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Editorial

Understanding post-cardiac arrest myoclonus

Myoclonus, the brief involuntary twitching of a muscle or group of muscles, occurs in about 20% of patients resuscitated from cardiac arrest [1,2]. It can be a manifestation of widespread and irreversible brain injury, or a "benign" clinical entity that does not portend a poor outcome. Distinguishing between these conditions is a common clinical problem early after resuscitation.

At one time it was said that all early, severe myoclonus after resuscitation was "myoclonic status epilepticus" (MSE), or "status myoclonus", and that the survival rate was close to zero [3]. In fact, some patients with severe early myoclonus after cardiac arrest have the benign form, and make a good functional recovery [1,2,4–6].

Myoclonus can arise from injuries to different regions of brain or spinal cord [7,8], including the ventrolateral thalamus [9,10], but the pathophysiology and localization of myoclonus–inducing lesions after cardiac arrest remain poorly characterized. Electroencephalography (EEG) was not traditionally required to make a diagnosis of MSE after cardiac arrest; the definition instead relied on the timing and classic motor activity [11,12]. Accordingly, the identification of benign and malignant EEG subtypes among patients with myoclonus after cardiac arrest is only now being elucidated. Interpreting the EEG in patients with myoclonus can be challenging, since muscle activity causes electrical artifact, and neuromuscular blockade is often needed to evaluate correlations between electrical discharges and muscle contraction.

A registry-based study of 2532 patients after cardiac arrest revealed myoclonus in 18%, and a higher incidence of good outcome (26/170 or 15%) if epileptiform activity on EEG did not accompany the myoclonus, compared to 2% (5/205, $p < 0.001$) when epileptiform correlates were present [1]. Such myoclonus with corresponding EEG features has been called "cortical" myoclonus, while "subcortical" myoclonus refers to the characteristic muscle activity without EEG findings, and presumably arises from injury to the brainstem or spinal cord.

Recent studies provide detailed EEG and neurological assessments at the patient level, and have focused on EEG and physical examination findings of patients with good outcomes despite myoclonus after resuscitation [5,6]. Elmer and colleagues evaluated EEG findings in 69 patients with myoclonus after cardiac arrest, including 7 that survived and 4 with good outcomes. In that study, two experts classified EEG recordings into four different phenotypes, and correlated those patterns with outcome. "Pattern 1" in which ≥50% of the EEG background was suppressed, interrupted by high-amplitude polyspikes in "lockstep" with myoclonic jerks, and "Pattern 2" in which narrow vertex spike-wave discharges occurred on a continuous EEG background, also in "lockstep" with myoclonus. Only patients with Pattern 2 survived with a favorable outcome, which occurred in 4 of the 8 patients (50%). Only two patients had "subcortical" myoclonus, and neither survived [5].

In this edition of *Resuscitation*, Dhakar describes myoclonus which occurred in 22% of their 280 patient cohort, focusing on 59 subjects with myoclonus and EEG data available [6]. This cohort included seven patients who regained consciousness (11.9%), including six whose myoclonus began within 24 h of resuscitation, putting to rest the idea that early myoclonus is always associated with poor outcome. Similar to findings by Dr. Elmer and his colleagues, only patients whose myoclonus occurred with normal voltage criteria in their EEG background survived; this included subjects with continuous, near continuous (< 10% of epoch time showing suppression or attenuation), or discontinuous (10–49% suppression or attenuation) backgrounds, but not those with > 50% of epoch time showing suppression or attenuation (all of whom died). The finding of better outcomes among patients whose EEG never showed suppression or attenuation > 50% of epoch time is consistent with prior publications including patients after cardiac arrest without regard to myoclonus [13–15]. Among the 39 patients with video files available, 5/18 (28%) patients with asynchronous involvement of > 2 body parts recovered consciousness, while none of the remaining 21 patients with isolated facial/ocular myoclonus, whole-body myoclonus, or limbs-only myoclonus recovered. In this small cohort, only patients in the "cortical" myoclonus subgroup survived, while those with "subcortical" myoclonus uniformly died. It is also notable that the EEG patterns identified in cardiac arrest survivors in both the Elmer and Dhakar cohorts are similar to those reported in the Lance-Adams syndrome [16].

It is important not to over-interpret these pioneering studies, with either small cohorts [5,6] or unconfirmed EEG interpretations [1]. Nonetheless, a more complex picture of myoclonus in cardiac arrest survivors is emerging, which will need further confirmation. Different EEG and clinical phenotypes of myoclonus exist, and they do not share the same pathophysiology or prognosis. This should make us feel humble in our knowledge, and cause us to act conservatively, especially in prognostication and the withdrawal of life-supporting therapies.

Complexity and heterogeneity within the cardiac arrest survivors with myoclonus should not be a surprise, given the great diversity of cardiac arrest etiologies and widely varying patient substrates. Consider the different types and severities of brain injury caused by sudden cardiac death (an immediate cessation of all blood flow), as opposed to drug overdose (a prolonged period of hypoxia and hypoventilation followed by a circulatory arrest), or near hanging (venous engorgement and ICP rise, followed by abnormalities of ventilation and then circulatory arrest) or pulmonary embolism (prolonged or brief hypotension and hypoxemia followed by circulatory arrest). When we add to these diverse etiologies dissimilar no-flow and low-flow intervals, variable CPR quality, profound differences in oxygenation and pH, and physiological variations inherent to the patients themselves, we should expect a lack of uniformity in the type of neurological injury after an arrest. The difficulty of our work as intensivists comes in interpreting this variation, while providing consistent, individualized, and high-quality patient care.

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To better standardize our current clinical efforts and research activities regarding myoclonus, it is important we use precise language. Strictly speaking, this is not "post-anoxic myoclonus", because more often it is a hypoxic-ischemic brain injury. This is not "myoclonic status epilepticus", because the myoclonus only occasionally coincides with the EEG findings of status epilepticus. The best way to think about and to discuss "post-cardiac arrest myoclonus" may be to characterize the movements themselves, the EEG correlates, and the EEG background. For example, a patient may have "heterogeneous myoclonic activity, with midline maximal spikes arising from a continuous background, corresponding with the abnormal movements" – a pattern associated with a more favorable prognosis, or perhaps "monolithic facial myoclonus, with corresponding epileptiform bursts arising from a pattern of > 50% burst suppression" – a very unfavorable phenotype. Only by embracing the complexity of myoclonus after cardiac arrest will we be able to offer that individualized and high-quality care we expect.

This new research is a welcome addition to existing scientific knowledge of the different patterns and outcomes of post-cardiac arrest myoclonus. Additional work that correlates these findings with MRI and autopsy results would be of great additional value. Our advice to clinicians is to characterize myoclonus after cardiac arrest carefully, but to rely on better established and multimodal approaches to prognostication, as per recent European guidelines [17], avoiding the temptation to oversimplify and assume that myoclonus after a cardiac arrest event invariably means the end. At our center (and we suspect many others), a small but growing cohort of cardiac arrest survivors with myoclonus and their families can clearly tell you how glad they are to be alive.

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