Author's response to reviews

Title: Use of screw locking elements improves radiological and biomechanical results of femoral osteotomies

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Author's response to reviews: see over
REVIEWER:
The authors present an animal study with the use of screw locking elements to improve radiological and biomechanical results of femoral osteotomies in sheep. The authors used a model of femoral osteotomies in sheep with four different plate configurations and two different endpoints at 8 and 16 weeks follow up. Altogether they created 4 different groups in 16 animals. The question of the authors was to evaluate radiological and biomechanical differences of the femoral bone after osteosynthesis with a DCP after 8 and 16 weeks. The focus in these 4 different groups was on the effect of two additional screw locking elements per plate osteosynthesis on the contralateral side of the osteosynthesis compared to an osteosynthesis without these screw nuts. The authors were able to present a favorabel outcome for the SLE in this sheep model compared to common DCP plates.

Nevertheless, the manuscript needs some revision and major improvements:

**Major Compulsory Revisions:**

*Background:*
- The authors claim in the conclusion of the abstract and the background that SLEs are cost effective compared to locking plates. This is part for the discussion, but it cannot be anticipated that the SLE are cheaper than all locking constructs on the market. Furthermore, it is not the hypothesis of the presented work to be cheaper on the market. This is an aspect for the discussion but nothing for conclusion. The statement to be cheaper is no justification per-se for the clinical application. The hypothesis of this work is not that SLE use is cheaper than locking plate use. However use of a technology that is cheaper than other, getting similar results, it is of increasing importance for surgeons of countries with limited budgets. In fact the cost-effective advantage of a technology introduced in their papers is outlined, both in the abstract and conclusions, by two papers quoted in our reference session, published in very important journals:

  Cost of this technology is out of our matter. However before writing our paper we compared the cost of a DCP with 8 not locked screws plus 2 SLE (provided by Surgival, Spain) with the cost of locking plates and 8 locked screws of different brands in Spain. Cost of locking plates constructs was between 3 and 5 times more expensive.

- Locking plates are not automatically abbreviated with LCP – these are locking compression plates from the Synthes branding. There are a couple more locking plates on the market with different locking mechanisms. The statement in the discussion is also false, that the locking mechanism “relies on screws threaded into the plate”. There are a couple more locking mechanisms on the market – the effect is the same, an angular stability to achieve the internal fixateur principle. We agree and have now changed to locking plates (LP).

- The introduction aims in a direction like the authors intend to compare LCP versus
SLE. The LCP plates are not part of the study or the results. They can be part of the discussion.

SLE concept was created to improve stability of traditional not locked plate-screw constructs, allowing enough micromovement to stimulate fracture healing at low cost. Currently locking plate technology is the gold standard of stability for osteosynthesis systems, mainly in poor quality bones. We summarize the principles, advantages and disadvantages of this technology to justify the introduction of a new and different system.

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Materials and Methods

- My major concern is the statistical pooling of the groups. The authors pool the results of the torsional stiffness of the DCP+6S+SLE and DCP+8S+SLE versus DCP+6S and DCP+8S on the other hand. Plus the 6S groups were sacrificed after 8 weeks and the 8S groups sacrificed after 16 weeks. I do not agree with this procedure and I am convinced that this is methodological not correct. The authors compare apple and oranges and the reason for this procedure is the low power of n=4 per group and p=0.068 (Wilcoxon Test) for all four groups. It’s a pity that the authors did a lot of nice experimental work in an elaborate animal model without regarding the minimum of “samples” to come to a positive result for the statistical testing. This makes me even more wonder, since the author obviously made their in vitro studies before (References no. 13-15 and 19).

We agree that the number of animals was small. However, according to the current tendency we tried to avoid more animal suffering. Although it was not pointed out in the manuscript, the initial setting for the study was of 6 animals per group. Four animals operated on without SLE died before the scheduled date due to excessive suffering and prostration in spite of veterinary care. So, we decided do not operate more animals without SLE. No animal operated on with SLE died before the scheduled date. To avoid unnecessary animal suffering we decided to operate on only 8 animals with SLE. We tried to show that SLE benefit was independent of the number of screws used in the construct. In fact it is showed that better results were observed when SLE was used both for 6 and 8 screws constructs in comparison with constructs without using SLE. The mean value and 95% confidence interval were quite similar in both groups, 6 and 8 screws, of the osteotomized bones operated on with SLE, and also in the osteotomized bones of both groups operated on without SLE. According to these results we assumed that number of screws used in the constructs and time passed after the operation had no influence on the final results. We have made some comments on this respect in the discussion.

- It is correct to assume that the data are non-parametric since only 4 samples are evaluated by the authors. Nevertheless, the differences between the groups DCP+6S vs. DCP+6S+SLE and DCP+8S vs. DCP+8S+SLE are significant with a t-Test for independent variables p=0.02 – and this is part of the authors hypothesis, to prove that the screw nut is better than the DCP alone. There is a little bit potential in the data, but the authors need to analyze their data more thoroughly.

We agree and have added some comments in the results and discussion.

- I do not understand exactly the principle of the SLE – is the mechanism a locking mechanism to avoid screw loosening of the nut, or is it a simple one by one thread with the same pitch of screw and nut?
The SLE acts locking the screw at the free end of this, beyond the far cortical, to avoid its loosening and stripping from the plate. The locked screw does not engage to the bone but just in the nut, allowing micromovement that stimulates healing of the osteotomy/fracture without impairing stability. As it has been shown with bone surrogates and now in this in vivo work one SLE at each side of the osteotomy is enough to allow stability of the construct.

- Implant failure in real life is not only associated with an insufficiency of bone or the construction material but with local infection of the bone. Were microbiological swabs or histological probes taken in those cases of failure to exclude this?

