obtained?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Section B: Data collection</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Are data collection methods clearly described?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>If a face-to-face survey, were inter-observer and intra-observer bias reduced?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Is the data collection instrument validated?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>If based on regularly collected statistics, are the statistics free from subjectivity?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Does the study measure the outcome at a time appropriate for capturing the intervention’s effect?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Is the instrument included in the publication?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Are questions posed clearly enough to be able to elicit precise answers?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Were those involved in data collection not involved in delivering a service to the target population?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Section C: Study design</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Is the study type/methodology utilized appropriate?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Is the study clearly defined?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Was ethics approval obtained?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Are the outcomes clearly stated and discussed in relation to the data collection?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Section D: Results</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Are all the results clearly outlined?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Are confounding variables accounted for?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Do the conclusions accurately reflect the analysis?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Is subset analysis a minor, rather than a major, focus of the article?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Are suggestions provided for further areas to research?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Is there external validity?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Calculation for section validity: $\frac{Y \times N + U \times T}{Y + N + U + T}$

Calculation for overall validity: $\frac{Y \times N + U \times T}{Y + N + U + T}$

If $\frac{Y \times T}{Y + T} < 75\%$ or if $\frac{N + U}{Y + T} > 25\%$ then you can safely conclude that the section identifies significant omissions and that the study’s validity is questionable. It is important to look at the overall validity as well as section validity.

Section A validity calculation:
Section B validity calculation:
Section C validity calculation:
Section D validity calculation:
Overall validity calculation:

Table (2): EBL critical appraisal check list 2009.

EBLIP Critical Appraisal Checklist
Lindsay Glynn, MLIS
Memorial University of Newfoundland
lglynn@mun.ca
After assessment of the validity, we excluded four articles. One from the articles related to the fat and three from those related to nasoseptal flap due to their invalidity. 

So, we finally have six related and valid articles which we can collect our data from.

Prisma flow chart for articles resulted from the search about the three methods of reconstruction:

Figure (1): Prisma flow chart for articles resulted from the search about the three methods of reconstruction.
4- Data Collection (Results):
From the (6) included articles the following will be recorded in a data collection form: A) Fat as a method of sellar reconstruction:

<table>
<thead>
<tr>
<th>Author /Year</th>
<th>Level of evidence</th>
<th>Intervention</th>
<th>Participants</th>
<th>Outcome (CSF leak)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trinh VT and Duckworth EA 2015(^{6}).</td>
<td>IV</td>
<td>Closure of sellar defect with abdominal fat only harvested from around umbilicus.</td>
<td>10 with small sellar defect</td>
<td>No patient with CSF leak</td>
</tr>
<tr>
<td>Jalessi M et al, 2013(^{7})</td>
<td>IV</td>
<td>1) A thin layer of fat applied on arachnoid membrane defect 2) a layer of fascia underlay 3) Covering the defect with a layer of Surgical 4)Filling the sphenoid sinus with Gelfoam</td>
<td>80 patients with either CSF leak from less than 1 mm defect (73 patients) or with no defects but a severe prolapse of the suprasellar components coming out of the Sella(2 cases) or in whom extra-pseudo capsular dissection performed</td>
<td>No patient with CSF leak</td>
</tr>
<tr>
<td>SciarrettaV et al 2010(^{8}).</td>
<td>IV</td>
<td>Abdominal fat was positioned within the Sella and subsequent repositioning of the previously undermined sphenoid mucosa.</td>
<td>123 with small dural defect, while 5 were due to a larger dural defect and 8 patients required repair because of an overt thin diaphragma sellae without a visible CSF leak (repaired with abdominal fat)</td>
<td>11 patients with postoperative CSF leak</td>
</tr>
</tbody>
</table>

Table (3) Included articles for the fat as a method of sellar

www.jiarm.com
Middle turbinate flap as a method of sellar reconstruction:

<table>
<thead>
<tr>
<th>Author/Year</th>
<th>Level of Evidence</th>
<th>Intervention</th>
<th>Participants</th>
<th>Outcome CSF leak</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sciarretta V et al 2010</td>
<td>IV</td>
<td>Middle turbinate flap as a part of multilayer reconstruction with fat inlay and cartilage on lay</td>
<td>11 patients with postoperative CSF leak after repair with fat need revision reconstruction</td>
<td>No patient with postoperative CSF leak</td>
</tr>
</tbody>
</table>

**Total**: 11

(c) Nasoseptal flap as a method of sellar reconstruction:

<table>
<thead>
<tr>
<th>Author/Year</th>
<th>Level of Evidence</th>
<th>Intervention</th>
<th>Participants</th>
<th>Outcome CSF leak</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eloy JA et al, 2012</td>
<td>IV</td>
<td>Nasoseptal flap with autologous fat in 24 patients and fascia lata in 13 patients inlay technique</td>
<td>37 patients with pituitary adenoma with sellar defect (average size 3.4 cm²)</td>
<td>No patient with postoperative CSF leak</td>
</tr>
<tr>
<td>Kim BY et al, 2013</td>
<td>IV</td>
<td>Bilateral nasoseptal flap with bone graft from the vomer put inlay manner</td>
<td>92 patients with pituitary adenomas (585), Rathke’s cleft cysts (55), lymphoma (51), and metastatic ductal carcinoma (51)</td>
<td>No patient with postoperative CSF leak</td>
</tr>
</tbody>
</table>

**Total**: 129

Table (4): Included articles for the middle turbinate flap as a method of sellar reconstruction.

Table (5): Included articles for the nasoseptal flap as a method of sellar reconstruction.
(5) Data Analysis:

<table>
<thead>
<tr>
<th>Method of reconstruction</th>
<th>Total patients</th>
<th>Post-operative CSF leak</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fat graft</td>
<td>226</td>
<td>11</td>
</tr>
<tr>
<td>Middle turbinate flap</td>
<td>11</td>
<td>0</td>
</tr>
<tr>
<td>Nasoseptal flap</td>
<td>129</td>
<td>0</td>
</tr>
</tbody>
</table>

*Table (6):* The data collected from all included articles.

The following software will be used *(Review Manager (RevMan) Version 5.0.25 Copenhagen: The Nordic Cochrane Centre, the Cochrane Collaboration, 2010).*

6) Reporting and interpretation:

We enter the results in table 11 to the above mentioned, meta-analytic software: Review Manager (RevMan 5.0.25) which resulted in the following graphs.

**Figure (2):** Forest plot graph comparing the nasoseptal flap with the fat

In figure (2) the meta-analytic software compared results of the fat and the nasoseptal flap which favors the nasoseptal flap with P value 0.07 and ODD ratio is less than 0.1 which is actually still not significant as the P value must be $\leq 0.05$.

**Figure (3):** Forest plot graph comparing the middle turbinate flap with the fat
But, in figure (3) the results of the fat is compared to those of the middle turbinate and this comparison showed that the middle turbinate flap is better than the fat with P value 0.78 and ODD ratio is near 1 which is not significant at all.

There is no figures comparing the results of the middle turbinate flap with that of the nasoseptal flap which is logic because that, in the both methods of sellar reconstruction there was no patients with postoperative CSF leak.

After interpreting these meta-analytical graphs we found that no one of the three methods of sellar reconstruction is statically significant which is due to low number of the patients in each one which is the main important point which the meta-analysis study depends on. But the nasoseptal flap shows the trend to be better than the other two methods because the number of the patient needed to be significant is so near the number of the patients resulted from the nasoseptal flap and the meta-analytic software would consider it the significant method of reconstruction if the number of the patients was more. But, it is still not significant.

But, from the statically point of view, we have considerations that make the evidence for the usage of the nasoseptal flap as the best method of sellar reconstruction after endoscopic transsphenoidal pituitary surgery is weak because of the following drawbacks:

- Limited number of valid, eligible and highly qualified articles from which we can get the data.
  As previously shown, there are only six available articles. THREE for the Fat, ONE for the Middle turbinate flap and TWO for the Nasoseptal flap.
  This is because we exclude a lot of articles because of their irrelevance or invalidity.
- The articles we found are case series studies which are of lower evidence than the randomized control trials and NO one article is randomized control trial which is of high evidence.
- Low number of patients in each article.
- Actually we can’t compare between the results of different articles as :
  - Articles that are concerned with the fat as a method of sellar reconstruction used the Fat as a layer of multilayered technique NOT the Fat alone as in the articles concerned with the other methods of reconstruction.
  - The sellar defects in different articles about the THREE methods are of different sizes.
- Intra-operative CSF leak is not present in all articles about different methods and furthermore, it is not present in all patients of the same article.
- In the article concerned with the Middle turbinate flap, it was revision reconstruction NOT primary reconstruction as in the articles concerned with the other methods of reconstruction.

Conclusion:

We can conclude that there is no statically difference regarding the outcome (CSF leak) between the three methods of sellar reconstruction after endoscopic transsphenoidal pituitary surgery (FAT, MIDDLE TURBINA TE FLAP AND NASOSEPTAL FLAP) which can’t make one of these methods superior to the others. Thereby, we can’t recommend any method of them as the best method of sellar reconstruction.

Recommendations:

Future studies with more effort should concentrate on developing well designed controlled human trials to provide more statistically valuable results. And these randomized control trials should compare between the three methods (fat, middle turbinate flap and nasoseptal flap) in reconstructing the sellar defects of the same size and with the same circumstances.

References: