Author's response to reviews

Title: A Cohort Study on the Incidence and Outcome of Pulmonary Embolism in Trauma and Orthopaedic patients.

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19 September 2013

Ursula D’Souza, PhD
Senior Editor
BMC Medicine

Dear Dr D’Souza,

Re: MS: 1681396363104819
A Cohort Study on the Incidence and Outcome of Pulmonary Embolism in Trauma and Orthopaedic patients
Suribabu Gudipati, Evangelos M. Fragakis, Vincenzo Ciriello, Simon J. Harrison, Petros Z. Stavrou, Nikolaos K. Kanakaris, Robert M. West and Peter V. Giannoudis

Thank you for your letter regarding the above manuscript. We have taken into consideration the reviewers comments and have responded as follows:

Reviewer 1

In principle I would ask for minor revision. My main query is how many PEs were diagnosed on VQ / echo (i.e. not picked up with the CTPA).

Thank you very much for your time and comments. In total 650 patients had been diagnosed with PE from different disciplines of medicine. Most of them had a diagnosis confirmed by CTPA and a small proportion had different interventions to confirm the diagnosis. However, as we only analysed patients admitted to trauma and orthopaedic department, we can confirm that all of these embolisms were confirmed by CTPA. No other modality was used to confirm the diagnoses in this cohort of patients.

Reviewer 2

Thank you very much for your time and comments.

1) Statistical analysis, pages 8–9

Revised and expanded section:

Statistical analysis
Continuous variables were summarized in terms of mean values with standard deviation and range as measures of variability. For variables that have skewed distributions, or otherwise may not be well represented by a normal distribution, medians and inter-quartile range are reported rather than mean and standard deviation. Categorical values were presented as absolute frequencies and percentages. Data were processed and analysed by MedCalc version 12.2.1 (MedCalc software bvda, Mariakerke, Belgium).
Mortality following PE was modelled using a multivariable logistic regression on potential risk factors. These were assessed using a Wald test with a p value of 0.05 or less considered to be statistically significant. Modelling was undertaken using the
software development environment R version 3.0.0 [24]. It is noted that the analysis is exploratory only, to identify those factors most strongly associated with mortality. A variety of plausible models, including and excluding covariates, were explored and the final model presented is a parsimonious one, which includes only statistically significant predictors.

2) **Fig 1 Lack of labels for 2 axes: one is AGE; the other is unclear, Frequency or Percentage?**
   Ans- Y axis is age range and the X axis is Number of patients, that is frequency. Page 29

3) 
   a) **It was improved but still not reported well, especially for the last column “Time of death after PE”.**
   Ans- It is time to death after PE diagnosis. (Page 31)

   b) **Top panel, e.g., there were exactly 112 (days) for each of all 3 patients with Spine?**
   Ans- It is the mortality duration after PE. One patient died at 140 days and the second one died after 84 days so the average was 112 days. Only 2 out of 3 spinal patients in the elective cohort died.

   d) **Only one number (112) was reported, then is the “Median: 112” in last line meaningful? Why so many blank / missing under this column?**
   Ans- Apart from spinal patients there were no recorded deaths in the other elective cohort of patients. Regarding 112 days this pertains only to patients who had spinal surgery as there were no recorded deaths in other group of patients.

   e) **Bottom panel, what did “(5.9%) 21 days” after the last column mean?**
   Ans- This corresponds to the combined fracture neck of femur patients (1.2% treated with CHS (cannulated hip screw) and 4.7% treated with hemi-arthroplasty.

4. **Table 3 Charlson Co-morbidity Index: Range 0-7. But in text: range: 0 – 10 (page 10).**
   Ans- Carlson co-morbidity index is 0-10, it was correct in the text. Mistake accepted in the table and corrected.

5. **Table 7 and Figure 2 The logistic modeling process was not very clear. What’s your final model and how many predictors/covariates in it?**
   If there only 3 predictors (Table 7), how to generate the Figure 2?
   Is there an AGE-by-DVT interaction term in the model?

   Ans- The logistic regression procedure is now explained in more detail in the Statistical Analysis section. There are relatively few events (11) for 3 predictors so that the findings may not be entirely robust. Nonetheless each of the predictors reaches statistical significance at the 5% level and so is established as strongly associated with the mortality outcome. The purpose of the modelling is exploratory only to identify such associations.
Figure 2 relates to further exploration of events, specifically the impact of subsequent DVT. In the presented model, DVT contributed little more above the included predictors and was dropped as an explanatory variable. No to cause any confusion and as Figure 2 is not relevant to the fitted model has been withdrawn. (Page 42)

Editor

Question 1: Please provide the name of the ethics committee that approved the study.

Reply: The study design and protocol involved reviewing clinical and radiological records of patients. When the local institutional board reviewed our application, it was felt that the study didn’t fall into the category for full ethical approval. The study was approved by our Institutional board committee and was given registration number IBR ‘10138’. This has been included in the section materials and methods.

Question 2: As patients were admitted for acute trauma or elective orthopaedic procedures were eligible to participate in the study then informed consent was not required. Please can you clarify this. Otherwise please add information on informed consent as follows: Informed consent must also be documented.

Reply: All the patients were consented for the relevant procedures during their admission and were well informed and made aware that the information will be used for research purpose without revealing their identity.

Question 3: Please format the author contributions based on the instructions.

Reply:

SG - Data collection, analysis, initial draft of the manuscript, revisions and prepared the final manuscript.

EMF - Data collection, analysis and initial draft of the manuscript.

VC - Data collection, statistical analysis and initial draft of the manuscript.

SJH - Data collection and initial editing of the manuscript.

PZS - Statistical analysis.

NKK - Study concept and design, critical review of the final draft.

RMW - Statistical analysis and final preparation of the manuscript.

PVG - Study concept and design, Coordination of all the aspects of the study, critical revision of the manuscript, administrative technical and material support.
Question 4: Please provide an acknowledgement section.

Reply: None

We hope that the above replies are to the reviewers’ satisfaction. Please let me know if you require any further clarification.

Best Wishes

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