We studied histologically all the osteotomized bones and did not observe inflammatory reaction. No signs of infection were seen in any of the specimens studied in our work, including those which died before the scheduled time. No microbiological swabs were taken.

Results
- The manuscript merely states that loads were applied using a rate of $10^\circ$ per minute at an axial preload of 20 N. The stiffness results are subsequently presented as Nm. This is not adequate, as the results are uninterpretable unless the lever arm, and therefore the bending moment, is known. Further, the missing information renders the experiment irreproducible and prohibits comparison with the results of other studies. If the authors indeed applied load through a standardized lever arm, they can salvage this portion of the study by converting their Nm data into Nm/degree of angulation based on the length of the lever.

We agree. It was a mistake and our results should be shown as Nm/dg. It has now been corrected.

- Why were the radiological pictures not analyzed by a blinded or independent radiologist and/or surgeon? Easy to perform – 32 femora in 2 planes – i.e. 64 radiographs to give a statement.

Radiological pictures were analyzed by Prof Enrique Rodríguez, Professor of Radiology at the Veterinary School of University of Las Palmas de Gran Canaria. He could not act as a blind observer since the radiographies show clearly the differences between bones operated on with and without SLE.

Discussion:
- 3rd para: “odd bones” – what exactly are odd bones?
This is a term frequently found in the medical literature. It refers to bones which are alone in a segment (example: femur, humerus).

- 4th para: “scientific literature” I assume the authors rely only on scientific literature – a reference is needed here and the same for the statement that “Failures occur mainly due to screw loosening before fracture consolidation” – I think this statement is not true. Screw loosening is one failure mechanism for non-angle stable constructs. Please reference this statement.

It is widely assumed that the main reason for failure of non-locked plate constructs, in bones of poor quality, is screw loosening and stripping. Following journal guidelines we tried to avoid excessive references and for that reason we considered unnecessary to reference those statements. We have now added some references:


- I am missing the discussion of the technique used by Hammad (Acta Orthop. Belg., 2008, 74, 630-635) who used a similar setup with the difference to place the nuts directly under the plate – the advantage of this technique could be less surgical site denudation and morbidity?

See comments below


As pointed out before, following the guidelines of the journal we tried to avoid excessive references and only used recent ones to write our paper. Both the relative recent paper by Hammad and those quoted by the referee use the concept of Schuhli locking nuts. These nuts are located between the bone and the plate, avoiding screw stripping by fixing the screw to the nut and theoretically preserving periosteal blood supply. However this concept like many others has been abandoned and now the technology relies on screws locked directly into the plate. To be more concise we avoided use of old references and centered our discussion in current concepts. Anyway following the suggestion we have now reference the Schuhli concept in the discussion session.

Tables
Table 2:
- The analysis in SPSS with exact the data of the authors of Table 1 produces different results:
  False 1,39±0,33 – Correct 1,39±0,34
  False 1,19 – 1,62 – Correct 1,11 – 1,68
  False 2,34±0,47 – Correct 2,35 ± 0,48
False 2,03-2,65 – Correct 1,95 – 2,74 etc.

We have checked it and corrected

**Minor Essential Revisions**

Was the manuscript read by a native speaker? I doubt it because some of the phrases sound unfamiliar to me. I suggest a proof reading.

The manuscript was revised by Dr Susmita Hunt, Chief Editor, Biomedical Correction

According to the information in Internet this is a British company offering professional, high-quality and cost-effective scientific editing services for academic and industrial scientists wishing to publish their work in English-based medical and science journals (www.biomedicalcorrection.com)

*Background*
- First line – Internal fixation of fractures……
  The open reduction and internal fixation of fractures is one of the common used options to treat instable fractures.
  Not every fracture needs to be operated and not every osteosynthesis is a plate. Only instable fractures have to be operated and sometimes we use intramedullary nails etc.
  It has been corrected according to the suggestion

*Materials and Methods*
- The specification of the plate system is missing. Which brand?
  The information has been added

- The discussion tries to explain the reason why the authors did not use a torque delimiter – but what was the real reason?
  Like in normal clinical setting we did not use torque delimiter for not locking plates.

*Discussion*
- The authors often refer in the background and discussion part to the locking plate systems. Why did the authors not compare the SLE versus a LCP construct – for example by using only 2 locking screws and the remaining plate holes with non locking screws?
  The aim of our work was to evaluate the osteotomy healing in our animals using one fixation system (DCP) with and without use of SLE. We refer to the locking plate systems since they are mostly used currently due to the stability they provide to fixation.

- The authors enunciate the cost effective technology – how do we know?
  As pointed out previously we asked for prices to the firm which commercialized the SLE system in Spain and to the companies which sell locking plates in Spain.

- I would not try to support the experimental findings of the SLE with unpublished results from field reports of human applications (probably no ethical approval, CE or DIN?)
  The main author has operated on 15 patients affected of unstable clavicle fracture using a standard reconstruction 3.5 plate with one SLE at each side of the fracture. The follow up is between 12 and 18 months. Complete active range of movement of the shoulder
and arm was reached in less than 6 weeks with good and excellent results according to DASH and Constant scores. The cost of these constructs was 5 times less than the clavicle locking plate constructs normally used in our hospital. All patients were informed and consented to participate in the study. Ethical approving was obtained by the Local Committee of the University of Las Palmas de Gran Canaria (Ref. CEIH-2013-01). One paper is been prepared to be published with this preliminary results. He has also operated on several patients with osteoporotic humeral fractures obtaining very good results, but not all of them have enough follow up. According to the guidelines of the journal we have referenced this experience as "unpublished results".

Table 1: the decimals of the percentage can be shortened to one –
It has now been corrected according to the suggestion