Comment on “Vasoplegic syndrome following cardiothoracic surgery-review of pathophysiology and update of treatment options”

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We read with great interest the article by Bousse et al. on vasoplegic syndrome after cardiothoracic surgery [1]. It provides an excellent review of alternative pharmacologic interventions when vasodilatory shock becomes refractory to usual measures of catecholamines and vasopressin. In the article by Busse et al., the following statement is made: “In a protocol by Ortoleva et al., non-catecholamine therapy is recommended to begin at norepinephrine doses of 0.5 μg/kg/min, which has been associated, at least in the distributive shock population, with an unacceptable level of mortality.” [1, 2]. We wish to provide a clarification on this reference to our algorithm on the management to vasoplegia [3].

Our article recommends the initiation of alternate therapy at the equivalent of 0.5 μg/kg/min of norepinephrine (or other agreed upon limit) and not when the norepinephrine dose by itself has reached that level. Our article also states that “The use of vasopressin, norepinephrine, or phenylephrine are left to the discretion of the clinician...” [3]. While we believe vasopressin is a valuable addition in vasodilatory shock, the recent price increase on vasopressin has sanctioned use at our and other institutions. Hence, we did not specifically mention the use of vasopressin and instead elected to use a norepinephrine equivalent dose of 0.5 μg/kg/min which, for example, could be 0.3 μg/kg/min of norepinephrine and 0.08 U/min of vasopressin, among other possible combinations.

The article by Svir et al. is an observational study of medical intensive care unit (MICU) patients receiving either no vasopressors, less than 40 μg/min norepinephrine or at least 40 μg/min of norepinephrine [2]. A mortality of 84.3% in the MICU and 90% for the hospitalization was noted in patients receiving at least 40 μg/min of norepinephrine. However, this study notes that 43% of patients receiving high dose norepinephrine were also receiving vasopressin versus 14% in the low dose norepinephrine group. Furthermore, no patient weights were available. Hence, this article cannot be used to justify a certain weight-based threshold of high or low dose catecholamine vasopressor support because no mention is made of patient weight. Multiple articles on the use of high dose weight based norepinephrine in intensive care units exist (0.9 μg/kg/min or more and 1 μg/kg/min or more), and 0.5 μg/kg/min of norepinephrine is not used as a cut off to define “high dose vasopressors” [4, 5].

In conclusion, we wish to clarify that our article uses norepinephrine equivalent doses which can include vasopressin to allow clinicians the freedom to select therapy that is in accordance with individual institutional guidelines.

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Authors’ response
Response to “Comment on Vasoplegic Syndrome Following Cardiothoracic Surgery—Review of Pathophysiology and Update of Treatment Options”
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We thank Dr. Ortoleva and Dr. Cobey for their clarifying letter and acknowledge that the definition of “high dose vasopressors” is variable and not quantitative. It should also be pointed out that individual patients may display the side effects of catecholamine therapy at different thresholds further aggravating the possibility of a consensus definition. The study by Sviri et al. is just one of many analyses which attempt to associate outcomes with doses of vasopressor therapy. Many authors describe a catecholamine threshold of 0.5 mcg/kg/min which was acknowledged by Ortoleva et al. as the point at which alternate therapy should begin [6–8]. Alternatively, “high-dose” therapy has been defined as the need for rescue therapy with vasopressin [9, 10]. Moreover, some thresholds are weight-based [5, 11, 12] while others are not [13, 14]. There can be no doubt, however, that high doses of catecholamines are associated with adverse events, including mortality [15] and organ failure [16]. Notwithstanding some of the economic pressures that Ortoleva et al. are right to point out (including the cost of vasopressin), it is our opinion that de-catecholaminization at lower cumulative doses may mitigate some of these adverse effects seen from high-dose therapy [17]. The non-catecholamine agents highlighted in our manuscript, including vasopressin, are distinctly different from catecholamines, and should be separately and thoughtfully deployed in the right circumstances.

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