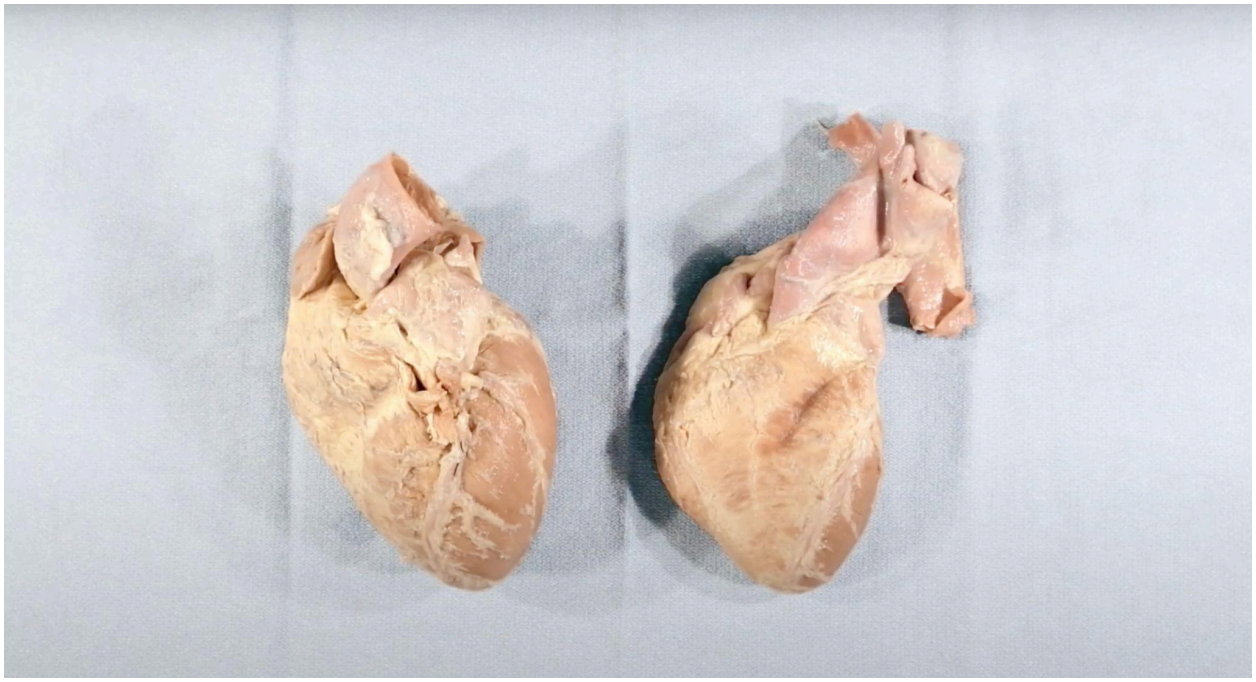

Sudden Cardiac Death
Meagan Chambers MD

Background

Sudden cardiac death (SCD) accounts for ~50% of total cardiovascular mortality and 10%–20% of all deaths (Zheng 2001). Most of the SCDs (70%–80%) are caused by coronary artery disease (CAD), whereas non-ischemic myocardial diseases account for approximately one-fifth of the cases, and the minority is caused by other cardiac conditions (e.g. primary arrhythmia syndromes, valve diseases, or myocarditis) (Huikuri 2001).

Sudden cardiac death (SCD) is a complicated topic but is also a hallmark of autopsy pathology. It is, by definition, a topic which can only be studied in the post-mortem setting as it is the first clinical manifestation of an underlying disease in previously asymptomatic, apparently ‘healthy’ subjects (Basso 2017).

There exists more than one comprehensive guideline which can help the unfamiliar autopsyist navigate the sudden cardiac death autopsy. The article therefore focuses on collating these resources and directing readers to them. Importantly, the article does not endorse any specific recommendations, but rather seeks to collect them for individuals to utilize and implement at their discretion. (That said, if you only have time to read one or two articles, the articles which cover topics similarly to how they are covered elsewhere in this website are under “THE COMPLETE SUDDEN CARDIAC DEATH AUTOPSY”).

Of note, not all cases of sudden death are cardiac and there is an autopsy textbook which takes an organ-based approach to sudden death.

Approach to Sudden Cardiac Death

Sudden cardiac death is defined as “a natural, unexpected fatal event occurring within one hour from the onset of symptoms in an apparently healthy subject or in one whose disease was not so severe as to predict an abrupt outcome” (Goldstein 1982). A case of “sudden cardiac death” may fall outside the jurisdiction of the forensic world, if the decedent had a period of hospital survival where a “cardiac” diagnosis was rendered. However, the question may remain as to *why* the person experienced a cardiac event. Recognizing sudden cardiac death prior to starting the autopsy is both critical and at times challenging. For example, a patient with a history of a fall at home and subsequent head bleed raises the question – did they fall and then die, or did they die and then fall? The latter could be a case of sudden cardiac death. The most important thing to do is to approach the autopsy with a broad differential. As the workup for sudden cardiac death can entail substantial ancillary testing, being alert to the possibility can mean the difference between finding an underlying cause of death and not. Similarly, if you reach the end of the autopsy procedure and don’t have a cause of death, that can be a good time to think about expanding the differential to include sudden cardiac death. By extension, even if you do have a cause of death, you may still need to think about sudden cardiac death – as in the example of a head bleed secondary to SCD. Additionally, examples such as severe coronary artery disease in persons under 40 should prompt deeper questions such as why? Does this person have severe coronary artery disease as a result of genetic influence, steroid abuse or “western diet?” Each of these answers prompts different reactions and contributions to the medical system.

Finally, a significant number of SCD workups may ultimately end up negative for a specific cause of death. But, while recognizing financial and system constraints, a careful negative workup still has more value than a limited SCD autopsy.

Autopsies for SCD are frequently not done at all or completed without a standardized protocol (Banner 2020). It is important to keep in mind that collecting that data that you can, within the financial and social limitations of your institution, is important. While you may not have an answer now, the quality of data that you have contributes to research in the future and/or the possibility of an answer later.

Recommended Resources:

THE COMPLETE SUDDEN CARDIAC DEATH AUTOPSY

- Basso C, Aguilera B, Banner J, Cohle S, d'Amati G, de Gouveia RH, di Gioia C, Fabre A, Gallagher PJ, Leone O, Lucena J, Mitrofanova L, Molina P, Parsons S, Rizzo S, Sheppard MN, Mier MPS, Kim Suvarna S, Thiene G, van der Wal A, Vink A, Michaud K; Association for European Cardiovascular Pathology. Guidelines for autopsy investigation of sudden cardiac death: 2017 update from the Association for European Cardiovascular Pathology. Virchows Arch. 2017

Dec;471(6):691-705. doi: 10.1007/s00428-017-2221-0. Epub 2017 Sep 9. PMID: 28889247; PMCID: PMC5711979.

- Kelly KL, Lin PT, Basso C, Bois M, Buja LM, Cohle SD, d'Amati G, Duncanson E, Fallon JT, Firchau D, Fishbein G, Giordano C, Leduc C, Litovsky SH, Mackey-Bojack S, Maleszewski JJ, Michaud K, Padera RF, Papadodima SA, Parsons S, Radio SJ, Rizzo S, Roe SJ, Romero M, Sheppard MN, Stone JR, Tan CD, Thiene G, van der Wal AC, Veinot JP. Sudden cardiac death in the young: A consensus statement on recommended practices for cardiac examination by pathologists from the Society for Cardiovascular Pathology. Cardiovasc Pathol. 2023 Mar-Apr;63:107497. doi: 10.1016/j.carpath.2022.107497. Epub 2022 Nov 12. PMID: 36375720.

- Wilhelm M, Bolliger SA, Bartsch C, Fokstuen S, Gräni C, Martos V, Medeiros Domingo A, Osculati A, Rieubland C, Sabatasso S, Saguner AM, Schyma C, Tschui J, Wyler D, Bhuiyan ZA, Fellmann F, Michaud K. Sudden cardiac death in forensic medicine – Swiss recommendations for a multidisciplinary approach. Swiss Med Wkly. 2015 Jun 22;145:w14129. doi: 10.4414/smw.2015.14129. PMID: 26098688.

Of note, these guidelines mention the possibility of cardiac conduction system dissections. There is a narrated video and a powerpoint to guide this dissection, as well as an excellent paper here for more information on cardiac conduction system dissection.

GROSS EXAMINATION

Cardiac Hypertrophy at autopsy:

- Cunningham KS, Spears DA, Care M. Evaluation of cardiac hypertrophy in the setting of sudden cardiac death. Forensic Sci Res. 2019 Aug 19;4(3):223-240. doi: 10.1080/20961790.2019.1633761. PMID: 31489388; PMCID: PMC6713129.

Concern for cardiomyopathies (Suggested by: cardiac hypertrophy and/or dilatation/scarring with normal coronary arteries):

- Sheppard MN, van der Wal AC, Banner J, d'Amati G, De Gaspari M, De Gouveia R, Di Gioia C, Giordano C, Larsen MK, Lynch MJ, Lucena J, Molina P, Parsons S, Suarez-Mier MP, Rizzo S, Suvarna SK, Te Rijdt WP, Thiene G, Vink A, Westaby J, Michaud K, Basso C; Association for European Cardiovascular Pathology (AECVP). Genetically determined cardiomyopathies at autopsy: the pivotal role of the pathologist in establishing the diagnosis and guiding family screening. Virchows Arch. 2023 Apr;482(4):653-669. doi: 10.1007/s00428-023-03523-8. Epub 2023 Mar 10. PMID: 36897369; PMCID: PMC10067659.

ANCILLARY TESTING:

For an introduction and overview of Molecular autopsies (i.e. post-mortem genetic testing), including a review of the diseases testing is meant to catch and existing guidelines, see:

- Martínez-Barrios E, Grassi S, Brión M, Toro R, Cesar S, Cruzalegui J, Coll M, Alcalde M, Brugada R, Greco A, Ortega-Sánchez ML, Barberia E, Oliva A, Sarquella-Brugada G, Campuzano O. Molecular autopsy: Twenty years of post-mortem diagnosis in sudden cardiac death. Front Med (Lausanne). 2023 Feb 10;10:1118585. doi: 10.3389/fmed.2023.1118585. PMID: 36844202; PMCID: PMC9950119.

To go directly to the guidelines for genetic testing:

- ACMG Guidelines: Deignan JL, De Castro M, Horner VL, Johnston T, Macaya D, Maleszewski JJ, Reddi HV, Tayeh MK; ACMG Laboratory Quality Assurance Committee. Points to consider in the practice of postmortem genetic testing: A statement of the American College of Medical Genetics and Genomics (ACMG). Genet Med. 2023 May;25(5):100017. doi: 10.1016/j.gim.2023.100017. Epub 2023 Feb 16. PMID: 36799919.

- NAME Guidelines: Middleton O, Baxter S, Demo E, et al. National Association of Medical Examiners Position Paper: Retaining Postmortem Samples for Genetic Testing. Academic Forensic Pathology. 2013;3(2):191-194. doi:10.23907/2013.024

- HRS/EHRA, Ackerman MJ, Priori SG, Willems S, Berul C, Brugada R, Calkins H, Camm AJ, Ellinor PT, Gollob M, Hamilton R, Hershberger RE, Judge DP, Le Marec H, McKenna WJ, Schulze-Bahr E, Semsarian C, Towbin JA, Watkins H, Wilde A, Wolpert C, Zipes DP. HRS/EHRA expert consensus statement on the state of genetic testing for the channelopathies and cardiomyopathies this document was developed as a partnership between the Heart Rhythm Society (HRS) and the European Heart Rhythm Association (EHRA). Heart Rhythm. 2011 Aug;8(8):1308-39. doi: 10.1016/j.hrthm.2011.05.020. PMID: 21787999.

Ethics of genetic testing in SCD:

- McGuire AL, Moore Q, Majumder M, Walkiewicz M, Eng CM, Belmont JW, Nassef S, Darilek S, Rutherford K, Pereira S, Scherer SE, Sutton VR, Wolf D, Gibbs RA, Kahn R, Sanchez LA; Molecular Autopsy Consortium of Houston (MATCH). The ethics of conducting molecular autopsies in cases of sudden death in the young. Genome Res. 2016 Sep;26(9):1165-9. doi: 10.1101/gr.192401.115. Epub 2016 Jul 13. PMID: 27412853; PMCID: PMC5052042.

- Michaud K, Fellmann F, Abriel H, Beckmann JS, Mangin P, Elger BS. Molecular autopsy in sudden cardiac death and its implication for families: discussion of the

practical, legal and ethical aspects of the multidisciplinary collaboration. Swiss Med Wkly. 2009 Dec 12;139(49-50):712-8. doi: 10.4414/smw.2009.12837. PMID: 20047134.

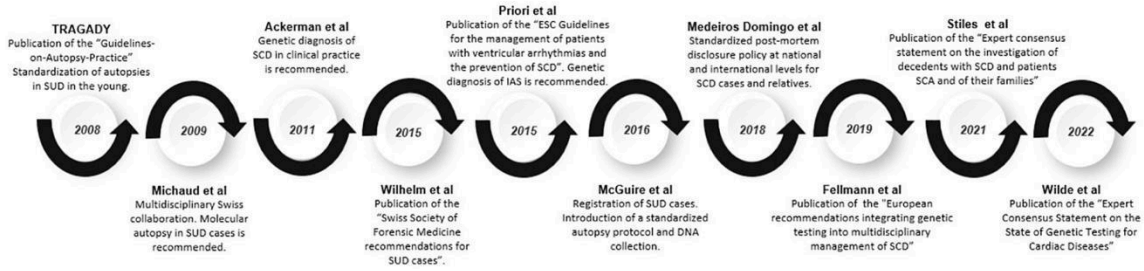

FIGURE 3
Timeline of guidelines and recommendations. Evolution of guidelines and recommendations on genetic testing and the standardization of molecular autopsy for the study of patients affected with SUD and their relatives.

(Figure credit: Martínez-Barrios 2023)

Additional Resources:

Definition of Sudden Death:

- Goldstein S. The necessity of a uniform definition of sudden coronary death: witnessed death within 1 hour of the onset of acute symptoms. Am Heart J. 1982 Jan;103(1):156-9. doi: 10.1016/0002-8703(82)90552-x. PMID: 7055041.

Sudden cardiac death in college athletes:

- Petek BJ, Churchill TW, Moulson N, Kliethermes SA, Baggish AL, Drezner JA, Patel MR, Ackerman MJ, Kucera KL, Siebert DM, Salerno L, Zigman Suchsland M, Asif IM, Maleszewski JJ, Harmon KG. Sudden Cardiac Death in National Collegiate Athletic Association Athletes: A 20-Year Study. Circulation. 2024 Jan 9;149(2):80-90. doi: 10.1161/CIRCULATIONAHA.123.065908. Epub 2023 Nov 13. PMID: 37955565.
- Han J, Lalario A, Merro E, Sinagra G, Sharma S, Papadakis M, Finocchiaro G. Sudden Cardiac Death in Athletes: Facts and Fallacies. J Cardiovasc Dev Dis. 2023 Feb 5;10(2):68. doi: 10.3390/jcdd10020068. PMID: 36826564; PMCID: PMC9965876.

Standardization of SCD practice:

- Banner J, Basso C, Tolkien Z, Kholova I, Michaud K, Gallagher PJ. Autopsy examination in sudden cardiac death: a current perspective on behalf of the Association for European Cardiovascular Pathology. Virchows Arch. 2021 Apr;478(4):687-693. doi: 10.1007/s00428-020-02949-8. Epub 2020 Oct 28. PMID: 33111163; PMCID: PMC7990811.

Other resources:

- Zheng ZJ, Croft JB, Giles WH, Mensah GA. Sudden cardiac death in the United States, 1989 to 1998. Circulation. 2001 Oct 30;104(18):2158-63. doi: 10.1161/hc4301.098254. PMID: 11684624.
- Huikuri HV, Castellanos A, Myerburg RJ. Sudden death due to cardiac arrhythmias. N Engl J Med. 2001 Nov 15;345(20):1473-82. doi: 10.1056/NEJMra000650. PMID: 11794197.