Author’s response to reviews

Title: Minimizing risk of customized titanium mesh exposures – a retrospective analysis

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Version: 2 Date: 18 Nov 2019

Author’s response to reviews:

Submission of manuscript

`Minimizing risk of customized titanium mesh exposures – a retrospective analysis`

Dear Prof. Mijiritsky,

On behalf of my coauthors, thank you again for considering our research article `Minimizing risk of customized titanium mesh exposures – a retrospective analysis` for publication in your journal BMC oral health pending satisfactory revision in response to reviewer’s comments. The manuscript has been revised to address the reviewer’s and your comments, and a detailed point-by-point response to each reviewer/editorial point is attached. A clean version of our manuscript is attached. We believe these changes have improved the manuscript, and reviewer’s comments are greatly appreciated.

Yours sincerely,

Dr. Amely Hartmann

Dear Editor/Reviewer,

Thank you for critically assessing our manuscript for publication in BMC oral health.

We wish to thank you for suggested improvements.
Editor

please revise your paper according to the indications of reviewer number 3

Reviewer 3 (Ausra Ramanauskaite)

Reviewer 3 - Suggestion 1:

Abstract:

1. Methods

Lines 14-15 - An exposure rate was investigated - perhaps this is what authors means. The impact of factors such as .... On the exposure rate was assessed - again, perhaps this is what authors meant.

The current formulation is not acceptable.

Response:

We corrected this according to reviewer´s suggestion.

Abstract Lines 12-13:

An exposure rate was investigated concerning surgical splint application, A®- PRF and flap design.

Reviewer 3 – Suggestion2:

Results

2. Lines 2-3: 'Surgical splints were not evaluated to reduce the exposure rate (p = 0.029)' - please double-check this. This must be a mistake.

Response:

We apologize for this inaccuracy.

Title page/p.1, l.25-p.2, l.1:

Surgical splints were not evaluated to reduce the exposure rate (p=0.239).
Reviewer 3 - Suggestion 3:

3. Introduction Page 2 L 4 - 'should be describes' - probably authors meant were assessed -mind the language!

Response:
We thank the reviewer for this comment, and we changed it according to the suggestion.

p.2,l.3-4:
The influence of various demographic, local and systematic factors were assessed.

Reviewer 3 - Suggestion 4:

Methods

4. P 3 L 23-24 - please, make one sentence out of two. Better use (e.g…) instead of separating the last sentence.

Response:
We made one sentence out of two.

p.3, l.19-21:
In general, patients with systemic or local diseases and malignancies were excluded before enrolment.

Reviewer 3 - Suggestion 5:

5. Outcome assessment section should follow after the Workflow and surgery section.

Response:
We changed the order of the sections mentioned above.

p.3, l.23- p.6, l.2:
Workflow and Surgery
After acquisition of a Cone Beam Computed Tomography (CBCT) dataset, a 3D-projection of the atrophied segment was obtained by using a reverse engineering software. The necessary bone volume was digitally added, and the individualized titanium meshes were designed. The inner contour of the lattice structure represented the desired augmentation volume. By using Computer-Aided Design/Computer-Aided Manufacturing (CAD/CAM) procedures and rapid prototyping the final design was achieved and confirmed interactively by the surgeon (figure 1 and 2). After a 3D-Printing Process (figure 3), the titanium mesh was sent to the surgeon and sterilized before use.

Surgery was performed under local anesthesia. The opening incision was carried out in accordance with the defect size and location of the neighboring anatomical structures of the region. Flap design was performed as appropriate in each case (full flap preparation, full flap and periosteal incision, periosteal incision, poncho/split flap or rotation flap). After preparation of the defect, scar tissue was removed. In the lower jaw, some cortex perforations were performed to boost the blood supply. The meshes were installed by using a mixture of autologous bone graft and bone substitute biomaterial (Bio Oss®, Geistlich, Wolhusen, Switzerland) in a 1:1 ratio (figure 4). Autologous bone was harvested from the conventional intraoral donor sites (n=59, external oblique line (n=50) and operation site (n=9)) or from the iliac crest (n=8). In one patient, only bone substitute (Bio Oss®) was used. Each mesh was fixed to the residual bone with titanium osteosynthesis screws. A resorbable membrane (Bio-Gide®, Geistlich, Wolhusen, Switzerland) was placed on top. In some cases (n=12), an Advanced-Platelet Rich Fibrin (A-PRF®) clot was applied according to manufacturers´ protocol following the in vitro-protocol of Choukroun [24] (figure 5 and 6). Flaps were adopted without tension by using deep mattress and single interrupted sutures (Seralon5/0). Vacuum form splints were adjusted to enhance soft tissue healing in n=22 (figure 7). Patients received instructions concerning a proper oral hygiene. They had to avoid brushing at the grafting area and to wear removable dentures. All patients underwent an oral antibiotic therapy (Amoxicillin® 1000 mg 1-1-1 or Clindamycin® 600 mg 1-1-1) for 5-7 days starting at time of the surgery.

