Author's response to reviews

Title: Clinical and radiographic outcomes of the treatment of adolescent idiopathic scoliosis with segmental pedicle screws and combined local autograft and allograft bone for spinal fusion: a retrospective case series

Authors:

Ming Li (lf0907@gmail.com)
Xiaoming Yang (tely@mail.asiamedcom.com)
Suxi Gu (526468809@qq.com)
Xiutong Fang (fanger2009@gmail.com)
Jingjie Wang (wendypol555@163.com)
Jianqiang Ni (184718969@qq.com)
Dajiang Wu (renmys2000@sina.com)

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Author's response to reviews: see over
April 23, 2010

Re: MS: 2058339075305438, “Treatment of adolescent idiopathic scoliosis with segmental pedicle screws and combined local autograft and allograft bone for spinal fusion”

Dear Dr Shipley:

Thank you the time and energy you have spent on our manuscript and for the thorough review. We have carefully read the reviewer comments and have revised the manuscript based on them. As requested, below we have included the comments and our point-by-point responses to them.

We look forward to you continued correspondence.

Sincerely:

Dr Yang

Point-by-point response to reviewer comments

Editorial Adviser comments:

"Thank you for giving me the opportunity for look at this submission which is a report on a series of cases of operative treatment of adolescent idiopathic scoliosis. The data are derived from a retrospective file review from a department of orthopedic surgery in Shanghai, China.

Not being an orthopedic surgeon myself, I will restrict my review to the scientific issues in the paper. I cannot comment on whether the clinical findings are of relevance but they appear to be."
First, it should be clarified in the title that this is a retrospective case-series. Therefore by definition the inclusion criteria are somewhat liberal which is a scientific weakness but on the other hand a reflection of the clinical reality. Furthermore the number of patients is relatively small. Therefore, if the paper is published, it is to be considered as preliminary evidence without much scientific weight. This should be mentioned specifically in the discussion.

Author Response: Thank you for the good suggestion. We have revised the title as suggested, and included the relatively small number of patients as a limitation to the study.

All operations were performed by the same surgeon which is a weakness and should be discussed specifically since it limits the generalizability of the results.

Author Response: It is true that different surgeons may have different results due to differences in technique, however, the variation in the outcome was minimized since all the operation performed by the same surgeon in this study. This shows the validity of the method. In addition, many studies report results in which surgeries were performed by only one or sometimes 2 surgeons. Two examples are given below. We do understand your comment, however, and have included this as limitation of the study


The most important weakness of the paper from my point of view is that there is no account of the evaluation of the outcome measures. How was it performed (for instance the measurement of back pain)? Was it systematic? Are these measurements reliable and valid in relation to pseudoarthrosis? Who did it (was it the surgeon who had performed the surgery or a blinded person)? How were differences between baseline and follow-up calculated? Were there really no missing data (I find that hard to believe in hospital files)? All of these issues need to be clarified in the text.

Author Response: All the evaluations of the outcome measures were performed according to conventional methods. Quality of life and functional outcome was evaluated by administration of a Chinese version of the SRS-22 survey (Cheung KM, Senkoylu A, Alanay A, Genc Y, Lau S, Luk KD. Reliability and concurrent validity of the adapted Chinese version of Scoliosis Research Society-22 (SRS-22) questionnaire. Spine (Phila Pa 1976).
2007; 32(10):1141-1145) at the last follow up visit. The results of the SRS-22 are presented in the table below. The information above and reference citation have been included in the manuscript and the table has been added as Table 2. No data of the study subjects were missing.

SRS-22 score at last follow-up

<table>
<thead>
<tr>
<th>Domain</th>
<th>Average Score</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain</td>
<td>4.32</td>
<td>3.8-5</td>
</tr>
<tr>
<td>Mental health</td>
<td>4.37</td>
<td>3.8-5</td>
</tr>
<tr>
<td>Function/activity</td>
<td>4.56</td>
<td>4.0-5</td>
</tr>
<tr>
<td>Self-image/appearance</td>
<td>4.48</td>
<td>3.8-5</td>
</tr>
<tr>
<td>Satisfaction of management</td>
<td>3.80</td>
<td>2.5-5</td>
</tr>
</tbody>
</table>

I find it very difficult to believe that? no patients had complaints of back pain?. That would make them healthier than the general population in spite of extensive back surgery!

