

COMMENTARY

Delirium and cardiac surgery: progress - and more questions

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See related research by Kazmierski et al., <http://ccforum.com/content/17/2/R38>

Abstract

Post-operative delirium is a common and dangerous complication of cardiac surgery. Many risk factors for delirium have been identified, but its pathogenesis remains largely elusive. A study by Kazmierski and colleagues investigates a more recently considered risk factor for delirium: perturbations in the hypothalamic-pituitary axis and depression. This and further work may help define novel prevention and treatment strategies for delirium.

Delirium is the most common neuropsychological complication following cardiac surgery, with most recent estimates of prevalence ranging from 25 to 50%. Post-operative delirium remains a clinical challenge to manage, and in and of itself is associated with increased mortality, hospital length of stay, costs, and other complications such as infection and stroke [1]. Explorations into the causes of post-operative delirium have considered myriad factors, including preexisting conditions, surgical and anesthetic management, and post-operative care. Despite the frequency of occurrence, the pathophysiology of postoperative delirium remains poorly understood.

In this issue of *Critical Care*, Kazmierski and colleagues [2] examine one potential mechanism for the development of post-operative delirium: disruptions in serum cortisol levels. An initial report demonstrating a link between disruptions and serum cortisol and the development of post-operative delirium in surgical patients was published in 1985 [3]. There has been, however, a paucity of new information since until recently. These investigations have endeavored to show a link between delirium and cortisol levels, though have missed critical

considerations, including the co-existence of other neurological conditions that play a role in the hypothalamic-pituitary-adrenal axis and hence cortisol secretion. Kazmierski and colleagues have added to this field by presenting the first analysis of the association between cortisol and post-operative delirium in cardiac surgery that assesses whether the association between cortisol and delirium is stress-related or mediated by other pathologies, such as major depressive disorder and cognitive impairment.

Consistent with previously published reports, in this study delirium was found to be associated with elevated pre-operative cortisol levels in those with major depressive disorder. While delirium was also associated with impaired pre-operative cognitive function, a more sensitive analysis considering the association between those two conditions and the development of delirium would have been informative. Other reports have demonstrated that elevated glucocorticoid levels can result in structural changes in the hippocampal neurons, thus suggesting a brain may be 'primed' for delirium [4] - a notion supported in the present work.

Of interest, Colkesen and colleagues [5] have investigated the interaction of elevated serum cortisol and the subsequent development of delirium following an acute myocardial infarction (MI) [5]. Similar to observations following cardiac surgery, post-MI delirium was more likely in those with elevated cortisol levels, demonstrating some biologic consistency in patients with significant coronary artery disease regardless of whether they underwent surgery. By extending this enquiry to the cardiac surgery patient, the authors had the opportunity to determine serum cortisol at the initial time of presentation.

An important limitation of the present study is the choice of biomarkers assessed, and the timeline over which they are considered. Plasma free cortisol, as the biologically active cortisol, would have been a preferable measure to serum cortisol, especially in light of the largely older, frail population studied - a population that likely has low albumin levels, significantly influencing laboratory values. Further, given that delirium did not

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necessarily develop on the first post-operative day, measures of cortisol outside of that initial time period would further inform the analysis. The authors also limited their choice of biomarkers to simply cortisol and IL-2. IL-2 has not previously been widely used in studies in this area, while pro-inflammatory cytokines such as IL-6, IL-8 and IL-10 have been associated with delirium [6]. Use of additional previously identified biomarkers would make this study more comparable to existing literature.

While the results of this study are interesting, it is likely premature to recommend routine pre-operative serum cortisol level testing for all subjects undergoing coronary artery bypass grafting. Rather, it seems more appropriate to suggest that the authors have unveiled a potential mechanism by which neuropsychiatric illnesses contribute to the development of delirium. Future work looking at mechanisms by which this stress response can be abrogated or perhaps avoided in the peri-operative setting may be the next logical step. Stress of any sort appears to contribute to the development of delirium. It is logical that limiting or reducing these stressors will likely be of benefit to patients in terms of both delirium and overall postoperative outcomes. Questions remain, however: can we intervene and, if so, what is the optimal time? What will decrease patient 'stress' levels?

As with low cardiac output state resulting in poor end organ perfusion potentially impacting all physiological symptoms, perhaps cardiac surgery stress and the resultant inflammatory cascade results in metabolic alterations impacting hemodynamics, immune response, respiratory function, and central neurological function. Given the advancing age and frailty of patients undergoing cardiac surgery, the present study and further work

are important for improving future peri-operative care and surgical outcomes.

Abbreviations

IL, interleukin.

Competing interests

The authors declare that they have no competing interests.

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References

1. Martin B-J, Buth K, Arora R, Baskett R: Delirium as a predictor of sepsis in post-coronary artery bypass grafting patients: a retrospective cohort study. *Crit Care* 2010, **14**:R171.
2. Kazmierski J, Banyas A, Latek J, Bourke J, Jaszewski R: Cortisol levels and neuropsychiatric diagnosis as markers of postoperative delirium: a prospective cohort study. *Crit Care* 2013, **17**:R38.
3. McIntosh TK, Bush HL, Yeston NS, Grasberger R, Palter M, Aun F, Egdahl RH: Beta-endorphin, cortisol and postoperative delirium: a preliminary report. *Psychoneuroendocrinology* 1985, **10**:303-313.
4. Fuchs E, Flügge G: Stress, glucocorticoids and structural plasticity of the hippocampus. *Neurosci Biobehav Rev* 1998, **23**:295-300.
5. Colkesen Y, Giray S, Ozenli Y, Sezgin N, Coskun I: Relation of serum cortisol to delirium occurring after acute coronary syndromes. *Am J Emergency Med* 2013, **31**:161-165.
6. van den Boogaard M, Kox M, Quinn K, van Achterberg T, van der Hoeven J, Schoonhoven L, Pickkers P: Biomarkers associated with delirium in critically ill patients and their relation with long-term subjective cognitive dysfunction; indications for different pathways governing delirium in inflamed and noninflamed patients. *Crit Care* 2011, **15**:R297.

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