PLOS NEGLECTED TROPICAL DISEASES

VIEWPOINTS

Use of minimally invasive autopsy during the COVID-19 pandemic and its possibilities in the context of developing countries

Deborah Nunes Melo[1,2], Tania Mara Coelho[3,4], Giovanna Rolim Pinheiro Lima[5], Carolina Gomes Fernandes[5], Bruno Cavalcante Fales de Brito Alves[5], Fernanda Montenegro de Carvalho Araújo[6], Renata Aparecida de Almeida Monteiro[7], Jaume Ordi[8,9], Paulo Hilário do Nascimento Saldiva[7], Luciano Pamplona de Góes Cavalcanti[1,3,5]*

1 Programa de Pós-graduação em Patologia, Universidade Federal do Ceará, Fortaleza, Brasil, **2** Serviço de Verificação de Óbitos Dr Rocha Furtado, Fortaleza, Brasil, **3** Programa de Pós-graduação em Saúde Coletiva, Universidade Federal do Ceará, Fortaleza, Brasil, **4** Hospital São Jose de Doenças Infecciosas, Fortaleza, Brasil, **5** Faculdade de Medicina, Centro Universitário Christus, Fortaleza, Brasil, **6** Fundação Oswaldo Cruz, Fortaleza, Brasil, **7** Departamento de Patologia, Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brasil, **8** Department of Pathology, Hospital Clínic, Universitat de Barcelona, Barcelona, Spain, **9** ISGlobal, Barcelona Institute for Global Health, Hospital Clínic, Universitat de Barcelona, Barcelona, Spain

* pamplona.luciano@gmail.com

Coronavirus Disease 2019 (COVID-19) cases have spread quickly across the globe, but the deaths are distributed unevenly. These differences are related to several reasons, including the lack of access to diagnosis and socioeconomic status [1–3].

In this scenario, despite the advances in diagnostic methods in recent decades, a well-performed autopsy remains the gold standard methodology for diagnosing the cause of death [4].

The value of the autopsy has been shown in recent epidemics such as dengue, influenza A/H1N1, Zika, HIV, and yellow fever [5–9]. The autopsy findings helped to clarify not only the basic cause of death, but also the pathophysiology of the disease. These discoveries were possible even after many years when new technologies became available, as exemplified by the studies on paraffin-preserved material from the Spanish flu pandemic of 1918 [10].

Also, autopsies make an indispensable contribution to medical education and training. They provide a unique situation to observe systemic manifestations of different diseases, providing the basis for a medical training.

However, the number of autopsies performed globally is decreasing progressively. This phenomenon is partly due to the lack of limited resources and technical challenges, especially in developing countries. Cultural barriers and the reluctance of families to provide informed consent are additional factors contributing to the decline in autopsy numbers.

Moreover, due to the COVID-19 pandemic, some countries have decided not to allow complete autopsies, which limits the proper investigation of the disease pathophysiology and the death confirmations that were not diagnosed during clinical evolution [11]. In this scenario, some countries are expanding the use of verbal autopsy complemented by specific laboratory tests with good results [12]. However, although verbal autopsy provides a broad approach, its performance for etiological diagnosis is still limited, as it may misclassify some deaths caused by infectious diseases [13].

Thus, the minimally invasive autopsy (MIA) has emerged as an innovative strategy. It is a simple systematic collection technique that utilizes tissue samples from various organs and

OPEN ACCESS

Citation: Melo DN, Mara Coelho T, Rolim Pinheiro Lima G, Gomes Fernandes C, Cavalcante Fales de Brito Alves B, Montenegro de Carvalho Araújo F, et al. (2021) Use of minimally invasive autopsy during the COVID-19 pandemic and its possibilities in the context of developing countries. PLoS Negl Trop Dis 15(8): e0009629. https://doi.org/10.1371/journal.pntd.0009629

Editor: Nelesh Premapragasan Govender, National Institute for Communicable Diseases, Johannesburg, South Africa, SOUTH AFRICA

Published: August 4, 2021

Funding: The authors received no specific funding for this work.

Competing interests: The authors have declared that no competing interests exist.

body fluids, configuring a fast, nondisfiguring procedure, with easy technical applicability that can provide robust data for surveillance, especially in regions with limited resources, being useful to guide strategies for prevention, control, and treatment of diseases [4,14–16].

In addition to health professionals considering it more acceptable, this technique stands out for overcoming the low acceptability and feasibility of a complete autopsy in some regions, which contributes to reducing the stigma of more invasive current practices [4,17].

