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# Respiratory Muscle Effort during Weaning: Reply

## In Reply:

We appreciate the interest of Özdemir *et al.* in our recent article.[1] They raise the interesting question of whether increased expiratory respiratory muscle recruitment in patients who fail a trial of spontaneous breathing is the result of increased respiratory loading and inspiratory muscle weakness or the reason of failure.

Undoubtedly, the inspiratory muscles of the patients in the failure group, including the diaphragm, were more weakened than in the success group and, among other factors, differences in duration of mechanical ventilation and underlying conditions may play a role in development of diaphragm weakness. In our study, we focused on the role of expiratory muscle physiology in weaning success and weaning failure patients. As pointed out in the discussion of our article, it has been reasoned that the goal of expiratory muscle recruitment is to assist the inspiratory muscles.[2,3] We demonstrated that in patients weaning from mechanical ventilation, a substantial amount of total energy expenditure is attributed to activation of the expiratory muscles. This is an important observation. Whether expiratory muscle recruitment is the reason or a result of failure cannot be derived from our study. However, we agree with Özdemir *et al.* that previous studies have demonstrated that increased respiratory loading, as occurs with exercise, low respiratory compliance, but also inspiratory muscle weakness results in the activation of expiratory muscles in fixed hierarchy.[4] Thus it is likely that expiratory muscles were recruited as a result of high loading. The interesting observation is the high energy expenditure by the expiratory muscles during weaning. We cannot directly derive from our data if expiratory muscle activation indeed improved diaphragm contractile efficiency. However, it is interesting to note that despite increasing activation of the expiratory muscles during the spontaneous breathing trial in weaning failure patients, diaphragm neuromuscular efficiency did not change and was still lower compared to weaning success patients.

We would like to stress that the arguments provided by Özdemir *et al.* concerning cardiac arrest or surgery in our study may not be valid. First, only three patients (33%) underwent cardiac surgery in the failure group. The risk of iatrogenic phrenic nerve injury as a result of cardiac surgery when using ice slush[5] is uncommon with the use of more modern cardioplegia techniques as used in our center (Radboud University Medical Center, Nijmegen, The Netherlands). Second, we found no evidence of increased pulmonary edema in the failure group during the weaning trial (*i.e.,* no differences in dynamic lung compliance between groups).

### Competing Interests

The authors declare no competing interests.

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# Delirium after Cardiac Surgery and Cognitive Change: Comment

## To the Editor:

We read with great interest the article by Brown *et al.*[1] that reported an association between delirium diagnosis and cognitive dysfunction at 1 month in patients

after cardiac surgery. The study is notable for its rigorous delirium assessment and thorough neuropsychologic battery testing at multiple perioperative time points. The conclusion that there is no difference in cognitive change at 1 yr between delirious and nondelirious patients, however, should be interpreted with caution. In addition to being potentially underpowered, the study measured delirium as a dichotomous yes/no despite previous findings that longer durations of delirium have greater impact on long-term cognitive impairment[2,3] and that increased delirium severity is associated with worse outcomes.[4,5] Brown *et al.*'s findings of lower cognitive function scores, starting with baseline assessments, for those who develop postoperative delirium are in agreement with other studies demonstrating the large contribution of preoperative cognitive performance to both acute and long-term brain dysfunction after surgery.[6–8] The question of whether this signifies a continuation of a downward trajectory initiated before surgery, is a reflection of greater baseline comorbidities, or has another explanation, has yet to be answered.

The description of resilience, or return to cognitive baseline after episode of postoperative delirium, has previously been described by Inouye *et al.*, who went on to show an accelerated cognitive decline at up to 36 months.[9] It would be interesting to see if these patients would have the same biphasic decline within domain-specific cognitive scoring. From a patient perspective, it would also be important to qualify the clinical impact of a lower overall cognitive Z-score and domain-specific cognitive scores. This could help answer whether statistically insignificant changes measured with composite cognitive scoring could potentially miss the clinical impact of delayed executive function, verbal fluency, and other domains that greatly impact patient life or whether statistically significant decline on robust in-depth testing during studies translates into appreciable deficits in the real world.

The study by Brown *et al.*[1] is important in adding to the growing body of literature attempting to define the interrelationship between postoperative delirium and cognitive decline, particularly regarding domain-specific analysis. Trials aimed at reducing delirium and postoperative decline that include similar rigorous assessments but also mechanistic testing are needed. We feel that it is essential to note the *potential* for recovery of cognition after acute brain dysfunction, but that the extent and quality of that recovery remains to be seen.

## Competing Interests

The authors declare no competing interests.

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# Delirium after Cardiac Surgery and Cognitive Change: Reply

## In Reply:

We thank Drs. Boncyk and Hughes for their letter and interest in the article, "Cognitive Decline after Delirium in Patients Undergoing Cardiac Surgery."[1] The research group at Vanderbilt University, Nashville, Tennessee, has conducted seminal work in understanding delirium and long-term cognitive change after hospitalization. We generally agree with the points discussed in the accompanying letter and are glad to see these points emphasized. Our results show a nonlinear trajectory of cognitive status after surgery up to 1 yr postoperatively. We agree that the findings of no difference in cognition by delirium status at 1 yr should be interpreted cautiously, since the 1-yr assessments were not the primary outcome and the study may be underpowered to demonstrate meaningful differences. Although we discussed this limitation and tried to be appropriately cautious in our interpretation of the 1-yr data, this letter highlights an important limitation of our results. We also agree that examining longer-term trajectories is critical, given that Inouye *et al.*[2] showed increased cognitive decline in delirious patients during extended follow-up—from 1 to 3 yr postoperatively. To this end, we are currently examining the feasibility of obtaining cognitive assessments in our study patients at time points greater than 5 yr after surgery. We also agree that patient-reported outcomes are important to consider to evaluate both statistical and clinical significance of our findings and will consider whether patient-related outcomes that we did collect could provide further insight. Finally, the importance of future observational and interventional studies to illuminate mechanisms for delirium cannot be overemphasized. The epidemiology and risk factors for delirium have been well described; a seminal current challenge is to understand mechanisms for the development and consequences of delirium after surgery and critical illness.

### Competing Interests

Dr. Brown has consulted for and received grant funding from Medtronic (Minneapolis, Minnesota). Dr. Hogue is a consultant and provides lectures for Medtronic/Covidien (Boulder, Colorado) and is a consultant to Merck (Kenilworth, New Jersey).

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