Author's response to reviews

Title: Lung ultrasound: a useful tool in diagnosis and management of bronchiolitis

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Author's response to reviews: see over
Dear Editor(s),

Enclosed please find the revised version of our paper entitled “Lung ultrasound: a useful tool in diagnosis and management of bronchiolitis” (MS: 8589807615185432) revised on the basis of reviewers’ suggestions.

We wish to thank you and the Reviewers for your interest in our paper and for the useful comments we received.

We have dealt with all the points of criticism raised by the Reviewers, and have modified our paper accordingly.

We look forward to hearing from you in due course.

Yours sincerely,

Mariano Manzionna
Referee #1

We thank this Referee for the constructive comments and suggestions. This is our point to point reply.

1. The authors state that the lung ultrasound “permits the identification of those infants that are in need of supplementary oxygen” but it is not clear if lung ultrasound identifies patients that will need oxygen not identified by clinical evaluation. Are ultrasound findings able to intercept patients that will need supplementary oxygen in the next hours or days also when saturation is more than 94% or capillary blood oxygen tension is more than 45 mmHg. This is very important and should be clarified. Otherwise the role of lung ultrasound is questionable because nothing is added compared with clinical evaluation.

We calculated the specificity, sensitivity, positive predictive value and negative predictive value of the sonographic profile to predict the need for supplementary oxygen also when, during the scan, saturation was more than 94% or capillary blood oxygen tension was more than 45 mmHg.

2. The pediatric sonographer found 9 normal ultrasound pattern, while 12 by radiologist sonographer in patients affected by bronchiolitis. This data should be explained and should be specified the clinical score in these patients.

The pediatric sonographer found 9 normal ultrasound pattern in patients clinically diagnosed with a mild bronchiolitis (clinical score: 1-4).
The radiologist sonographer found 12 normal ultrasound pattern in patients clinically diagnosed with a mild bronchiolitis (clinical score: 1-4).
Three of the 12 infants scanned by the radiologist were considered with a mild bronchiolitis by pediatric sonographer.
None of the 12 infants with normal ultrasound pattern need oxygen supplementation in the next hours or days, despite diagnosed as affected by bronchiolitis.
Maybe the pediatric sonographer overdiagnosed US data because avoid observing the infants.

3. Was lung ultrasound examination performed every day? Is it possible to know if these normal ultrasound infants developed ultrasound abnormalities during the next days?

Yes, we performed ultrasound examination everyday.

None of the 12 infants with normal ultrasound pattern need oxygen supplementation in the next hours or days (or developed ultrasound abnormalities during the next days) despite diagnosed as affected by bronchiolitis and hospitalized.

4. The “discussion” legend has been forgotten.

We added the “Discussion” legend.

Referee #2
We thank this Referee for the constructive comments and suggestions. This is our point to point reply.

1. The aim of the investigation is not phrased correctly. The authors might consider (line 127-129):” ..the agreement between a lung ultrasonography and clinical scores in the ... of infants with suspected bronchiolitis”

We modified the aims of the study.

2. There no reference to how much the ultrasound findings may be specific for bronchiolitis. Has the proposed score been validated?

The proposed score has not been validated before this study. We decided to adopt it according to specific US findings for bronchiolitis published in ref 18.

3. Patient enrolment in the suspected bronchiolitis group includes both RSV positive and negative infants. Yet, the vast majority of RSV negative patients has a normal ultrasound scan and 9% of their total series has a normal chest auscultation. Their age span is considerably wide. The authors should comment on these points.

We acknowledge that the wide age span of the patients enrolled may be a limitation of the study. Because some bronchiolitis cases have normal chest auscultation and only other clinical signs of bronchiolitis (respiratory rate, use of accessory respiratory muscles etc) we speculate that the attending physician over-assessed the clinical impression and decided to hospitalize the patients.

4. Diagnostic accuracy might be ill defined since ultrasound score (>3 cut-off for moderate bronchiolitis) is used to predict oxygen requirement, a variable that is not in the study aims or elsewhere in the manuscript. Also in this respect, there is no reference to a sample size calculation that might support this observation.

We added diagnostic accuracy in the study aims.

According to literature, 25% of infants hospitalized for bronchiolitis need oxygen supplementation. With an α level of 0.05 and a power of 90% a sample size of 19 infants was needed.

5. Both ultrasound and clinical scores are composed by several items and are not of immediate comprehension. The authors should comment on the practical use of their results in daily neonatal practice.

We clarified practical use of our results in daily practice: ultrasound findings are able to intercept patients that will need supplementary oxygen in the next hours or days also when saturation during the enrollement is more than 94% or capillary blood oxygen tension is more than 45 mmHg. Use of LUS for safely reducing hospitalization, might have a great impact on socioeconomic aspects of this disease.

6. The Abstract paragraph is poorly informative on both LUS and clinical examination. Second sentence is out of context (line 58-59).
We deleted the second sentence and added supplementary information on both LUS and clinical examination.

7. Please report consistent terminology : VRS is SRV twice in line 205 and elsewhere.

We corrected terminology throughout the manuscript.

8. There is no Discussion paragraph between “Methods” and “Conclusions”. References on lung ultrasound in the neonatal period should be implemented.

We appropriately added the “Discussion” paragraph. We add recent references on LUS in neonatal period (ref. 7,23)

9. Typos and short forms are scattered throughout the manuscript. Cfr line 235, 244, 276 and 287 (it is ); line 260 please explain “artifactual landmarks”.

We revised typos and short forms throughout the manuscript. We changed landmarks with signs.

Referee #3

We thank this Referee for the constructive comments and suggestions. This is our point to point reply.

1. Minor essential revisions:

- Page 2, line 59: LUS - It's better to explain the acronym when it appears for the first time
- Page 2, line 72: it's better to write "statistically significant"
- Page 3, line 100: it is better to cite a bibliographic reference
- Page 6, line 193: it's better entitle the chapter "Statistical Analysis"
- Page 7, lines 212-215: the text is unclear. How many infants are VRS positives?

We performed these minor essential revisions throughout the manuscript

Editorial Request

1. Acknowledgements:
We strongly encourage you to include an Acknowledgements section between the Authors’ contributions section and Reference list. Please acknowledge anyone who contributed towards the study by making substantial contributions to conception, design, acquisition of data, or analysis and interpretation of data, or who was involved in drafting the manuscript or revising it critically for important intellectual content, but who does not meet the criteria for authorship. Please also include their source(s) of funding. Please also acknowledge anyone who contributed materials essential for the study.

Authors should obtain permission to acknowledge from all those mentioned in the Acknowledgements. Please list the source(s) of funding for the study, for each author, and for the manuscript preparation in the acknowledgements section. Authors must describe the role of the funding body, if any, in study design; in the collection, analysis, and interpretation of data; in the writing of the manuscript; and in the decision to submit the manuscript for publication.

We add an Acknowledgements section.

2. Please provide the name of Institutional Review Board and confirm if it was written informed parent consent that was obtained.

The Institutional Review Board is the local Ethical Commitee. We had a written informed parent consent.

3. We would like you to confirm the registration date of your TRN (trial registration number).

ClinicalTrials.gov Identifier: NCT01993797