In the study carried out in Southeastern Brazil during the yellow fever epidemic of 2018, the ultrasound-guided MIA (MIA/US) proved to be effective in both diagnosing the underlying disease and the cause of death and had a 100% diagnostic agreement when compared with conventional autopsy [9]. Similar findings were recently reported in Barcelona with 6 deaths by COVID-19, but without the use of an image resource [16].

The application of imaging techniques may create the impression that MIAs are expensive. However, the adaptation of methodologies and adequate personnel training proved cost-effective diagnostic tools in less developed regions [18,19].

Specifically, in the case of COVID-19 pandemic, in addition to being efficient in establishing the diagnosis of infections, it is a method that offers more safety to the professionals and can be performed with the body closed and surrounded by a plastic cover.

In 2020, the first autopsies using MIA technique were promoted in COVID-19 victims by the project Plataforma de Imagens na Sala de Autópsia (PISA), in the city of São Paulo. A year later, aiming to clarify the role of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) in lung and systemic injures, MIA was started in the state of Ceará, at the Serviço de Verificação de Óbitos Dr Rocha Furtado [20,21].

The wide acceptance of MIA in combination with simple imaging methods such as ultrasound scan offers a readily available, affordable, and safe postmortem diagnostic technique. Implementing MIA in developing countries can increase the accuracy of epidemiological surveillance indicators and overcome several barriers that prevent the performance of complete autopsies.

This tool can play an important role in improving the surveillance of causes of death in locations where infectious diseases are a common cause of mortality. The application of MIA should not eliminate the need of reinforcing death verification services or performing public verbal autopsies, even though it demonstrates limitations at the individual level, but which are still useful in low-budget situations. It is necessary to increase access to this technique, making it possible to expand the knowledge about the pathophysiology of these emerging diseases that lead thousands of people to death. In addition, its use can expand the range of pathologies that can be seen in biopsies, in the detection of emerging diseases, and even in the diagnosis of chronic diseases.

References

1. Okonjil EF, Okonji OC, Mukumbang FC, Wyk BV. Underestanding varying COVID-19 mortality rates reported in Africa compared to Europe, United States of America and Asia. Tropical Med Int Health. https://doi.org/10.1111/tmi.13575 PMID: 33733568
2. Mwananyanda L, Gill CJ, Macleod W, Kwenda G, Pieciak R, Mupila Z. COVID-19 deaths detected in a systematic post-mortem surveillance study in Africa. 2020. https://doi.org/10.1101/2020.12.22.20248327
3. Rocha R, Atun R, Massuda A, Rache B, Spinola P, Nunes L, et al. Effect of socioeconomic inequalities and vulnerabilities on health-system preparedness and response to COVID-19 in Brazil: a comprehensive analysis. Lancet. https://doi.org/10.1016/S2214-109X(21)00081-4 PMID: 33857500
4. Bassat Q, Castillo P, Alonso PL, Ordi J, Menéndez C. Resuscitating the Dying Autopsy. PLoS Med. 2016; 13(1):e1001927. https://doi.org/10.1371/journal.pmed.1001927 PMID: 26756992
5. de Góes Cavalcanti LP, de Melo Braga DN, de Lima Pompeu MM, Bezerra Lima AA, da Silva LMA, Aguiar MG, et al. Evaluation of the World Health Organization 2009 Classification of Dengue Severity in

Autopsied Individuals, During the Epidemics of 2011 and 2012 in Brazil. Rev Soc Bras Med Trop. 2015; 48(6):658–64. https://doi.org/10.1590/0037-8682-0287-2015 PMID: 26676489

