Dr. Jin-Xin Kong
Science Editor
World Journal of Orthopedics

11/22/2016

Dear Dr. Kong,

Re: Manuscript reference No. 29710

Please find attached a revised version of our manuscript “Ponseti Method Treatment of Neglected Idiopathic Clubfoot: Preliminary Results of a Multi-Center Study in Nigeria”, which we would like to resubmit for publication as a retrospective study in the World Journal of Orthopedics.

Your comments and those of the reviewers were highly insightful and enabled us to greatly improve the quality of our manuscript. In the following pages are our point-by-point responses to each of the comments of the reviewers as well as your own comments.

Revisions in the text are shown using yellow highlight for additions, and strikethrough font *[~~example~~]* for deletions. In accordance with reviewer 2’s suggestion, we removed table 4. We hope that the revisions in the manuscript and our accompanying responses will be sufficient to make our manuscript suitable for publication in the World Journal of Orthopedics.

We shall look forward to hearing from you at your earliest convenience.

Yours sincerely,

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Responses to the comments of Reviewer #1

1. In the Materials and Methods: ? “All patients were treated on an outpatient basis. “ However, In the discussion you stated that “with very rare cases being done in the operating theatre.” Will be interesting to know how many cases went to theater for tenotomy and what was the indication for this in terms of age or socioeconomic standard. ?

Response: Because of the limited access to sterile instruments and the ability to set up a sterile field, two of the twelve centers performed tenotomies in the operating theatre. Text has been added to reflect this.

2. After tenotomy protocol was not clear. It will be more interesting to define the percentage of patients were using the brace and who that you couldn’t provide them the brace due to limited resources. Also, for the patients used the brace, no data regards the bracing compliance or bracing schedule as mentioned, only night bracing (No full time bracing for 3 months as was defined in the original reports of Ponseti). ?

Response: At the time of the study, each of the centers used their own local orthotics/cobblers for brace creation so it’s very difficult to standardize. In 2016, all centers have been provided with “Iowa braces” provided by the Ponseti International Association. It is correct that the providers did not use full time bracing for 3 months as defined by Ponseti. This is due to the age of the patients as many of them are walking and running (providing their own dorsiflexion and stretching) and would not be compliant with full-time bracing. Because our study is only focused on the initial correction of the deformity, we did not follow up with compliance and bracing specifics. Future research into these outcomes will be interesting.

3. The statement that Pirani and Dimeglio scoring system have not been validated for the neglected population requires reference.

Response: This statement has now been referenced and two sources added concerning Pirani scoring.

4. In the Results: ? It is essential to analyze the 26 patients underwent surgeries, which of them had received only tendon transfer and which had only tendon Achilles lengthening, in one side and which of them needed extensive soft tissue release or boney surgery on the other side. As the first group you can`t consider them of the failure group, as it is known that the tendon transfer is considered a part of the Ponseti protocol, as this was reported in 20-40% in the original Ponseti reports. ?

Response: We do not have the data on which procedure the patients received. And although it’s true that tendon transfer can be considered part of the Ponseti protocol, one of the main objectives of this study is to show that neglected clubfoot can be corrected non-operatively as that is most beneficial in the low resource setting. Text was added to Materials and Methods section to reflect this.

5. It is interesting finding that the older age group required more number of casts/foot. However, a statistical correlation will be required to prove your finding whether it will be statistically significant or not (P-value). ?

Response: Single factor between-group ANOVA was performed on the data and there was found to be no statistically significant difference between the groups (p=0.78). This has been added to the text and the table.

6. How did you define failure in the PAT? Did you consider complications, as infection, bleeding, important structures injury or incomplete tenotomy?

Response: Failure of PAT was defined as an attempt at the procedure that did not result in at least 0° plantigrade correction of the foot. Complications were not recorded so we do not have data on them.

7. In the Discussion: ? You stated that "PAT's were nearly all performed under local anesthesia with very rare cases being done in the operating theatre." It will be interesting to define the number of patients taken to operating theater for PAT and the indication for that, either the age or the socioeconomic standard.

Response: As discussed in the response to comment 1, two of the twelve centers performed tenotomies in the operating theatre for better infection control. Because of the limited resources available at these two hospitals, policy was to only use sterilize instruments in the operating theatres and not in clinics. Text added to reflect this.

Reviewer 1, thank you very much for your questions and input on this paper. We would be glad to respond to any further questions and comments that you may have.

Responses to the comments of Reviewer #2

1. I enjoyed reading the manuscript illustrating success with the Ponseti method in yet another LMIC environment, which is very encouraging. My chief concern is that there is no data presented on grading of the feet, and that we are unable to evaluate the response to treatment based on severity and age.

Response: Thank you very much for your comments and insight on our paper. We agree that this is a weakness of the paper but unfortunately, there was little to no Pirani or Dimeglio scoring data available from treatment in these centers. At the time of this study, practitioners in Nigeria were only entering into the clubfoot registry information on patient characteristics (M/F, age at beginning treatment, other health conditions), number of casts required for each clubfoot, tenotomies, and defaults on treatment (loss to follow up before treatment completion or opting for surgical intervention). Although Pirani scoring is part of the International Clubfoot Registry, because of the time constraints and lack of adequate support staff in the lower resource setting, logging the scoring data at each visit for each patient is extremely difficult at most centers.

2. Materials and methods: Page 2, line 18: Does this represent all cases done at each site, or a consecutive series of all patients treated during those years?

Response: This indeed represents all cases treated by Ponseti-trained providers at each site from January, 2010- July, 2015.

