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(Accepted for publication June 7, 2019.)

Cardiac Events after Electroconvulsive Therapy: Reply

In Reply:

We appreciate Dr. Østergaard and Dr. Kellner's comments on our article. The mortality rate in Tørring *et al.*[1] was 2.1 deaths (95% CI, 1.2 to 3.4) per 100,000 electroconvulsive therapy treatments and 6.0 deaths (95% CI, 2.0 to 23.0) per 100,000 electroconvulsive therapy treatments in our meta-analysis.[2] The difference may appear large; however, the 95% CIs overlap and thus, the two studies are less discrepant than they appear at first sight. Three primary reasons may explain the difference between the two studies. First, as pointed out by Østergaard and Kellner, there are statistical differences. Second, our study aimed at all-cause mortality to obtain an unbiased estimate of risk after electroconvulsive therapy. Trying to identify a causal relationship between electroconvulsive therapy and death from a retrospective review of the literature is difficult at best, and exposes the analysis to bias, which we wanted to avoid.[3] Third, we included all studies regardless the sample size (Tørring *et al.* included only studies with a minimum of 3,000 electroconvulsive therapy treatments). We choose to include all studies to limit selection bias but accept the concern of a small study bias.

The mortality rate per patient undergoing electroconvulsive therapy is not reported in the study by Tørring *et al.* The reason that the reported risk[2] per patient is proportionally higher than per electroconvulsive therapy treatment, is that most patients undergo a series of electroconvulsive therapy treatments. In Tørring *et al.*'s study (table 1 from Tørring *et al.*[1]), each patient underwent, on average, 8 to 12 treatments, which may translate into a higher mortality rate per patient compared to per electroconvulsive therapy treatment.[2]

We completely agree with Østergaard and Kellner's statement to "avoid unfounded fear of electroconvulsive therapy—especially among patients with life-threatening mental disorders where this treatment can be life-saving—it is of utmost importance that the mortality related to electroconvulsive therapy is calculated and presented in a meaningful manner." This was our goal and we stand behind the findings of our study.

Competing Interests

The authors declare no competing interests.

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DOI: 10.1097/ALN.0000000000002928

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(Accepted for publication June 7, 2019.)

Delays Decrease Survival in Cardiac Arrest: Comment

To the Editor:

I read with interest the recent article by Bircher *et al.* regarding survival after in-hospital cardiac arrest.[1] The article, like others from the Get With The Guidelines–Resuscitation Investigators, continues to disseminate

inaccurate time-interval data from in-hospital resuscitation attempts. To their credit, the authors do acknowledge (more clearly than in some other Get With The Guidelines–Resuscitation articles) the limitations of their data, most importantly "the lack of independent verification of the times recorded." But taking inaccurate time-interval data from Get With The Guidelines–Resuscitation or other sources at face value hides serious delays in response to in-hospital cardiac arrests. It can also lead to flawed studies and questionable conclusions.

In the case of the present article, the conclusion that survival rates after both cardiopulmonary resuscitation (CPR) and defibrillation or epinephrine are time-dependent is hardly surprising; indeed, it would be astonishing if this were not the case, in view of the overwhelming evidence of the relationship (at least for starting CPR and first defibrillation) from out-of-hospital and animal studies.[2] The inaccuracy of the underlying data from this study limits the yield of useful information, leading to the limited and unsurprising conclusion that longer times to emergency interventions are worse for survival.

The time data reported here and in other Get With The Guidelines–Resuscitation studies only loosely represent reality. Current Get With The Guidelines–Resuscitation data include a figure from all hospitals for times to first defibrillation of 1 minute median and 0 minutes first interquartile. Such numbers are typical, when they are tracked at all—but they strain credulity.[3] The time intervals are imprecise—typically based on a handwritten record marking only the nearest whole minute—and the reported time intervals are often so short as to be simply impossible. Data-acquisition methods are not standardized across hospitals and wide variation is unavoidable, as evidenced by the 5,036 instances of *negative* times to start of CPR. Although there is no direct statistical evidence to show the inaccuracy—no one is reporting better data for comparison—some clinicians will no doubt recognize simply by reflecting on their own clinical experience that the reported intervals are impossible. Additional *prima facie* evidence is available at most clinical simulation centers simply by timing simulated defibrillation attempts under realistic conditions, as in "mock codes."[4,5]

Inaccurate time data is a major impediment to resuscitation research, offering only a blurred image of clinical reality. The authors state that "causal factors for delays and…other unknown factors that may influence timeliness of CPR or defibrillation and epinephrine treatment…remain areas of active investigation within Get With The Guidelines–Resuscitation." Those efforts are welcome, but such factors are not going to be revealed by the current numbers—far better data quality is required. Equally important is that the poor time data obscure the problem of serious delays in cardiac arrest response.

