

## ANSWER TO THE REVIEWERS

We would like to thank to the reviewers for their careful perusal of our manuscript. Definitely, the manuscript will be improved after the revision, and we the authors hope that with the changes made the manuscript will have enough quality to be eventually published. In the following pages we address each of the reviewers' comments and the changes made to the manuscript.

### Reviewer No 1

#### **1. How were the 66.7% out-of-hospital cardiac arrests witnessed?**

Answer: This is an excellent appreciation. Due to the study characteristics (observational study performed with patients with sudden cardiac arrest who underwent to coronary angiogram during admission), there is a selection bias (survival bias), as physicians tend to perform coronary angiography to patients in which you expect to have a good neurologic prognosis. We suspect this explains the high rate of witnessed cardiac arrest in the study. This bias was commented in the limitations section

#### **2. The overall 5-year mortality of 37.4% should be stated that is the percentages of the resuscitated patients otherwise it appears to be very low especially with a 66.7% of the arrests being out of hospital arrest.**

Answer: We modified the following the manuscript as follows:

-Overall 5-year mortality *of the resuscitated patients* was 37.4%.

#### **3. "In survivors of out-of-hospital cardiac arrest, immediate coronary angiography and revascularization, if appropriate, should be considered irrespective of the ECG pattern if no obvious non-coronary cause of the arrhythmia is present" Class IIa in 2014 ESC revascularization guidelines.**

Answer: This is a good appreciation. In contrast to the new 2015 AHA and European Resuscitation Council resuscitation guidelines, in 2014 ESC revascularization guidelines, immediate coronary angiography after sudden cardiac arrest should be considered (Class IIa) for all patients if no non-coronary cause is present. As you comment, this decision should be performed irrespective of the ECG pattern and, in our opinion, this a general recommendation that is ultimately individualized for each patient, so, for these reasons, we decided to cite the specific resuscitation (and not revascularization) guidelines.

**4. The phrase: “Statistical methods were reviewed by Pablo Salinas, MD, PhD and Carlos Ferrera, MD, PhD; both bachelor degree in biostatistics” could have been omitted and the names can be mentioned in acknowledgements.**

Answer: We removed this phrase from the text.

#### **Reviewer No 2**

Comments: This observational, single-center study compared two groups of patients hospitalized for cardiac arrest: those presenting with an initial “shockable” rhythm, i.e. ventricular fibrillation, vs. those presenting with “non-shockable” pulseless electrical activity or asystole. Of particular interest was the comparative incidence of coronary artery disease (coronary angiogram) in the two groups. As expected, the ventricular fibrillation cohort collectively had more favorable outcomes, including higher survival to discharge, better neurological status (cerebral performance score) at discharge, and lower five-year mortality. Although the incidence of coronary stenosis did not differ between groups, the ventricular fibrillation group showed a strong trend toward a higher incidence of acute coronary lesions, and a statistically significant higher need for percutaneous coronary intervention. On the basis of

these findings, it is concluded that cardiac arrest victims should be considered strongly for early coronary angiography, especially those patients with initial ventricular fibrillation. The manuscript is well-written, the statistical analysis is appropriate, and the data support the conclusions.

**Although the study is rather small, it would be worthwhile to show if acute PCI produced any improvement in outcomes, or even a trend in that direction. Of the patients with significant coronary artery disease, did those receiving acute PCI show a greater survival rate and/or good neurological outcome?**

Answer: Thank you for the positive comments. As you recommend, we added a sentence commenting on PCI prognostic value:

Interestingly, in patients with shockable rhythm, those who underwent *ad hoc* PCI of the acute coronary lesions had a trend towards improved survival compared to patients with untreated acute coronary lesions (mean all-cause survival  $41.3 \pm 5.4$  months vs.  $29.7 \pm 6.9$  months;  $p=0.147$ ). *However, in patients with initial non-shockable rhythm, ad hoc PCI did not improve survival rates ( $p=0.948$ ).*

**Minor edits: Second paragraph of Discussion: Change 'definite' to 'definitive' Fourth paragraph of Discussion: "In our study, five-year survival rates were also higher... ...as previously reported [cite reference]." Fifth paragraph of Discussion: delete "derived" (second line) Table legends should appear at the bottom of the respective tables, not with figure legends.**

Answer: We modified the manuscript including all the proposed changes.

### Reviewer No 3

**Very interesting study important topic the impact of coronary artery disease in a cohort of patients resuscitated from cardiac arrest with non-diagnostic ECG is studied in a rather large group of patients the outcome of the patients**

**is remarkably good the major message is that the threshold for coronary angiography in both groups (shockable or not/ irrespective of initial rhythm) should be low. Limitations of this study are well documented**

Answer: We thank the reviewer for their thoughtful comments

#### **Reviewer No 4**

**Thank you for writing this nice manuscript. Apart from some small spelling errors, the manuscript looks fine. I have some comments.**

- 1. Please add the acronym "PEARL" to reference 25.**
- 2. Please mention the COACT trial among the studies currently including OHCA patients with nondiagnostic EKG (Lemkes et al., Am Heart J 2016).**

Answer: We modified the manuscript to add the acronym PEARL and the reference of Lekmes et al.

- 3. The paper describes a cohort of patients with SCA who underwent cor angiography. Do the authors know how many patients presented with SCA and did not undergo CA? Please report and add to Figure 1.**

Answer: We really apologize for not being able to contribute this data to the manuscript. Management of cardiac arrest patients in our center is carried out by several (three) independent intensive care units directed by anesthesiologists, intensive care physicians and critical care cardiologists. According to the cardiac arrest occurring out-of-hospital, in-hospital, in the peri-operative setting or at a referral hospital, as well as depending on the suspected origin of the cardiac arrest, the patient might be directed to one or another. Therefore, is somewhat difficult to assess a realistic total number of cardiac arrest. We conducted this study starting from a prospective,

comprehensive, multipurpose database of the Interventional Cardiology Department, including only patients referred for cardiac catheterization.