ANSWERING REVIEWERS

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Risk of ventricular arrhythmia in patients with Myocardial Infarction and Non-Obstructive Coronary Arteries and normal ejection fraction

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We would like to thank the editorial board for giving us the opportunity to resubmit our paper. We provide in the present "reply to reviewers" a point-by-point answer to all concerns and criticisms raised by the reviewers.

Please find bellow the answers to all issues raised by reviewers:

Reviewer 1

In this retrospective study, Bière et al tried to assess the arrhythmic determinants and prognosis of patients presenting a Myocardial Infarction and Non-Obstructive Coronary Arteries (MINOCA). There were 131 patients included and follow-up for 1 year. They showed that ST elevation on admission and LGE transmural extent appear to be good markers for identifying patients at risk of ventricular events in the early stages of disease. The manuscript provided a timely study on this field. I am interested in the percentage of your patients who were included into the study.

We understand the comment of the reviewer to discuss the representability of the population studied here. This issue is inherent to every retrospective studies.

The retrospective nature limits the possibility to provide a reliable-enough study flow chart. Indeed in-hospital coded nomenclature for diagnosis is not accurate enough to identify these patients. Our inclusion criteria were "(a) hospitalization for acute anginal chest pain, (b) increase in troponin rates superior to the normal range, (c) left ventricular ejection fraction (LVEF) ≥45%, and (d) absence of coronary artery stenosis or thrombosis (stenosis <50% of the diameter of the epicardial vessel)." These criteria are not formally included in common diagnosis such as "acute coronary syndrome", "myocarditis", or "myocardial infarction".

We believe our study to be representative of today populations with MINOCA because (1) the study was conducted in two university hospital. Both centers do provide evidence-based medicine and the best standard of care in the area. In this centers, patients with chest pain, troponin increase and normal coronary angiogram will be most likely referred for CMR in order to elucidate the underlying mechanism of the event. (2) Inclusions in our study were driven by final diagnosis listings, as completed by physicians of the Cardiology department. Among our inclusion criteria, absence of coronary angiogram (n=30), absence of troponin measurement (n=30), absence of relevant chest pain (n=22), LVEF <45% (n=3), and absence of CMR scan (n=2) were the one that lead us to exclude the greater number of patients after first-line screening. In the end, the present analysis was set on 131 patients, out of 254 patients screened. Numbers for excluded patients are given in the manuscript.

In the end, we cannot provide strong numbers of patients presenting MINOCA with depressed LVEF in our institutions but we believe selection bias to be minimized by the specific population we studied in highly-specialized centers.

Reviewer 2

1) Were the patients of the study taking any anti-arrhythmic medications and, if so, which one(s)?

We agree with the comment of the reviewer that anti-arrhythmic medications is lacking in our report. Thought it is very relevant for arrhythmic events, we forgot to report the fact that none of our patients received ant-arrythmic medication during the one-year follow-up (except beta-blockers, of course) (page 10 line 25). Of note, none presented atrial fibrillation, and patients with initial sustained ventricular tachycardia were excluded for analysis.

2) The authors should (briefly) comment on the ethnicity/racial characteristics of their study population and how those may have factored into their observed results/findings.

We totally agree with the reviewer that ethnicity/racial characteristics may impact on the kind of findings we provide. For example, McNamara et al (J Am Coll Cardiol. 2011 Sep 6;58(11):1112-8) found that African American may present lower functional outcome after the diagnosis recent onset dilated cardiomyopathy (at some point this study included cases of myocarditis). Nevertheless, data are scarce on this topic, and social factors may play a massive role in the context of cardiovascular disease (Bucholtz et al, J Am Coll Cardiol 2015;66:645–55). That's why and in accordance with the reviewer remark we discussed this point very carefully in the limitation section (page 14 line 17).