After a two-week healing period, sutures were removed. Outcomes were also assessed one week after surgery and during follow-up each month. The Re-opening and removal of the titanium mesh was after approximately 4-8 months depending on size of the defect. Implant placement subgroups (Camlog Screw Line®, Camlog, Wimsheim, Germany) were equally distributed (implantation performed either simultaneously with mesh insertion (44.1%) or after a healing period of 4-8 months combined with the removal of the mesh (44.1%)).
Outcome assessment

The primary aim of the study was to describe the population concerning the grafting success. Success of the augmentation procedure was defined as the feasibility of implant placement in the planned position and achievement of an adequate primary stability (15Ncm-35Ncm) until the re-entry and to finalize with the individual prosthetic supraconstruction. Failure was defined as complete loss of the graft. Outcomes and possible healing difficulties were assessed one week after surgery and during follow-up each month. Patients were instructed to contact the surgeon if any disturbances occurred.

Secondary aim of the study was to assess possible risk factors (defect regions, defect and mesh sizes, smoking, tissue phenotype (thin and fragile phenotype, thick phenotype[25]), diabetes) for grafting success and developing an exposure. Exposure rate and impact of such factors as Vacuum form splint, A-PRF® and flap design on the exposure rate should be assessed. Exposures of the titanium mesh were classified concerning their size. “A” was a punctual exposure, “B” an exposure like one premolar size and “C” a complete one whereas “D” was no exposure[26]. Mesh size was defined according to the missing teeth.

Reviewer 3 - Suggestion 6:

6. P 4 L3-4 - please, define your primary outcome? Was it grafting success? Was it exposure rate? Was it the assessment of factors such as A-PRF.. etc on the exposure rate? There are 3 different outcomes. Elucidate it and please report in understandable manner. At what time points were these different outcomes assessed - after 2 weeks? After 4-8 weeks? This must be very clear.

Response:

The reviewer is right; we rewrote this section and included the information of former L17-21.

p.5, l.11-p.6, l.2:

Outcome assessment

The primary aim of the study was to describe the population concerning the grafting success. Success of the augmentation procedure was defined as the feasibility of implant placement in the planned position and achievement of an adequate primary stability (15Ncm-35Ncm) until the re-entry and to finalize with the individual prosthetic supraconstruction. Failure was defined as complete loss of the graft. Outcomes and possible healing difficulties were assessed one week after surgery and during follow-up each month. Patients were instructed to contact the surgeon if any disturbances occurred.
Secondary aim of the study was to assess possible risk factors (defect regions, defect and mesh sizes, smoking, tissue phenotype (thin and fragile phenotype, thick phenotype[25]), diabetes) for grafting success and developing an exposure. Exposure rate and impact of such factors as Vacuum form splint, A-PRF® and flap design on the exposure rate should be assessed. Exposures of the titanium mesh were classified concerning their size. “A” was a punctual exposure, “B” an exposure like one premolar size and “C” a complete one whereas “D” was no exposure[26]. Mesh size was defined according to the missing teeth.

Reviewer 3 - Suggestion 7:

7. P 4 L 10 - opportunity -* perhaps authors meant 'feasibility of implant placement'

Response:

We thank the reviewer for this comment. We changed it according to your suggestion.

p.5, l.13-16:

Success of the augmentation procedure was defined as the feasibility of implant placement in the planned position and achievement of an adequate primary stability (15Ncm-35Ncm) until the re-entry and to finalize with the individual prosthetic supraconstruction.

Reviewer 3 - Suggestion 8:

8. P 4 L 11 - was primary stability assessed: Ncm?

Response:

Primary stability was assessed in Ncm.

p.5, l.13-16

Success of the augmentation procedure was defined as the feasibility of implant placement in the planned position and achievement of an adequate primary stability (15Ncm-35Ncm) until the re-entry and to finalize with the individual prosthetic supraconstruction.

Reviewer 3 - Suggestion 9:

9. P 6 L 4-6 - See comment Nr 6!

Response:
The reviewer is right; we clarified this issue.

p.5, l.3-6:

After a two-week healing period, sutures were removed. Outcomes were also assessed one week after surgery and during follow-up each month. The Re-opening and removal of the titanium mesh was after approximately 4-8 months depending on size of the defect.

Reviewer 3 - Suggestion 10:

10. P 6 L 7 - what is well-balanced - perhaps authors meant equally distributed?

Response:

The reviewer is right; we added this information.

p.5, l.6-9:

Implant placement subgroups (Camlog Screw Line®, Camlog, Wimsheim, Germany) were equally distributed (implantation performed either simultaneously with mesh insertion (44.1%) or after a healing period of 4-8 months combined with the removal of the mesh (44.1%)).