**Author Response:** We have described the patients’ responses exactly, and no patients had complaints of back pain. Perhaps adolescents are more concerned with the correction of their body shape and appearance and are thus more tolerant of pain. We have found adult patients with scoliosis often complain of back pain during follow-up.

Table 1 and 2 can be collapsed into one which in turn should be expanded to account systematically for the outcome measures.

**Author Response:** Thank you for this suggestion and we understand your concern. We have reviewed the tables and have deleted Table 1 and described its information in the text.

If the authors are able to deal with all the above issues, in my opinion the conclusion should be rephrased into something like: This retrospective case-series indicates that in situ autograft bone combined with allograft bone may be a promising method to be used in AIS treated with pedicle screw placement. Further prospective studies using systematic inclusion criteria, systematic follow-up and control groups, preferably in a randomized design, are needed to determine just how useful this procedure is."

**Author Response:** Thank you for the comments. We have rewritten the conclusion as follows: In summary, this retrospective case-series indicates that in situ autograft bone
combined with allograft bone may be a promising method to enhance spinal fusion in AIS treated with pedicle screw placement. By eliminating the need for iliac crest bone harvesting, significant morbidity may be avoided. Further prospective, randomized, case controlled studies using systematic inclusion criteria and follow-up are needed to determine the usefulness of the procedure.

Comments:
Abstract:
Results- there is no mention about average follow-up. Follow-up is very important on such paper. How did you analyze the fusion? How can there not be any revision surgery, complications or pseudarthrosis?

**Author Response:** All patients had a minimum follow-up of 18 months (range, 18 to 40 months). This was stated in the Results, and we have included this in the abstract. No revision surgery and pseudarthrosis were found during the follow-up. We have included this in the Results section.

Manuscript
Background: authors mentioned that search for other substitute was necessary due to high morbidity associated with iliac crest bone graft. So please give information regarding other bone graft substitutes and associated complications, so that you are using allograft mixed with autograft.

**Author Response:** Studies have indicated the risk of disease transmission is greater with fresh and fresh-frozen allograft bone than with freeze-dried bone. We have rewritten the sentence to focus on the topic of the study, the use of allograft bone mixed with autograft bone.

The purpose of this study is to determine the effectiveness of combined local autograft bone and freeze-dried cancellous allograft bone in the treatment of AIS with segmental pedicle screws and dual rod instrumentation. - Purpose is not clear. This is clinical results which will be excellent whatever may be the bone substitute. Purpose should be comparing complications, pseudarthrosis, or risk factors for non-union or infection like that. Clinical results cannot be compared for the success of a bone substitute.

**Author Response:** We have restated the purpose of the study as follows: Our aim in this study was to determine the presence of complications, pseudarthrosis, non-union, and infection using combined in situ local autograft bone and freeze-dried cancellous allograft bone in patients undergoing posterior spinal fusion for the treatment of adolescent idiopathic scoliosis.
Methods
Retrospective study- effectiveness of bone substitute cannot be checked by retrospective study.

**Author Response:** Thank you for the comment and we understand your point. We have rephrased the aim of the study. Please see our response above.

Criteria for surgical correction of AIS included- criteria are not clear. It is general. Suppose patient with 90# curves with Risser sign 0 or 1, what will you do? The study was approved by the Institutional Review Board of our hospital and informed consent was obtained from all patients and their parents.- How preoperatively or postoperatively. How can IRB approved a retrospective study without any case-control and measuring the effect of bone substitute in fusion.

**Author Response:** This situation described above is not common in AIS. It appears more frequently in children with idiopathic and congenital scoliosis. No patients with the situation described were in our cohort, however, if it had been encountered, surgical treatment would have been recommended. We believe that we have clearly stated the criteria for the surgical correction of AIS of the patients that were included in the study. The IRB of our hospital approved our retrospective review of medical records. We have rewritten the sentence for clarity.

