Author's response to reviews

Title: Cotrel-Dubousset instrumentation for the correction of adolescent idiopathic scoliosis. Long-term results with an unexpected high revision rate.

Authors:

Franz Mueller (muellerfj5@aol.com)
Herbert Gluch (bhz.wirbelsaeule@schoen-kliniken.de)

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Author's response to reviews: see over
The authors address the comments in the revised manuscript and provide a cover letter giving a point-by-point response to the concerns.

**First Reviewer's report; Reviewer: Jens Ivar Brox**

Reviewer's report:

**Major Compulsory Revisions.**

First, this is not the first 10-year follow-up. The first was published by Bjerkreim et al. in 2007.

*Authors comments:*

This is absolutely correct, and we have changed the text due to the follow up rate.

The conclusion is not supported by the data. The present study is a small retrospective review of 40 patients and only 35% reported patient related outcome which means that SRS-24 is not valid for the whole sample.

*Authors comments:*

This exception is correct, and we have changed the conclusion.

The poor results may be related to the surgical method applied, to patient selection or to the surgeons conducting the operations. This is not discussed.

*Authors comments:*

This exception is correct: The poor results are not directly related to the CD-system, but may be related to the surgical method used (long segment fusion with 13 segments), or due to the long surgical time. Therefore we have corrected the section „discussion“ completely.

Reference to other surgical methods has not been made.

*Authors comments:*

The study is due to the (historical) CD instrumentation, therefore it makes no sense to discuss other surgical methods like Harrington rod or so called third generation implants.

The design of the present study is weak and no firm conclusion can be made, but the authors should be able to better discuss their results.

*Authors comments:*

Without doubt, our study has only evidence level 4. On the other side and due to scoliosis surgery there exist no study with evidence level 1 or 2. We have completely changed the section „discussion“.

From the literature discussed, the reoperation rate is variable but low in most studies, in particular in the large studies. The present study reports the worst results of all, and most likely this is attributed to patient selection or the surgeons. As compared with Bjerkreim operation time was 325 min versus 202 min, and 13 versus 9 segments were fused, the age of the patient was 16 versus 16.8, 23/40 versus 99/100 had King-Moe II-III, the major curve was reduced 48% from 69 degrees versus 66% from 56 degrees. In particular the discussion and the conclusion in the manuscript and the abstract needs a major revision.

*Authors comments:*

We have changed the section „discussion“ and „conclusion“ in the manuscript completely.

**Minor essential revision:**

The primary and secondary goal of the study is not stated, just that the authors conducted a retrospective study.

*Authors comments:*

The primary aim of the study was the long term outcome of patients with AIS surgical treated by CD instrumentation. Due to high revisions rate, the secondary aim was the analysis of the the complication. We have changed the text.

The treatment method and the patients is adequately described, but SRS-24 is not described.

*Authors comments:*

Due to the lengths of the manuscript, we think it is not necessary to describe the SRS-24 in detail.

**Thank you very much for the review.**
The authors address the comments in the revised manuscript and provide a cover letter giving a point-by-point response to the concerns.

**Second Reviewer's report; Reviewer: Jack Cheng**

Reviewer's report:
There are a number of major concerns:

1. Small series of patients with mixed age of operation - from 13-21 yrs old
   **Authors comments:**
   *It is in accordance with many other studies (e.g. Bjerkeim et al. 2007; Boss et al. 2007), the mean age at surgery was 16.0 years.*

2. Mixed curve type included - from right thoracic, left thoracic to thoracolumbar, lumbar and double curve. Severity of curve ranged from 50 to 100 deg Cobb angle!
   **Authors comments:**
   *It is in accordance with many other studies, too. Moreover, the most curve type in the study included typically right thoracic curve.*

3. Construct of CD instrumentation not analysed
   **Authors comments:**
   *The construct of the CD is analysed sufficient, e.g. length of segments, cross rods.*

4. Very high rate of revision 47.5% and infection accounting for 25%. Are they related to the severity of curve, curve type, instrumentation segment....... These have not been analysed - only average figures were provided
   **Authors comments:**
   *This comment is absolutely correct: The poor results are not directly related to the CD-system, but maybe related to the surgical method used (long segment fusion with 13 segments), and maybe due to the long surgical time. Therefore, we have completely changed the section „discussion“.*

5. Only 14/40 completed to SRS 24 questionnaire, the latest clinical outcome and functional status not clear
   **Authors comments:**
   *We have given sufficient results of the SRS, in accordance with other studies. 14 out of 40 patients (35%) completed the SRS-24 questionnaire after a mean of 14.3 years postoperatively. In the SRS-24 questionnaire, the total score averaged 93.3 points out of a maximum 120 points (min. 71 to max. 106 points) at the follow-up. The analysis of the questionnaire showed no significant differences between the 5 patients with instrumentation still in situ (average 96.4 points) and the 9 patients after the removal of the instrumentation (average 91.5 points).*

Quality of written English: Needs some language corrections before being published
   **Authors comments:**
   *The written English language is acceptable rated by the other five reviewers; moreover the language was checked by a native speaker!*

*Thank you very much for the review.*
The authors address the comments in the revised manuscript and provide a cover letter giving a point-by-point response to the concerns.

