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Editorial

Mode of death after cardiac arrest: We need to know

Even if obtaining a stable return of spontaneous circulation(ROSC) is the major endpoint of cardiopulmonary resuscitation (CPR), the following outcome is poor in many cardiac arrest patients with a return of cardiac activity. During their subsequent in-hospital course, many of these victims will die as illustrated by a very high mortality rate in ICU, reaching up to 60–70% in both in-hospital cardiac arrest (IHCA) and out-of-hospital cardiac arrest (OHCA).[1–3] In patients with a sustainable ROSC, a complex pathophysiological process commonly occurs, called post-cardiac arrest syndrome, which involves in various degrees both hemodynamic disturbances and anoxo-ischemic brain injuries.[2] In addition to pre-existing comorbidities, the severity of this post-resuscitation syndrome may be further worsened by the persistence or the recurrence of the cardiac arrest cause (such as coronary occlusion or pulmonary embolism). The pathophysiology of the post-resuscitation shock usually combines vasoplegia and myocardial dysfunction, that can result in a refractory circulatory failure and multiple organ dysfunctions. Specific treatments can be proposed to prevent and manage these cardio-circulatory complications, such as coronary reperfusion,[4] fibrinolysis,[5] mechanical support if refractory myocardial dysfunction,[6] and antiarrhythmic drugs to prevent recurrent arrhythmia.[7] Anoxo-ischemic brain damages can be fatal, causing brain death or irreversible lesions that lead to withdrawal of life sustaining treatment (WLST). Accordingly, neuroprotection is a main issue in post-cardiac arrest care, using pharmacological interventions, temperature management, restauration of homeostasis and adequate prognostication.[8] Overall, an adequate appraisal of causes of death is a cornerstone in the management of the post-resuscitated patient in order to identify potential therapeutic tools.

Despite being crucial, data regarding mode of death after cardiac arrest remain sparse. In a pioneer study, Laver et al.[9] assessed the mode of death in 126 patients admitted in ICU after a cardiac arrest (both IHCA and OHCA). They used a quite simple classification (multiple organ failure versus cardiovascular versus neurological) and they reported that the most common cause of death was related to irreversible brain injuries (46% in the whole population). In another study, Dragancea et al.[10] reported the cause of death of 86 post-cardiac arrest patients, classified as brain-related (71%), cardiovascular, or other cause. Finally, in a larger study, Lemiale et al.[11] assessed the mode of death in 768 OHCA patients. This study revealed that one-third of these deaths were related to shock and multiple organ failure and two-thirds were attributable to neurological injury (including 12% of brain deaths). On the whole, these studies firmly confirmed the prominence of brain damages, but details regarding withdrawal of life sustaining treatments (WLST) were lacking, although most of these "brain-related deaths" are known to be the consequence of active WLST.[2,12] Obtaining more detailed information regarding decisions of WLST is needed in this setting. In parallel, death from cardiovascular causes can encompass different situations, which may require different specific treatments. Finally, even if 2015 guidelines recommend collecting the cause of death as an Utstein element,[13] there is no consensus regarding definition and no standardized classification. An improved methodology for categorizing modes of death after cardiac arrest is necessary.

In the study published in *Resuscitation* (March 2019, Volume 136) Witten et al.[14] propose a new and very interesting classification for modes of death after IHCA or OHCA, using five predefined categories (WLST for neurological reasons, WLST due to comorbidities, refractory shock, recurrence of sudden cardiac arrest and respiratory failure). They evaluated this classification in a monocentric population of 408 patients (182 IHCA and 226 OHCA) who died in hospital after sustained ROSC. Two reviewers classified patients in the predefined categories, resulting in an acceptable agreement (κ between 0.61 and 0.62). Interestingly, causes of death differed between IHCA and OHCA: whereas a strong majority of OHCA (73%) died from neurological WLST, reasons of death after IHCA were more disparate (one third of WLST due to comorbidities, one quarter of WLST due to neurological failure, and one quarter of refractory shock). This offers interesting information, which is consistent with the specificities of each setting. Schematically, the outcome after OHCA appears mainly driven by brain anoxo-ischemic lesions (as described in previous studies[9–11]). By contrast, IHCA patients seem more likely to present with pre-existing comorbidities, which is a strong determinant for WLST in these patients. This study adds to the existing literature, as it provides a more precise description of causes of death, suggesting that different algorithms for management and decisions of WLST should be used for IHCA and OHCA. The classification into 5 categories that was used by Witten and al. will appeal to clinicians, and its ability to discriminate WLST according to their cause (brain injury vs comorbidities) is an important added value compared to previous categorizations. These results, although interesting, must be interpreted in the light of limitations. First, interrater reliability is slightly better than moderate, underlining the difficulty to classify several cases. As underlined by authors, another strong limitation is related to the monocentric design of this study. The classification will require an external validation to assess its generalizability in other settings and other countries, with different systems of care. Third, causes of death are strongly related with initial aetiology: for example

patients with neurological causes of arrests[15] may require specific classification. Finally, "granularity" of the classification should be enhanced, and specific identification of brain deaths (accounting for up to 10–12% of patients after cardiac arrest[16]) would be useful.

Beyond these limitations, authors should be congratulated since they indubitably fill in a gap. In OHCA patients, brain damages are by far the first cause of death during in-hospital course, and research should therefore focus on prevention and treatment of cerebral injury provoked by the circulatory arrest. On the opposite, IHCA prognosis is strongly mediated by comorbidities, and this might be considered in a specific WLST algorithm. Improving the description and establishing an accurate classification of causes of death after cardiac arrest will be very helpful, and the present study offers interesting clues that should be pursued to improve taxonomy of cardiac arrest research.

Conflict of interest

None.

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