3. Page 2, line 34. Statement about validation for neglected can be left for the discussion under limitations, probably not best to leave in method section. Or, is this being used to justify that there is no data in the results section concerning initial grading of severity?

Response: The latter suggestion is correct. Although some of the literature on neglected clubfoot treatment uses Pirani or Dimeglio scoring data, these systems were developed in the grading and monitoring of improvement during casting in newborn populations. There is no literature currently on whether they have similar reliability in older populations such as in this study. We felt it was necessary to include this piece of information in the methods section to clarify that although we did not have data on severity grading in our results, these forms of grading have not been validated for our study population.

4. Results: Page 3, line 5. So data was available for all 225 patients who met the inclusion criteria?

Response: That is correct.

5. Page 3, lines 4-7. By correction do you mean a plantigrade foot? The rates of initial correction seem excellent. How do the authors define failure? One could suggest that failure would be the need for intra-articular surgery (PMR or PMLR), and that the choice to do a tendoachilles lengthening might not be a failure since it's extra-articular?

Response: Yes, by complete initial correction, we indicate a plantigrade foot (text added to manuscript to clarify). You are also correct that an Achilles lengthening or tendon transfer are part of the Ponseti protocol. However, we elected to define failure as any need to resort to these more intensive procedures as one of the goals of this study was to show that neglected clubfoot could be treated non-operatively in the low resource setting (text added to Methods section to define failure).

6. No data is given on the initial Pirani or DiMeglio scores, and many feel that it is flexibility rather than purely age that determine the response to treatment. Rather than breaking down the age ranges into 1-2, 3-9, and > 10, might be nice to simply make a table which shows years 1 through 13 or whatever the maximum was, what the mean Pirani/DiMeglio was for each age, # casts, and tenotomy versus Achilles lengthening or whatever surgery was performed. This would allow the reader to grasp the data.

Response: Because of the lack of scoring data and the lack of scoring system validation for the neglected clubfoot population, we chose to split our data into these three groups, essentially toddlers, children, and adolescents. We felt that this would best illustrate to the reader the effectiveness of Ponseti method in each age group and maintain large enough group sizes so that outliers would not skew the average casts. We have added in the max age (16) into the text and Table 2. Also, we do not have data on which surgery was performed, just if it was performed so we cannot add that information to the table.

7. Page 3, line 13. Overall rate of tenotomy is very low, which underscores the need to represent the data on initial Pirani or DiMeglio scores. It is likely that a subset of cases were positional equinovarus rather than true clubfoot. Recognizing that in either case the deformities needed to be corrected and that treatment was successful, it would still be nice to reader to know the breakdown by severity. This could be accomplished by revising Table 2 as suggested.

Response: We agree that it is possible some cases may have been less severe equinovarus, but because scoring data was so severely limited, this analysis is not possible with this study. And as you mention, in either case the deformity requires successful treatment which can be accomplished with the Ponseti method as described in this study. With more resources and support staff in Nigerian clubfoot clinics, we hope to look into these factors in future research.

8. Discussion: Page 3, Line 30. There are several other recent references concerning Ponseti in older age groups including Banskota et al Bone Joint J 2013

Response: We have already cited the Banskota 2013 article (source 10). Two sources for neglected clubfoot treatment with Ponseti from 2016 added.

9. Page 4, line 27. Not sure what you mean by phenotype. The main question is that of flexibility/rigidity of the deformities treated, which can be illustrated by showing the data for Pirani/DiMeglio scores as suggested in Table 2 and in the results section.

Response: Because we do not have the grading system data, we are illustrating that the biological characteristics of our population such as sex distribution and laterality of clubfoot are similar to newborn populations and there is no cultural gender bias or skew in treating neglected bilateral vs unilateral clubfoot.

10. Page 4, line 37. Not sure what you mean by provider preference? There are clear indications for tenotomy using Ponseti method. Could a number of patients may have had an untreated positional equinovarus deformity? This is why reader needs to know the grading for the feet.

Response: "Provider preference" may not have been the best phrasing for our intended meaning. The providers in some of the treatment centers are limited in their ability to perform tenotomies because of lack of adequate sterile instruments and local anaesthetic. It's also correct that some of these patients could have had positional equinovarus deformity and text has been added to reflect this.

11. Page 5, line 8-10. Need to know how many patients were left out because of "variable data collection", and how many patients had grading data available.

Response: Text added to include this. No patients had grading data available.

12. Page 5, lines 12-19. This information is not related to the research study and should probably be deleted.

Response: Paragraph has been cut.

13. Page 5, lines 20-26. This might be included in acknowledgments but is not related to the research question

Response: Paragraph has been moved to Acknowledgments.

14. Figure and Tables: Table 2. The rate of tenotomies is quite low relative to Ponseti's work and that of other studies except in Malawi (Tindall et al). Perhaps there were many positional clubfeet.

Response: We agree and attempt to address this in the Discussion and in Response #10 above.

15. Figure 3 is a nice algorithm but does not relate to present research study, except that all patients were treated by Ponseti method. Does not add to paper and can consider deleting it

Response: We feel that the algorithm in Figure 3 is helpful in guiding clinicians working in Nigeria and other low resource settings in treating neglected clubfoot. We would prefer it remain with the text if possible.

16. Table 4. Not sure how this technique guide fits in the setting of a research study. Some of these points may be discussed as lessons learned but otherwise table does not add to the paper and should be deleted.

Response: Table 4 deleted.

Reviewer 2, thank you very much for your questions and input on this paper. We would be glad to respond to any further questions and comments that you may have.