Reviewer 1 – blue
Reviewer 2 – orange
Reviewer 3 – purple
Authors – green

First of all congratulations for Authors. The subject of sudden cardiac death (SCD) constitutes a major clinical and public health problem, whose death burden is estimated for four million SCDs worldwide every year. The review of this paper presents accomplishments of the molecular autopsy. I appreciate, it was real pleasure and an honour.

We would like to thank the Reviewer for their kind words and thoughtful feedback. We truly appreciate their recognition of the significance of sudden cardiac death and the role of molecular autopsy in advancing our understanding of its causes. Their support and appreciation mean a lot to us.

The changes include under your reccomendations were made in orange color.

Specific comments to authors :

1. What is the cost of molecular autopsy? Please include this information in discussion section.

Thank you very much for the suggestion. In response, we have introduced the following paragraph

(lines 416 - 422) The cost of a molecular autopsy can vary based on factors such as the number of genes analyzed, the specific methodology and platforms used, and regional pricing differences. The estimated cost per analysis is estimated to vary between US$240–297 for targeted panels, US$604–1932 for WES, and US$2006-3347 for WGS. Cost proportions were highest for library preparation and sequencing materials (average 76.8% of total costs), sample extraction (8.1%), data analysis (9.2%) and data storage (2.6%). Capital costs for the sequencers were an additional US$24–67 per person (PMID: 32493298 – Gordon, 2020).

2. In up to 30% of SCD cases in young individuals, no cause of death is identified post-mortem, referred to as autopsy-negative or sudden arrhythmic death syndrome (SADS). In instances where the cause of death remains unknown, post-mortem genetic testing, also known as molecular autopsy, may identify a cause of in up to 30% of SADS cases . On the basis of the above, in my opinion it would be usufull for the manuscript to include some relevant information for educational purpose for the readers, let's hope wide medical community, concerning treatment options: ICD/SICD/VEST defibrillator.

Thank you for your valuable feedback and thoughtful suggestion. We appreciate your emphasis on the importance of providing educational information for the wider medical community. In response to your recommendation, we have added the following paragraph (lines XX - XX).

(lies 497- 501) In cases where a molecular autopsy identifies a genetic predisposition to sudden arrhythmic death syndrome (SADS), implementing preventive strategies for at-risk family members is crucial. One primary intervention is the use of defibrillator devices, which monitor heart rhythms and deliver shocks to correct life-threatening arrhythmias.The main types of

defibrillators include Implantable cardioverter-defibrillators (ICDs) and wearable cardioverter-defibrillators (WCDs), which are powerful tools in preventing SCD due to ventricular arrhythmias in carefully selected patients. (PMID: 31950276 – Beg 2020)

I truly recommend this paper for publication in in the present form after just a minor revision, with few sentences added in discussion section mentioned above, if the authors agree to do so. I recommend this paper for publication because every new data and diagnostic perspectives in SCD prevention is extremely important. The presented study is easy to read, interesting and extremely helpful in understanding genetic sequencing techniques, such as next-generation sequencing (NGS). This methodology gives hope for relatives of SCD victims, especialy in young SCD cases.

We sincerely thank the Reviewer for their thoughtful feedback and support of our work. Your insights and suggestions have been invaluable in enhancing the quality and educational impact of our manuscript. We truly appreciate your time and expertise in reviewing our study.

3. Biological samples should be collected from all individuals aged 40 or younger who experience sudden and unexplained deaths. In cases of out-of-hospital cardiac arrest in the young, Stanasiuk et al. recommended the collection of a 2 mL blood sample (in an ethylenediaminetetraacetic acid - EDTA tube) by the emergency medical service (EMS). If blood samples in EDTA tubes are not collected by the EMS, blood or tissue suitable for DNA extraction should be obtained during the autopsy process. This statement is so important and should be emphasized. I agree it should be repeated in the text but my advice is to transfer this from discussion section to conclusions.

Thank you very much for your suggestion. We agree that this statement is importante and should be emphasized. To do so, we have included the following paragraph to conclusions.

(lines 512 - 517) A crucial factor in ensuring the success of molecular autopsy is the proper collection of biological samples, particularly in individuals aged 40 or younger who experience sudden and unexplained deaths. EMS should collect a 2 mL EDTA blood sample whenever possible. If unavailable, blood or tissue should be obtained during autopsy to ensure high-quality DNA for genetic analysis. This practice enhances diagnostic accuracy, facilitates family risk assessment, and supports prevention strategies.