6. Arévalo E, Argueta V, Orozco R, Aplicano RM. Hallazgos en necropsias realizadas a pacientes diagnosticados con influenza A (H1N1). Rev Esp Patol. 2010; 43(4):187–90.
7. Schwartz DA. Autopsy and Postmortem Studies Are Concordant: Pathology of Zika Virus Infection Is Neurotropic in Fetuses and Infants With Microcephaly Following Transplacental Transmission. Arch Pathol Lab Med. 2017; 141(1):68–72. https://doi.org/10.5858/arpa.2016-0343-OA PMID: 27557413
8. Arteaga Hernández E, Capó de Paz V, Pérez Fernández-Terán ML. Opportunistic Invasive Mycoses in AIDS. An Autopsy Study of 211 Cases. Rev Iberoam Micol. 1998; 15(1):33–5. PMID: 17655402
9. Duarte-Neto AN, de Almeida Monteiro RA, Johnsson J, Dos Passos Cunha M, Pour SZ, Saraiva AC, et al. Ultrasound-guided minimally invasive autopsy as a tool for rapid post-mortem diagnosis in the 2018 Sao Paulo yellow fever epidemic: Correlation with conventional autopsy. PLoS Negl Trop Dis. 2019; 13(7):e0007625. https://doi.org/10.1371/journal.pntd.0007625 PMID: 31329590
10. Sheng Z-M, Chertow DS, Ambroggio X, McCall SH, Przygodzki RM, Cunningham RE, et al. Autopsy Series of 68 Cases Dying Before and During the 1918 Influenza Pandemic Peak. Proc Natl Acad Sci U S A. 2011; 108(39):16416–21. https://doi.org/10.1073/pnas.1111179108 PMID: 21930918
11. Argueta V. La importancia de la autopsia en epidemias. Rev Méd (Col Méd Cir Guatem). 2020; 159 (1):2–3.
12. de Souza PMM, Gerson G, Dias JS, de Melo DN, de Souza SG, Ruiz EM, et al. Validation of verbal autopsy and nasopharyngeal swab collection for the investigation of deaths at home during the COVID-19 pandemics in Brazil. PLoS Negl Trop Dis. 2020; 14(11):e0008830. https://doi.org/10.1371/journal.pntd.0008830 PMID: 33147211
13. Castillo P, MartõÂnez MJ, Ussene E, Jordao D, Lovane L, Ismail MR, et al. Validity of a Minimally Invasive Autopsy for Cause of Death Determination in Adults in Mozambique: An Observational Study. PLoS Med. 2016; 13(11):e1002171. https://doi.org/10.1371/journal.pmed.1002171 PMID: 27875530
14. Saldiva PHN. Minimally invasive autopsies: a promise to revive the procedure. Autops Case Rep. 2014; 4(3):1–3. https://doi.org/10.4322/acr.2014.021 PMID: 28573111
15. Bassat Q, Castillo P, MartõÂnez MJ, Jordao D, Lovane L, Hurtado JC, et al. Validity of a minimally invasive autopsy tool for cause of death determination in pediatric deaths in Mozambique: An observational study. PLoS Med. 2017; 14(6):e1002317. https://doi.org/10.1371/journal.pmed.1002317 PMID: 28632739
16. Rakislova N, Marimon L, Ismail MR, Carrilho C, Fernandes F, Ferrando M, et al. Minimally Invasive Autopsy Practice in COVID-19 Cases: Biosafety and Findings. Pathogens. 2021; 10(4):412. https://doi.org/10.3390/pathogens10040412 PMID: 33915771
17. Maixenchs M, Anselmo R, Sanz A, Castillo P, Macete E, Carrilho C, et al. Healthcare providers' views and perceptions on post-mortem procedures for cause of death determination in Southern Mozambique. PLoS ONE. 2018; 13(7):e0200058. https://doi.org/10.1371/journal.pone.0200058 PMID: 29979720
18. Wagensveld I. How to implement a Minimally Invasive Autopsy (MIA) procedure in a hospital setting; a practical guideline for radiologists. ECR. 2016 [cited 2020 May 22]. https://doi.org/10.1594/ecr2016/C-1235 Available from: https://epos.myesr.org/esr/viewing/index.php?module=viewing_poster&task=&pi=132972.
19. Castillo P, Ussene E, Ismail MR, Jordao D, Lovane L, Carrilho C, et al. Pathological Methods Applied to the Investigation of Causes of Death in Developing Countries: Minimally Invasive Autopsy Approach. PLoS ONE. 2015 [cited 2020 May 22]. https://doi.org/10.1371/journal.pone.0132057 Available from: https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0132057. PMID: 26126191
20. Monteiro RAA, Duarte-Neto AN, Silva LFF, Oliveira EPP, Filho JT, Santos GAB, et al. Ultrasound-guided minimally invasive autopsies: A protocol for the study of pulmonary and systemic involvement of COVID-19. Clinics (Sao Paulo). 2020; 75:e1972. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7233669/.
21. UFC. Universidade Federal do Ceara. 2021 [cited 2021 Apr 10]. Available from: http://www.ufc.br/noticias/15437-projeto-coordenado-por-professor-da-ufc-resulta-em-primeira-autopsia-minimamente-invasiva-da-historia-ceara.