Reviewer 3 - Suggestion 11:

11. P 6 L 20 - a possible exposure rate - perhaps authors meant exposure rate.

Response:

According to reviewer’s suggestion, we changed this.

p.6, l.8-10:

Grafting success, exposure rate and impact of such factors as Vacuum form splint, A-PRF® and flap design on the exposure rate.

Reviewer 3 - Suggestion 12:

12. P 6 L 20 - methods to reduce - perhaps authors meant impact of such factors as XXXX on the exposure rate.

Response:
We thank the reviewer for this suggestion and changed the information accordingly.

p.6, l.8-10:

Grafting success, exposure rate and impact of such factors as Vacuum form splint, A-PRF® and flap design on the exposure rate.

Reviewer 3 - Suggestion 13:

Results

13. P 8 L 22 - no failures occurred - did you mean no implants failed? Or it is meant the same as in line 5?

Response:

The reviewer is right; the information is the same. That’s why we deleted this sentence.

p.7, l.20-22:

Associated with these exposures, no loss of grafting material (86.8%, n=59), partial (11.8%, n=8) and complete in 1.5% (one case) was evaluated. A therapy according to the planned treatment protocol was possible in all the cases.

Reviewer 3 - Suggestion 14:

14. P 8 L 23 - see comment Nr 2.

Response:

We checked and double-checked the data.

p.7, l.23-p.8, l.3:

A®-PRF provided significantly less exposures of the titanium meshes (76.5% no exposure vs. 23.5% yes, p=0.029) (Table 1). Other parameters like tobacco abuse (p=0.669), diabetes (p=0.568) or surgical parameters (mesh size, defect region, flap design p=0.368) did not influence the exposure rate. Surgical splints were not found to reduce the exposure rate (p=0.239).
Reviewer 3 - Suggestion 15:

Discussion

15. P 11 L 1 - you mean perhaps - no measurements of the defect were assessed! Description provided by the surgeon mean nothing when it comes to the publication. Consider reformulation.

Response:

We did a reformulation according to reviewer´s suggestion.

p.9, l.25-p.10, l.1:

First, the study focused on augmentation procedures in three-dimensional defects. No measurements of the defect (in mm3) were assessed.

Reviewer 3 - Suggestion 16:

16. P 12 L 5-12 - this paragraph is hard to understand. It must be rewritten in a readable way. What is the link between the scar tissue and biotype?

Response:

We rewrote this section.

p.11, l.3-13:

One might assume that a thin tissue phenotype[25, 41] is much more difficult to handle than a thick one. Scar tissue will develop easily because of an earlier mucosal rupture. An adequate aesthetic outcome may be difficult to achieve. This was evaluated in previous studies[42]. They described thick gingival phenotypes associated with additional blood support during wound healing because of the missing periodontal ligament support in implant therapies. These findings are contrary to the results at hand. A possible reason for this may be in the patient group itself. Large three-dimensional defects like described in this study, are the result of numerous preceding surgeries like teeth extraction, inflammation processes or others. According to authors opinion, scar tissue as a result of these former interventions – in thin and thick tissue phenotype – might be the real reason for developing an exposure.

Reviewer 3 - Suggestion 17:

17. P 12 L 19 - how gender female and steroid hormones may influence exposure rate.

Response:
We specified these benefits according to reviewer’s suggestion.

p.11, l.16-p.12, l.6:

In their study, they also evaluated no relationship between gender and the risk to develop an exposure. This goes along with other studies[43] but is not in accordance with findings of this study where we were able to find a significant relationship between male gender and the development of exposures. Male patients were already described to suffer from an increased potential infection rate after implant placement by Figueiredo et al.[44]. This is in accordance with Kim et al.[45] who evaluated male gender to have the highest risk of wound dehiscence in guided bone regeneration. These results are in line with our findings. The same observation was also described in dermatology. Dao et al.[46] reported about gender differences in skin regeneration. They described modified immunological processes in elderly men caused by an increasing testosterone level. Male-specific instructions on postoperative care may help to overcome these healing difficulties.

On the other hand one might assume that especially steroid hormones in female patients appear capable of influencing the normal bacterial flora and the subgingival ecology [47, 48]. Consecutively, healing difficulties may arise. This is not according to the results of this study. Female gender was significantly associated with less exposures. Further gender-specific studies in intraoral healing processes are needed.

Reviewer 3 - Suggestion 18:

18. P 14 L 9 - An obvious trend to reduce - what exposure rates were reported without the use of surgical splints? Be specific.

Response:

The reviewer is right; we modified these sentences according to the correct data.

p.13, l.11-17:

The use of surgical splints must be evaluated in prospective studies with more patients. According to authors opinion, these surgical splints may provide a better wound healing although the results being not significant in this study.