**Third Reviewer's report; Reviewer: Toru Maruyama**

**Reviewer's report:**
This is an interesting abstract regarding the complication with CD instrumentation for scoliosis surgery. The authors reported exceptional high rate of complications, especially late infection. There are some points to be clarified.

**Major Compulsory Revisions**

1) The latest radiological follow-up was 57 months after surgery. Clinical outcome in terms of SRS-24 score was obtained in only 35% of the cases. So it is difficult to consider this study as “with a minimum of 10 years for the entire study group” described in conclusions section.

*Authors comments:*
*This is absolutely correct, we have changed the text due to this exception.*

2) As adolescent idiopathic scoliosis, patients over the age of 18 should be excluded from the study population.

*Authors comments:*
*It is in accordance with many other studies (e.g. Bjerkeim et al. 2007; Boss et al. 2007), the mean age at surgery was 16.0 years, including only some patients older than 18 years.*

3) Without bacteriological findings of any pathogens, how could the authors diagnose infection? Please describe in detail. Were there other findings suggesting infection?

*Authors comments:*
*First, infection is typically a clinical diagnosis, by pus, fistula, redness of the skin, e.g.. Second, the histological results showed in all cases putrid webs.*

Where were the fistulae located? Sometimes we experience the breakdown of the skin over the prominent implant in thin patients.

*Authors comments:*
*The most fistulae (5 out of 7 fistulae) were located at the distal end of the instrumentation.*

Were there obvious abscess formations around the implants?

*Authors comments:*
*The most fistulae were without obvious abscess.*

What kind of antibiotics was used for how many days?

*Authors comments:*
*Only cephalosporin third generation was used for 5 to 7 days.*

4) Do the authors mean that there are a single case of metallosis, a single case with loosening of the pedicle screws, and almost all cases with breakage/fractures of the transverse connectors?

*Authors comments:*
*We have changed the text, with more detail information due to the patients treated for LOSP.*

5) Sometimes it is difficult to remove CD systems. Are there any specific technique used by the authors?

*Authors comments:*
*This is absolutely correct. Implant removing of CD is often very difficult, however we have no specific techniques, only „keep cool“!*

6) Regarding the patients with LOSP, did the implant removal well relieve them of pain?

*Authors comments:*
*We saw no significant difference between patients after removal of implant or patients with implant in situ, however we achieved only 14 out of 40 patients for SRS-24 and 14.3 years post surgery.*

**Thank you very much for the review.**
The authors address the comments in the revised manuscript and provide a cover letter giving a point-by-point response to the concerns.

Fourth Reviewer's report; Reviewer: Behrooz Akharnia
Reviewer's report:
I enjoyed reviewing this manuscript. I have always felt that we need more long term follow ups to have a better understanding of the results of treatment methods we use. I congratulate the authors for this undertaking.

My general comments are:
1. Although there is no question that this study is a long term follow-up, I am not clear what the actual clinical and radiographic follow-up was. The medical files were studied at 14.3 years. In the next sentence the average follow-up was noted was 57.4 months. Does this mean that the patients were seen in some points and did not have radiographs or they were lost?
I suggest that the authors clarify this by indicating when the patients were seen and when the radiographs were taken so the reader understands what the true nature of the follow-up is.
Authors comments:
We have changed the text, due to the follow up.

2. I understand that the preoperative SRS 24 may not be available for the group which would have provided an excellent comparison. However, the low rate of follow-up SRS 24 data reduces the quality of the study and raises concerns of how the other 65% are doing long term. Any attempt to raise this follow-up will improve the quality of the study.
Authors comments:
We tried our best, however it was not possible to follow up more patients 14 years postoperatively for different reasons. Sorry!

3. The rate of revision is interesting since it is a high rate and almost all occurred within the first 4 years. Other studies with comparable follow-up (over 4 years) did not report such a high revision rate in the first few years of follow-up. I wonder if the authors have any explanation.
Authors comments:
We tried to have any explanation, however we documented only one significant influence. We have changed the section „discussion“ completely.

4. The same concern is for infection rate of 25% which I believe is one of the highest reported for AIS patients. Although in conclusion they state that the reason for high rate of infection is unclear, this high rate of infection combined with other implant issues may need more explanation in discussion.
Authors comments:
This is absolutely correct, therefore we have changed the section „discussion“ completely.

5. Conclusion should have a take home message from the data they presented. What the reader is getting is that there is a high rate of revisions and implant removal (more than any previous reports) but the reason will remain unclear and reader may not get any information what to expect and what they should do differently or if any other implant system would show the same results if studied long term.
Authors comments:
This is absolutely correct, therefore we have changed the section „discussion“ and conclusion completely.

Minor issues:
Please check the references again. There were few references that did not match the numbering such as Cook (19) which was actually (20).
Authors comments:
This is correct, thank you very much.

Also the review of the literature can be shorten for better reading.
Authors comments:
Therefore we have changed the section „discussion“ completely.

