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Resuscitation

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Editorial

On prognostication and withdrawal of life sustaining treatment after cardiac arrest: Does the "thin gray line" between life and death (too often) wear white?

Initial, successful, resuscitation after cardiopulmonary resuscitation in patients with sudden cardiac arrest is increasing, as well as their survival through admission to Intensive Care Units (ICU).[1,2] However, what happens then? Between 50 and 89% of these survivors will die in-hospital and this number is not improving in parallel with initial success.[3,4] More than 40% of deaths following cardiac arrest patients admitted to ICU can be attributed to withdrawal of life supporting therapy, typically due to expectations of poor outcome.[5]

In this edition of Resuscitation, May et al. study our ability to select patients for early withdrawal of life supporting therapy (eWLST), based on data from real clinical practice.[5] Their findings are reason for serious reflection.

Is this just another statistical approach to a database investigation? No! May et al. focus carefully on common practice in hospitals, where consideration of when to continue or stop treatment (WLST) are real issues. This paradigm has a large and abiding impact on survival after resuscitation from cardiac arrest. They offer a unique, high level, insight into this difficulty in the role of critical care staff and into which factors play a role in the selection process.[6,7]

Underlying early withdrawal of life-supporting/sustaining therapy (eWLST) is the concept of prognostication. This concept, as applied to medicine, refers to a judgment which directs therapy based on expectations of outcome. In many cases, prognostication is expressed as limiting or withdrawing technical support or interventions, including WLST.[5,6,8,9] Prognostication, by extension, is about the *right care for the right person at the right time* and is expectation driven. Its implied focus is avoiding "bad outcomes" such as late deaths, a low quality of life, the unintended need for chronic care, etc. and contains the ability to allow for humane, timely and worthy, death if this endpoint seems inevitable. It suggests the ability to objectively predict the course of disease based on its component parts as they apply to that specific patient and also in some regard deals with resource management.[10]

Current guidelines strongly suggest that prognostication after cardiac arrest be multi-modal and include clinical examination, electrophysiological assessment (EEG, SSEPS), biomarkers, and imaging (CT or MRI).[6,11,12] Ideally, entry into any critical care, post resuscitation, pathway will allow for 'opting out' as time progresses and more information becomes available.[13,14]

eWLST is defined as do not attempt resuscitate orders (DNAR), withdrawal of life support, and death within 72 h of the cardiac arrest. This form of prognostication remains under careful scrutiny since high quality, unequivocal, multi-factorial evidence essential for this choice remains hard to come by.[14] The multi-organ involvement after cardiac arrest further complicates this as for example metabolism of sedatives may delay awakening without impacting final outcome. The 72 h period reflects an interval within which temperature management has been finished and clinical, electrophysiological, and biomarker results become (more) reliable.[6]

In their manuscript, May et al. describe data from 2688 patients in the INTCAR database and were able to match patients with eWLST to patients with full supportive care. Endpoints were clinical outcome (Cerebral Performance Category (CPC) classes 1–2 versus CPC classes 3–5. Using propensity matching they found that fully 19% of patients in the eWLST group could have been predicted to survive with good neurological outcomes.[5]

Disturbingly, this high percentage is in line with the 16% found by Elmer et al.[16] using specific trial registries. Elmer et al. extrapolated this to 1500 excessive deaths in the USA per year.[16] Remember that while initial treatments such as CPR are focused on reestablishing effective circulation and oxygenation, critical care is focused not only on treating the root causes, but also on the ability of the patient to achieve an acceptable neurological recovery and a good quality of life, after the arrest, the resuscitation and after ICU care.[10] This with background knowledge that as many as 90% of definitive CPR survivors have some neurological consequences.[5,8,10]

Central to the issue May et al. describe and to our interest, is that prognostication and WLST is self-fulfilling: if life support is withdrawn, the patient will typically die. Whether an expected bad outcome actually would have occurred therefore remains unknown. So how could May et al. compare?[5] They used propensity matching. Characteristics which are in the database and describe the patients are carefully selected. For example, if the arrest was witnessed, length of any no-flow period, initial rhythm, time to ROSC, volume of adrenaline, whether targeted temperature management was used, type of sedation used, pre-existing burden of disease, etc. may be used.[17] May et al. decided on 12 variables. Patients were matched in a 1:2 ratio based on the overall similarity using all the variables to give the most robust analysis.[5]

In their manuscript, May et al. note that 42% of patients (1162 of the 2688) patients were exposed to WLST at some point during their

treatment. They found risk factors for consideration of eWLST such as age, female gender, increasing ischemic time, and US center, among others.[5] Their manuscript contributes to our understanding of how we do things and re-alerts to subjectivity.

Why, do you ask, would critical care staff use eWLST if its base in evidence is so slim? Why 72 h as 'early'? Well, withdrawal of life support is only of consequence if it has impact.[13] After 72 h, strategies for weaning and extubation, and organ support become relevant. Once life support has been stopped, a natural course can only be changed by (active) interventions, potentially lengthening suffering and loss of dignity for both the patient and their kin.

May et al. work carefully, as their manuscript reflects and the topic warrants. They review missing data, and select co-variables based on their overlapping characteristics, such as witnessed arrest is closed linked to early defibrillation. Are there limitations to their study?[5] Some of the important considerations were not noted in the database: were there living wills or was medical futility clear early on? Was there an entry bias to the database, in which patients who survived only briefly in the ICU, for any cause, were not registered?[15] These aspects remain, due to the very observational nature of the study, unknown. Propensity matching is intended to allow retrospective analysis in situations which, ethically or practically, are simply not possible to achieve prospectively. Indeed, this goes to the heart is the concern: are we, as staff involved in resuscitation, letting death happen in (too) many, with the hope of preventing bad outcomes in some?[15] May et al. offer us food for thought.

Is the study relevant for all those involved in the chain of survival, including those in the pre-hospital setting? Yes, we think so! Without the understanding of the full course of resuscitation, caregivers may hold back initial care, or not recognize the importance of their contribution to good outcomes. Investment in early, intense and aggressive, care could be lost if unexpected deaths in the hospital or to WLST are not understood. High quality information from the scene can impact choices later. The difficulty in offering appropriate care should be understood by all, hopefully focusing further attention on prognostication and eWLST.

Yes, the manuscript contains statistics. However, it is well written and accessible. Read beyond the methodology to the message and its motivation. Accept that important knowledge can be gained using data analysis including propensity matching in databased investigations, and that we all must learn to understand this. The manuscript is insightful and provocative: we trust you will enjoy its reading.

Conflict of interest statement

Neither of the authors have any conflict of interest or financial interest in the manuscript or the subject describes therein.

We received no intern or external funding for this project.

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Received 23 March 2019
Accepted 25 March 2019

http://dx.doi.org/10.1016/j.resuscitation.2019.03.034