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**ARTICLE DETAILS**

<table>
<thead>
<tr>
<th>TITLE (PROVISIONAL)</th>
<th>The accuracy of postoperative, noninvasive Air-Test to diagnose atelectasis in healthy patients after surgery – a prospective, diagnostic pilot study.</th>
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<tr>
<td>AUTHORS</td>
<td>Ferrando, Carlos; Romero, Carolina; Tusman, Gerardo; Suarez-Sipmann, Fernando; Canet, Jaume; Dosdá, Rosa; Valls, Paola; Villena, Abigail; Serralta, Ferran; Jurado, Ana; Carrizo, Juan; Navarro, Jose; Parrilla, Cristina; Romero, Jose; Pozo, Natividad; Soro, Marina; Villar, Jesús; Belda, Francisco</td>
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**VERSION 1 - REVIEW**

| REVIEWER            | Elsayed Elmestekawy  
Cardiac surgery division,  
Ottawa Heart Institute  
Ottawa  
Canada |
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<td>REVIEW RETURNED</td>
<td>17-Feb-2017</td>
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</table>

| GENERAL COMMENTS | The manuscript is well written, the method is clear, the results are well presented and the conclusion is sound and reflect the work they done. They also listed the number of limitation for this study  
Few points:  
1-Although the authors provided flow diagram is clear; the authors need to clarify that on the abstract and the text.  
Examples  
i-in the abstract page 2 line 14 participants; it need to be clear that out of 300 patients, 170 patients were included …  
ii-In the abstract page 2 , line 37 …and in 5 patients out of 29 patients (17%)...  
2-A Guerrero has to be expanded the first time it is mentioned in the text such as in page 5, line 32 …PACU  
3- In page 6, line 46 :….. adaptive randomization Can the authors discuss that and how they applied it?  
4-Page 6, line 56 CT-scans were obtained with 16-detector row/ 32 slices…did the authors choose this one or this what was available? was any difference expected in term of atelectasis diagnosis if used higher resolution CT scan?  
5-The sample size was not done and this should be also included in the study limitation |
|---------------------|------------------------------------------------------------------|

| REVIEWER            | Raffaele Giordano  
University of Naples Federico II, Italy |
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| GENERAL COMMENTS | The authors performed a prospective, cohort study. |
The authors hypothesized that change in oxygens induced by shot maneuver of FIO2 reduction to 0.21 can be used to detect the shunt related to postoperative atelectasis. Thus, the aim of this study was to determine whether SpO2 recorded by pulse oximetry after breathing room-air for 5 min ("the Air-Test") can reveal the presence of atelectasis and to establish the relation of the SpO2 value to the presence of atelectasis assessed by CT-scan. At the post-surgical recovery unit of the Hospital Clínico Universitario, Valencia, Spain, from January 12 to February 7, 2015. 170 patients scheduled for surgery under general anesthesia admitted into the postsurgical unit were included. The primary study outcome was the accuracy of the Air-Test for the detection of postoperative atelectasis assessed by reference standard. The secondary outcome was incidence of positive Air-Test. The Air-Test was performed in awake extubated patients after a 30 min stabilization period receiving supplemental oxygen therapy via a Venturi mask. The Air-Test was defined positive when SpO2 was ≤96% and negative when ≥97%. Arterial blood gases were measured in all patients at the end of the Air-Test. Within the next 25 min, the presence of atelectasis was evaluated by computed tomography scan in 59 randomly selected patients. The Air-Test diagnosed postoperative atelectasis with an area under the receiving operating curve of 0.90 (95% confidence interval: 0.82 to 0.98) with a sensitivity of 82.6% and a specificity of 87.8%. The presence of atelectasis was confirmed by computed tomography scan in all patients (30/30) with positive and in 5 patients (17%) with negative Air-Test. Based on the Air-Test, postoperative atelectasis were present in 36% of the patients (62 out of 170). In conclusions the authors demonstrated that the Air-Test is an accurate, simple, inexpensive, non-invasive and readily available method for diagnosing postoperative atelectasis. There are some limitations that are well explained in the text. The most important that this study was a pilot study and a large external validation study is needed. The article is interesting, well written, and we recommend publication.

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1
Elsayed Elmestekawy
Cardiac surgery division, Ottawa Heart Institute, Ottawa, Canada
Please state any competing interests or state 'None declared': No conflict of interest
Please leave your comments for the authors below
The manuscript is well written, the method is clear, the results are well presented and the conclusion is sound and reflect the work they done. They also listed the number of limitation for this study

Few points:

1-Although the authors provided flow diagram is clear; the authors need to clarify that on the abstract and the text.
Examples
I-in the abstract page 2 line 14 participants; it need to be clear that out of 300 patients, 170 patients were included …
II-In the abstract page 2 , line 37 …and in 5 patients out of 29 patients (17%).
- Following reviewer’s recommendation we have tried to be clearer in the abstract and in the text.
In the last version of the manuscript the abstract reads (page 2, lines 14-16 and 36):
“Of the 350 patients scheduled for surgery from January 12 to February 7, 2015, 170 patients with all the inclusion and none of the exclusion criteria who gave their consent were included.”

“Of the 59 patients evaluated with a CT-scan (29 with positive and 30 with negative Air-Test), all those with a positive Air-Test and 5 of those with a negative Air-Test (17%) had measurable atelectasis (area >2% of the whole lung) on the CT-scan.”

In the previous version was also included (page 9, lines 4-8):

“A total of 181 out of 350 eligible patients scheduled for surgery were enrolled, from whom 170 underwent the Air-Test in the PACU. Thirty randomly assigned patients from the 62 with positive and 29 from 108 with a negative Air-Test were assessed with CT (Figure 1).”

2- Abbreviation has to be expanded the first time it is mentioned in the text such as in page 5, line 32 …PACU

- Thank you for this appreciation. We have cheeked all the abbreviation and now are expanded the first time they appear in the text.

3- In page 6, line 46: …… adaptive randomization Can the authors discuss that and how they applied it?

- It was decided an adaptive randomization to minimized CT-scan exposure to those patients not expected to have atelectasis (positive Air-Test) following the guidance for industry: adaptive design clinical trials for drugs and biologics published by the FDA (Brannath W, et al. J Biopharm Stat 20:1125-31). One the objectives of this randomization as is described is: “to minimize exposure of potentially toxic or ineffective treatment” (Lin J, Lin L-A, Sandkoh S. A general overview of adaptive randomization design for clinical trials. J Biom Biostat 2016; 7:2)

In this study we initially set a maximum sample size of 30 patients with CT-scan per arm for two reasons: First, it was 5 patients over the minimum sample size we decided as a pilot study (25 patients with positive Air-Test and 25 with negative). Second, the daily clinical assistance scheduled in the radiology department did not allow us to perform a higher number of CT-scan during the recruitment period.

Following reviewer´s request we have described in the last version how randomization was performed and we have added in the randomization section the next sentence (page 6, lines 49-55):

“In this study we set a maximum sample size of 60 patients with CT-scan and a maximum sample size of 30 per arm (positive and negative Air-Test). We equally assigned the first 15 patients of each arm to two groups (CT-scan or no CT-scan) and started using the adaptive randomization at the next 16th patient on each arm.”

In the last version we also added the reference of the FDA for the adaptive design clinical trials (Brannath W, et al. J Biopharm Stat 20:1125-31. Reference 15 in the last version of the manuscript.

4- Page 6, line 56 CT-scans were obtained with 16-detector row/32 slices…did the authors choose this one or this what was available? was any difference expected in term of atelectasis diagnosis if used higher resolution CT scan?

- The 16-detector row/32 slices is the one we had available in our hospital at that time. Current CT scanners are capable of axial images as thin as 0.5 mm (compared with 10 mm of previous CT-scanners) and voxels would be smaller. Smaller voxels increase spatial resolution, decrease volume averaging, and improve the reliability of CT density readings. However, with the 5 mm reconstruction we performed the volume of a voxel is higher than the volume of an acinus at functional residual capacity (end-expiration) and therefore is considered adequate for this analysis (Gattinoni L et al. Am J Respir Crit Care Med 2001; 164:1701). We have now included this consideration in the methods section (page 7, lines 4-12):

“CT-scans were obtained with 16-detector row/32 slices Aquillion LB (Toshiba) located at the
Radiology Department. Scans (120 kV, 100-140 mA and 0.5 sec rotation time) were obtained during an expiratory hold after a normal inspiration. The images were reconstructed in 5mm thickness slices with 5mm interval and a depth of 12 bits per pixel, which is considered adequate for the analysis we performed18

5-The sample size was not done and this should be also included in the study limitation
-Following reviewer’s recommendation we have included the absence of simple size calculation as a limitation of the study. In the last version of the manuscript reads (page 13, line 55):
“Finally, as sample size calculation was not performed, this study can only be considered as a pilot study.”

Reviewer: 2
Raffaele Giordano
University of Naples Federico II, Italy
Please state any competing interests or state 'None declared': None declared

Please leave your comments for the authors below
The authors performed a prospective, cohort study.
The authors hypothesized that change in oxygens induced by shot maneuver of FIO2 reduction to 0.21 can be used to detect the shunt related to postoperative atelectasis. Thus, the aim of this study was to determine whether SpO2 recorded by pulse oximetry after breathing room-air for 5 min ("the Air-Test") can reveal the presence of atelectasis and to establish the relation of the SpO2 value to the presence of atelectasis assessed by CT-scan.

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Carlos Ferrando, Carolina Romero, Gerardo Tusman, Fernando Suarez-Sipmann, Jaume Canet, Rosa Dosdá, Paola Valls, Abigail Villena, Ferran Serralta, Ana Jurado, Juan Carrizo, Jose Navarro, Cristina Parrilla, Jose E Romero, Natividad Pozo, Marina Soro, Jesús Villar and Francisco Javier Belda

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