Surgical Technique:
Anterior discectomy and release was performed in patients with rigid major curves >75° with a correction <50% in bending radiograms.- This means that this study is not with segmental pedicle screws. This is about just treatment of scoliosis with posterior/posterior and anterior combined approach.

**Author Response:** The number cases with the criteria described above was very small.

Local autograft bone was cut into match-like sticks, combined with freeze-dried allograft bone, and carefully packed onto the prepared surfaces.- this is the only line in a paper where authors compared the effectiveness of allograft in fusion. I think paper is just clinical and numbers of papers have reported clinical results with allograft mixed with autograft from laminae, pedicle or facet etc.

**Author Response:** To prepare a bone planting bed, the autograft bone was lifted with a bone chisel. Just prior to beginning the procedure of bone planting, allograft bones were soaked with 0.9% physiological saline for several minutes. The allograft bones were then imbedded within the autograft bones. The purpose of this allograft bone included here was to be as the scaffold for bone growth. We have attempted to clarify this in the manuscript.
Possible pseudarthrosis was determined by 1) persistent midline moderate-to-severe back pain, 2) a defect in the fusion mass or an unfused facet visible on radiograph, and 3) curve progression >10° from the initial erect postoperative radiograph-in this short follow-up it is not possible to comment about pseudoarthrosis on radiograms unless you have CT scan evidence. And criteria of possible pseudarthrosis are just assumption not confirmed by operative procedure.

**Author Response:** I agree with the above points of view. However, if the patients don't have the above three mentioned signs and symptoms during the follow-up process, additional CT examination not only increases the cost but also increase the possibility of radiation-induced adverse effects on children’s development and growth. In my personal experience the extra CT examination may increase a child’s concerns about the surgical effects.

Results-
All patients had a minimum follow-up of 18 months (range, 18 to 40 months).- too short follow-up. Minimum follow-up should be at least 3-5 years to comment on fusion.

**Author Response:** I agree. We have revised the conclusions regarding this issue. Please see our response above. No complete spinal fusion was evaluated in this study.

At the last follow-up, fusion was found to be complete in all patients, and no cracks were noted. No neurologic, cardiac, pulmonary, or infectious complications occurred. No Cobb angle change >10° between an immediate postoperative radiograph and the last follow-up erect radiograph was found.

There was no obvious loss in the correction, and the average loss of correction was 1.1° (range, 0° to 4°). No pull-out of pedicle screws or broken rods was discovered during the follow-up period. No patients had complaints of back pain and all returned to normal school study a month after surgery.- there is no complication in any system in patients with scoliosis which is unbelievable to me.

I think patients’ selection must be biased or included only those who did not have any complications. It is not consecutive series.

**Author Response:** No major complications described in the text appeared in the patients in our study. This might be related to the relatively mild disease of the patients, but also might be related to the reduced surgery time or other factors.

Discussion
First paragraph- authors might have noticed the follow-up periods. And what is different from those in this paper. All had used allograft mixed with local bone graft. I think most of the
patients having scoliosis are being operated with the same method, i.e. local bone with allograft mainly because associated poor bone quality could not give enough amount of bone graft.

Allograft bone is available in a number of shapes, sizes, and types, including fresh, fresh-frozen, or freeze-dried cancellous or cortical bone. Reference is mandatory. Asselmeier et al. [10] reviewed more than 1,000,000 freeze-dried allograft transplantations performed since 1951 and found no documented cases of HIV or other viral transmission. This is not the main concern but persistent serous discharge from the wound or increased wound infection should also be concerned.

Author Response: We have included a reference regarding the types of allograft bone. With respect to serous discharge, allograft bone does increase the amount of tissue exudate. Initially, the exudate drains via the drainage tube. In our patients, the drainage tube was removed after the volume of exudate decreased. There were no cases of infection or other adverse consequences due to excessive exudate in this study.