The flawed data can also lead to dubious conclusions. A recent study of Get With The Guidelines–Resuscitation's pediatric data found no evidence that defibrillation success decreases with time. This astonishing finding must be questioned in light of the limitations of the underlying data.[6]

In 2000, the American Heart Association (Dallas, Texas) and International Liaison Committee on Resuscitation called for better time-interval data from in-hospital resuscitation attempts. The 2000 Emergency Cardiac Care Guidelines stated:

> Documentation of in-hospital resuscitation events is often inaccurate and therefore unreliable in making quantitative assessments of such critical components as time to defibrillation and other interventions during resuscitation. This must be corrected [in order]… to provide accurate assessment of resuscitation practices.… Accurate time-interval data must be obtained because it is the key to future high-quality research.[7]

Unfortunately, nothing meaningful has been done to address the problem in the years since the 2000 statement. This is a serious impediment to hospital quality improvement and resuscitation research—even more so because fixing the problem can be relatively simple.[8] In addition to conducting studies based on their current data, Get With The Guidelines–Resuscitation researchers should endeavor to improve the quality of their future time data. In so doing, they can increase the probability of finding new clinical approaches that will increase survival.

Competing Interests

The author declares no competing interests.

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DOI: 10.1097/ALN.0000000000002914

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(Accepted for publication July 11, 2019.)

Delays Decrease Survival in Cardiac Arrest: Reply

In Reply:

We thank Mr. Stewart for his interest in our article[1] and for his comments. We agree that accurate and precise data are always desirable for testing of hypotheses. However, we believe that it is not "relatively simple" to acquire accurate time data for the response to in-hospital cardiac arrest. Indeed, Mr. Stewart also acknowledges that no one else is reporting data better than the Get With The Guidelines–Resuscitation registry. The reality is that time data are difficult to capture accurately given the chaotic nature of an emergency response to in-hospital cardiac arrest. Therefore, some degree of inaccuracy likely exists. Furthermore, recorded clock times are impossible to validate as there is no gold standard with which to make comparisons.

Part of Mr. Stewart's comments arises from our full disclosure of the distribution of times to cardiopulmonary resuscitation and subsequent times to either defibrillation or epinephrine. Our intention was clear: to fully inform the readers so that they may judge the validity of the conclusions themselves based on the best available, although imperfect, time data. Importantly, in performing our analysis, we excluded values that were implausible at face value, and meticulously documented exactly what exclusions had been made at each stage of analysis. Therefore, we believe our findings are unlikely to be invalidated by a relatively small subset of aberrant data. In addition, we posit that any misclassification of time delays in our data would be nondifferential and would bias the results toward the null hypothesis, (*i.e.*, toward no effect of delay on survival). Therefore, our results represent a conservative estimate of the harm caused by the delays. The actual impact of delays in care on survival is likely to be larger.

The value of the Get With The Guidelines–Resuscitation database is to allow compilation of a large number of cases from multiple centers to ensure generalizability of study inferences. Despite some imperfections, this allows for the development of testable hypotheses as well as identifying limitations in the current standard of care. Such a database is arguably better and more clinically informative than expert opinion alone. The database and its analyses also provide a framework for refinement of the data gathering mechanism. Only by publication of analyses based on this set of data, and candid discussions such as this one, can improvements in data quality be made. At present, however, the data represent our best opportunity to understand the impact of delays in key processes on resuscitation outcomes and therefore provides valuable information. That information not only tells us what we know (that delays can lead to adverse outcomes for patients), but also quantifies to what degree delays lower the likelihood of survival.

Competing Interests

The authors declare no competing interests.

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DOI: 10.1097/ALN.0000000000002915

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(Accepted for publication July 11, 2019.)