In summary, I feel that the paper provide a long term follow-up in a consecutive series of AIS patients treated with CD instrumentation and should be published with above suggested revisions.

Thank you very much for the review.
The authors address the comments in the revised manuscript and provide a cover letter giving a point-by-point response to the concerns.

Fifth Reviewer's report: Lawrence Lenke
Reviewer's report:

What type of bone graft was used for the fusions?

Authors comments:
We have used only autologous bone grafting from spine/lamiae and or pelvis.

It is a bit confusing as it says that at the time of the empiric data collection, after an average period of 14.3 years post surgery, it was attempted to contact the patients via telephone…it was only possible to assess 14 out of 40 patients (35%). So can the authors detail exactly how long of a radiographic and clinical follow-up for most of these patients?

Authors comments:
This is absolutely correct, therefore we have changed the text.

I am very surprised by the high infection rate early on, which was listed as 25%. Can I assume these were all chronic indolent late infections from skin flora? In addition, I am a little surprised of the 20% implant removal rate for late operative site pain (LOSP). Do the authors have any thoughts as to why these patients experienced pain?

Authors comments:
Maybe, the late infections were all chronic indolent infection from skin flora, however, we incubated all swabs 48 hours only at this period (1990-1992!), therefore it was not possible to detect e.g. P. acnes.
Due to these results, we have changed the section „discussion“ completely.

For the SRS scores, was there a statical significance in the patients with instrumentation still in place versus those with removal? If so, would you please list the p values?

Authors comments:
We found no statistical significance between patients with or without instrumentation in situ.

In addition, were the late infections or LOSP patients correlated with crosslinks at all? We’ve seen that anecdotally increase with chronic infections over crosslinks in our patients recently.

Authors comments:
The high revisions rate due to infection and/or LOSP was not significantly influenced by crosslinks.

Thank you very much for the review.
The authors address the comments in the revised manuscript and provide a point-by-point response to the concerns.

**Sixth Reviewer’s report:**

Page 1. The article in Spine by Wood KB, et al. demonstrates that C-D rotates the entire spine and not selective derotation of the apical vertebrae.

Authors comments:
Maybe this is a mistake, this conclusion is neither directly nor indirectly mentioned in the article and moreover not the topic of our study. On the other hand, we like to point out, that rotation by posterior instrumentation is more translation than rotation proved by many other authors/studies.

Page 2. This is an interesting admission that prophylactic antibiotics were not given immediately pre-operative and intra-operative if needed. The literature does not support the efficacy of post-operative antibiotics. Because the follow up is 35%, this report is Level IV significance. Is the follow up determined by the time to last x-ray or time of the telephone follow up?

Authors comments:
Maybe this is a mistake, too. We have given antibiotic all patients preoperatively as a single shot, as described in section „Materials and Methods“ clearly.
It is correct, we conducted only a study with an evidence level 4. On the other hand, due to CD instrumentation, there are no Level 1 or 2 studies in the literature.

Page 3. Are the statistics for the secondary curve those that were instrumented or spontaneous correction? Was there a uniform loss of correction or did some not progress as in Lenke’s report and others progress significantly implying failed fusion?

Authors comments:
The secondary curves were instrumented, because we fused 13.4 segments at average. We documented only significance influence due to distal end of instrumentation, therefore we completely changed the section „discussion“.

Page 4. An infection rate of 10% is alarming. Was the time to revision for infection different from those for other indications, i.e. were they early or late infections? Loose or broken implants and metallosis all imply motion suggestive of failed fusion. Were x-rays obtained at 14.3 years?

Authors comments:
Within the first 30 days post surgery, 3 out of 40 patients (7.5%) received early operative revision for the dislocation of hooks or rods. At an average of 45.7 months (range 11 to 142 months), 19 out of 40 patients (47.5%; including 2 patients with early revision) received late operative revisions. The reasons were late infection (10 out of 40 patients; 25%) with the development of fistulae (7 cases) or purulent secretion (3 cases), which was resolved with the complete removal of instrumentation after all. The average time until revision was 35.5 months (range 14 to 56 months) after CD instrumentation.
There were no bacteriological findings of any pathogens after a maximum time of cultivation of 48 hours. Furthermore, complete implant removal was necessary in 8 out of 40 patients (20%) for late operate site pain (LOSP).
We have changed the text due the the follow up.

Page 6. Soft tissue rubbing on metal causes a burse. Metal on metal movement causes fragmentation or metallosis. Lenke’s report (22) of no broken implants or correction loss at 6 years implies a solid fusion.

Authors comments:
This is absolutely correct, that soft tissue rubbing on metal causes a burse, and metal on metal movement causes fragmentation or metallosis. However it is still not clear, if these both irritations can induce late infection.

Page 7. Fastidious and exotic organisms require prolonged incubation and or different media for identification.

Authors comments:
This is absolutely correct, however, at the study period (1990 to 1992) all swabs were incubated routinely 48 hours only. Since some years, all swabs are incubated for 14 days, routinely; e.g. for Propionibacterium acnes.

Thank you very much for the review.