Author’s response to reviews

Title: The role of cervical Electrical Impedance Spectroscopy in the prediction of the course and outcome of induced labour.

Authors:

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Author’s response to reviews:

COMMENTS
Reviewer 1

We welcome the comment of this reviewer that this is a novel method of assessing the cervix with regards to its inducibility. This is the principal reason we are of the opinion that the study will be of interest to the readership of BMC Pregnancy and Childbirth.

Concerns about the data analysis and writing:

The reviewer repeats several concerns and we have categorised them:

1) A very large number of analyses were performed - this would greatly increase the risk of spurious significant results.

Response: We do not understand how extensive data analysis leads to spurious significant results. We studied probes of 4 different dimensions but detected significant results with only the 12mm probe at a very specific frequency range. Our modelling studies had predicted that cervical stromal changes were most likely to be identified by this probe which delivered the highest stromal fraction of injected current and at these frequencies. These electrical frequencies at which we detected significant results also demonstrated differences in CR with parity and duration of labour. It would therefore be extremely unlikely that all our observations simply occurred by chance. It is noteworthy that this probe dimension, at exactly these frequencies, has also demonstrated the best repeatability and reproducibility (inter-class coefficient of correlation >0.95, coefficient of variation <5%) of all probe designs employed in our experiments, consistent with our clinical observations in this study. The report of the good reliability of this probe is under review in a technology and measurement journal.

2) The outcomes highlighted (labour > 12 hrs and all cause Caesarean delivery) are not appropriate outcomes for assessing cervical favourability (inducibility). The most appropriate measures are e.g. vaginal delivery within 12 or 24 hours, induction to vaginal delivery interval (perhaps also including cases of Caesarean for failure to progress).
Response:

- The numbers of women who had CS for failure to progress in labour and failed induction were small for extensive analysis. In the light of this reviewer’s suggestion, also alluded to by Reviewer 2, we have now report the predicted outcome of vaginal delivery rather than all cause CS and have clarified this in the entire manuscript.

- There is no universally agreed outcome for assessing inducibility on the basis of which this reviewer can make the assertion he/she makes. Indeed the age-old controversy regarding whether “failed induction” relates to failure to initiate labour or to failure to achieve vaginal delivery when labour has been successfully initiated (MacVicar 1971, BJOG Vol. 78. pp. 1007-1009) remains without resolution. Over the last 40 years individual authors have therefore pre-defined labour outcomes for their studies. All such outcomes are valid. The outcomes we have described have been employed in several other studies which we have referenced in this manuscript in relation to the Bishop score and ultrasound cervical length. We encourage this reviewer to read these references. We have opted for 2 outcome measures which really do not differ materially from the suggested outcomes by this reviewer: the “time to onset of labour (ripening)” added to the “time from onset of labour to the end of labour (the duration of labour)” equals the “induction to delivery interval” which the reviewer suggests! However whilst time to onset of labour and the induction to delivery interval are closely related they are, in fact, different as one relates to the preparation for labour whilst the other summarises the labour itself. Analysing them separately may answer 2 potentially different questions: prediction of pre-labour uterine preparation (including final phase of cervical remodelling) and prediction of duration of labour. The reviewer also suggests vaginal delivery as an outcome measure. We agree with this suggestion and have included this in this version. Predictive accuracy for all cause vaginal delivery would be exactly the same as for all cause caesarean section- a case of whether the glass is half full or half empty. Nonetheless, for clarity, we have now also reported data on vaginal delivery within 24 hrs of assessment in the entire manuscript.

We fail to see the logic of “perhaps including cases of CS for failure to progress into data regarding the duration of labour” since one is a categorical variable and the other a continuous variable. Once a decision has been made to deliver by CS it becomes impossible to determine the duration had labour continued.

3) Length of labour is largely dependent on efficiency of uterine contractions and degree of cephalopelvic disproportion (due to absolute sizes as well as baby posture) - it is not that relevant to state of the cervix (after all the starting point of active labour is at least 3 cm dilatation where cervical resistance is no longer the issue).

Response:

Length of labour is a complex multifactorial process that depends on the passenger, the passages, and the powers. The cervix is a main player as innumerable studies have shown. The efficiency of uterine contractions cannot be divested from the state of the cervix. We consider the studies by Uldberg et al

4) It must also be said that the number of total Caesarean delivery is low (33) and I suspect the number of women with active labour > 12 hours (it should be stated) is also low given that mean (sd) labour duration was 329.2 (194.8) minutes. Hence with such low numbers, multivariate logistic regression analysis results will not be that robust. Also the dependent covariates used should be stated.

Response:
We agree with this point and have added some comment in the results and the discussion as suggested. However despite the small numbers who had CS we still found some association between resistivity and mode of delivery. We have also added the dependent covariates that were used.

Response to comment number 5 and 6:
Our discussion did cover these comments and have been further clarified. Prior vaginal delivery was a variable controlled for in the logistic regression model and we stated this in the results. We also did include data on resistivity by parity but needed to remain brief and concise as required by the Journal’s instructions to authors.

Reviewer 2
This reviewer’s comments were very constructive and helpful. The suggestions, which were all minor, have been incorporated into the manuscript.

1) Please do not use reference No. 4 to describe Bishop score.
Response: We agree and have moved Ref 4 to the category on ultrasound cervical length.

24(7):933-9. Probably it is better to write that there is conflicting data concerning predictive values of the cervical ultrasound measurements.

Response: We could not agree more. We are highly conversant with these references but restrictions on numbers precluded us citing all of them. Nonetheless we have modified the write up on ultrasound to indicate that data is conflicting.

3) There is nothing written about induction in the paper No. 16

4) Figure 1. The picture has already been shown in your previous paper (reference No. 16). I suggest not to use the same picture again. Instead of this it would be better to refer to your previous paper.

Response:
Paper number 16 referred to the unripe cervix by the Bishop score in that cohort. We have referred to it as one of the previous studies during pregnancy which involved the EIS technique. We think this is appropriate. Figure 1 is a newer version of the probe and differs from that shown in our previous manuscript. However we have removed this since the basic principle is the same and we have referred to previous work. We will be happy to re-include this if the editors request us to.

5) It is not a good idea to mix various methods of induction in one study. To achieve more accurate results, it would be better to analyze one method of induction at once. For example, you could either use methods with prostaglandins or only those with ARM.

Response:
Since the clinical assessment is used to determine both those who require prostaglandin induction and those who have amniotomy (ARM) we feel it is appropriate to analyse all participants together. Our objective was to study resistivity and bishop score for all indicated induction of labour irrespective of method ultimately employed since this is the process routinely employed in clinical decision-making.

6) Major Compulsory Revisions:

Response;
These are highly helpful comments for which really minor revisions were requested. Many of these were already in the text but we have included the details requested in the methods and discussion as appropriate. We have included analysis for prediction of all vaginal delivery. Analysis for prediction of CS for failure to progress was limited by the small sample size for women who were delivered for solely this indication.