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## Cardiac Events after Electroconvulsive Therapy: Comment

To the Editor:

We read the recent paper “Major Adverse Cardiac Events and Mortality Associated with

Electroconvulsive Therapy” by Duma *et al.*<sup>1</sup> published in *ANESTHESIOLOGY* with great interest. We recently wrote an article entitled “The Mortality Rate of Electroconvulsive Therapy: A Systematic Review and Pooled Analysis,”<sup>2</sup> which has a very similar focus to that of Duma *et al.*, but the results are strikingly different. According to Duma *et al.*, “All-cause mortality was 0.42 (0.11 to 1.52) deaths per 1,000 patients and 0.06 (0.02 to 0.23) deaths per 1,000 electroconvulsive therapy treatments,”<sup>1</sup> which is substantially different from the results from our analyses “...yielding an [electroconvulsive therapy]–related mortality rate of 2.1 per 100,000 treatments (95% CI, 1.2 to 3.4).”<sup>2</sup> The main reason for this discrepancy (there are also differences in the statistical approach) is that we focused exclusively on deaths that were plausibly causally related to electroconvulsive therapy, *i.e.*, taking the timing (during or relatively soon after electroconvulsive therapy) and cause (*e.g.*, cardiac arrest or aspiration pneumonia) into account, while Duma *et al.* focused on all deaths that were reported in studies of electroconvulsive therapy—irrespective of the timing and cause of death. As evident from the mortality estimates previously noted, this distinction has important consequences.

In order to understand how the distinction between “[electroconvulsive therapy]–related mortality”<sup>2</sup> and “mortality associated with electroconvulsive therapy”<sup>1</sup> has resulted in the very different mortality estimates reported in the review by Tørring *et al.*<sup>2</sup> and Duma *et al.*,<sup>1</sup> respectively, let us look at the study by Shiwach *et al.*<sup>3</sup> In this study, it was reported that “Only one death, which occurred on the same day as the electroconvulsive therapy, could be specifically linked to the associated anesthesia. An additional four deaths could plausibly have been associated with the anesthesia.”<sup>3</sup> These five deaths were included in the analyses by Tørring *et al.*,<sup>2</sup> while Duma *et al.* included all 30 deaths occurring within 14 days of an electroconvulsive therapy session, irrespective of the cause<sup>1</sup>—for example, eight suicides (suicidal ideation/intent is among the prime indications for electroconvulsive therapy—so these death are highly unlikely to be caused by electroconvulsive therapy), a death due to cancer, and a death due to an auto accident that took place 4 days after the last electroconvulsive therapy session.<sup>3</sup> As related examples, Duma *et al.*<sup>1</sup> included data from the relatively small studies by Tecoult and Nathan,<sup>4</sup> and Martinez *et al.*<sup>5</sup> in their assessment of mortality associated with electroconvulsive therapy. We did not include data from these studies in our review<sup>2</sup> because we required a study to report on at least 3,000 electroconvulsive therapy treatments in order to avoid inclusion of deaths due to chance findings or selection or publication bias.<sup>6,7</sup> However, even without this sample size restriction, we would not have included the deaths reported in these two studies in the calculation of electroconvulsive therapy–related mortality, as their causal relation to electroconvulsive therapy is highly doubtful. In the study by Tecoult and Nathan,<sup>4</sup> the one death that occurred was described as follows: “One patient aged 42 years, died at home from

pneumonia 4 days after electroconvulsive therapy. She had previously had several bowel obstructions due to the large amount of antipsychotic medication she was taking. Unfortunately, we have no information to judge whether the pneumonia was related to electroconvulsive therapy or not.”<sup>4</sup> In the study by Martinez *et al.*,<sup>5</sup> the two deaths that occurred were described as follows: “Two of the patients with elevated cTn (cardiac troponin) subsequently died. No other clinical events were noted during follow-up of 18 months after reviewing the electronic medical record.”<sup>5</sup> According to the corresponding author of the Martinez *et al.* study, these two deaths were unlikely to be directly related to electroconvulsive therapy (written personal communication, December 2018, with Allan S. Jaffe, M.D., Division of Cardiovascular Diseases, Department of Internal Medicine, Mayo Clinic, Rochester, Minnesota). Consequently, that Duma *et al.*<sup>1</sup> consider these deaths to be associated with electroconvulsive therapy seems unreasonable.

To summarize the previous paragraph, Duma *et al.*<sup>1</sup> have shown that people receiving electroconvulsive therapy die at some point—from a variety of causes. They acknowledge this lack of causal link to electroconvulsive therapy in a short passage in the Discussion section of their paper: “Deaths may occur after electroconvulsive therapy because of many other factors and may only be temporally observed but not causally related to the electroconvulsive therapy treatment.”<sup>1</sup> That patients receiving electroconvulsive therapy die at some point is hardly a surprise, and as we pointed out in our recent review, “...the association between [electroconvulsive therapy] and death is very likely to be confounded by indication for the following reasons: [electroconvulsive therapy] is often used for patients with mental disorders who cannot tolerate medications due to cardiovascular or other general medical conditions or for patients with life-threatening disorders such as neuroleptic malignant syndrome (NMS), malignant catatonia, or delirium. Such patients are inherently at a relatively high risk of dying due to their overall disease burden.” In other words, patients receiving electroconvulsive therapy are very likely to die from the conditions that electroconvulsive therapy is used to treat and not *due to* electroconvulsive therapy itself. In fact, not receiving electroconvulsive therapy when the treatment is indicated may be a life-threatening situation for a patient.<sup>8</sup>

Since we took the timing and the cause of death into account in our review of the electroconvulsive therapy literature, we were able to document that dying *due to* electroconvulsive therapy is an extremely rare event, as supported by the fact that we found only one electroconvulsive therapy–related death (in 414,447 treatments) reported in the literature in the period from 2001 to the date of our review (August 5, 2016). We believe that this is a highly relevant finding that can be used to reassure concerned parties, including patients in need of electroconvulsive therapy and their relatives.

Many people fear electroconvulsive therapy,<sup>9,10</sup> and even the fear of actually dying due to electroconvulsive therapy is not uncommon.<sup>9</sup> This is likely a contributing

factor to patients in dire need of electroconvulsive therapy occasionally refusing to receive the treatment, with potentially fatal consequences.<sup>8</sup> Therefore, in order 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. We believe that the paper by Tørring *et al.*<sup>2</sup> provides the most useful estimates in this regard.

### Competing Interests

Dr. Kellner reports personal fees from UpToDate (Waltham, Massachusetts), Psychiatric Times (Cranbury, New Jersey), Northwell Health (Manhattan, New York), and Cambridge University Press (Cambridge, United Kingdom). In addition, Dr. Kellner has a patent for a foam bite block for electroconvulsive therapy (U.S. patent No. 6098627). Dr. Østergaard declares no competing interests.

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## 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.*<sup>1</sup> 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.<sup>2</sup> 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.<sup>3</sup> 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<sup>2</sup> 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.*<sup>1</sup>), 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.<sup>2</sup>

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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## 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.<sup>1</sup> The article, like others from the Get With The Guidelines–Resuscitation Investigators, continues to disseminate