Reviewer's report

Title: Non-diagnostic autopsy findings in sudden unexplained death victims

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Reviewer: Pietro Francia

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Yazdanfard et al. describe autopsy findings in 99 sudden unexplained deaths. They report that one third of victims had normal cardiac findings while two thirds had non-normal but non-diagnostic findings (mainly LV hypertrophy, coronary atherosclerosis and cardiac fibrosis). They discuss that non-diagnostic/non-normal findings may be early markers of structural heart diseases.

Albeit non original (Eur Heart J. 2018;40(10):831-838), the manuscript is interesting. However, I have major concerns.

The major study limitation is the unavailability of (a) clinical information on approximately half of sudden unexplained death (SUD) victims and (b) family screening. It is discussed that in patients without apparent autopsy-confirmed HCM, fibrosis and non-diagnostic hypertrophy may represent early markers of HCM when cardiomyocyte disarray may have been missed due to selection of sites for microscopical examination. Clinical phenotype is crucial in these circumstances to substantiate a diagnosis. Likewise, non-diagnostic LV hypertrophy is discussed as a possible substrate of SUD due to ventricular arrhythmia. However, mild LV hypertrophy may represent an incidental finding in hypertensive patients with inherited electrical heart diseases. Indeed, the concept that victims of inherited arrhythmogenic diseases are mostly free from any cardiac findings on autopsy is not supported by Authors' findings.

More in general, the lack of clinical information, family screening and molecular autopsy makes conclusions purely hypothetical.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes
Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

No

Are the conclusions drawn adequately supported by the data shown?
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No

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