Other paragraphs are related with the advantages of segmental pedicle screw and authors said that segmental pedicle screw is associated with less pseudarthrosis. In such situation, what is the purpose of writing about allograft?

Author Response: Segmental pedicle screw fixation can achieve good stability. However, failure can occur if adequate inner fixation does not occur. The application of allograft bone can contribute to good integration and fusion of the fixed segments.

In limitations: authors agreed that follow-up is very less and curves were very small. These limitations are enough to say that the study is inappropriate. Another thing is that whenever reporting about effectiveness of bone substitute, it is important to have 1) follow-up of at least 3-5 years; 2) all surgeries with the same approach; 3) two groups: one treated with allograft with local bone and the other with only iliac crest grafts; 4) all parameters in both groups should be similar; 5) compare the complications and pseudarthrosis or infections in both groups. So it is highly recommended that such study should be case-control study with good follow-up.

Author Response: We agree with your points and have revised the purpose of the study (see our response above) and the limitations of the study.

Tables are inappropriate and do not give much information.

Author response: Table 1 has been deleted and its information is described in the text. We have included a table of SRS-22 scores at last follow-up.

Level of interest: An article of insufficient interest to warrant publication in a
Reviewer's report:
Li et al. performed a retrospective cohort study of 50 consecutive patients with AIS treated with posterior pedicle screw-rod instrumentation and fusion with a combination of allograft and local autograft bone. The purpose of their study was to compare the efficacy of this combination of allograft and autograft. Their primary outcome measures were pseudoarthrosis and Cobb angle correction. No clinical outcome data were collected. They reported no pseudoarthrosis cases at a minimum follow-up of 18 months and noted an average loss of correction of 1.1 degrees, with an average Cobb angle correction of 77.8%. No instrumentation failures occurred.

While this study is concise and fairly well written, the question posed by the authors is not well-defined. What do they mean by “effectiveness?” It seems that they will only be able to draw conclusions on radiographic outcomes. A better definition of their question is necessary.

Author Response: We have rephrased the purpose of the study. Please see our responses above. In addition, quality of life and functional outcome was evaluated by administration of a Chinese version of the SRS-22 survey (Cheung KM, Senkoylu A, Alanay A, Genc Y, Lau S, Luk KD. Reliability and concurrent validity of the adapted Chinese version of Scoliosis Research Society-22 (SRS-22) questionnaire. Spine (Phila Pa 1976). 2007; 32(10):1141-1145.) at the last follow up visit. The results of the SRS-22 score at the last follow-up are presented in Table 2.

The methods are appropriate. Was any standardized clinical outcome data collected?
Author Response: Quality of life and functional outcome was evaluated by administration of a Chinese version of the SRS-22 survey at the last follow up visit. The results of the SRS-22 score at the last follow-up are presented in Table 2.

The data are sound. Can the authors provide data on how much allograft was used per case.
How did they decide how much to use?

**Author Response:** The amount of allograft was determined by the length of the fusion segment such that the allograft combined with autograft completely covered the whole bone bed. We have included this in the manuscript.

Manuscript adheres to the relevant standards for reporting and data deposition. With regard to discussion and conclusions, I think the authors should include a section comparing their results to previous reports using iliac crest autograft. Also a section on what new data their study provides, as the ability to achieve fusion with allograft in AIS surgery has been reported by several prior studies.

**Author Response:** We did not find any studies specifically addressing iliac crest autograft, posterior fusion, and pedicle screws. A study by Betz et al. (listed below) found that pedicle screw fixation can be effective with the use of allograft bone only. We have included this reference in the discussion. Our current study was the first time to apply the Chinese version of the SRS-22 to evaluate the quality of life after surgical management of AIS.


Limitations are clearly stated. An additional limitation the authors should mention is the fact that this is a retrospective series with a relatively small n. Title should be “Radiographic outcomes after treatment of adolescent idiopathic scoliosis with segmental pedicle screws and combined local autograft and allograft bone for spinal fusion.”

**Author Response:** We have revised the title based on your suggestions and that of reviewer 1.