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Goal-Directed Fluid Therapy: What the Mind Does Not Know, the Eye Cannot See

Hedefe Yönelik Sıvı Tedavisi: Aklın Bilmediği ve Gözün Göremediği Nedir?

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Dear Editor,

Your recent first (1, 2) and second (3, 4) round fluid debates were enjoyable and interesting. The editor and authors are to be congratulated for an excellent distillation of the key elements of this important discussion. We have a few comments relative to key points that were made.

First, Drs. Della Rocca and Vetrugno state that dynamic indices cannot be used as indicators of fluid responsiveness (FR) during open chest conditions. Respectfully, we disagree. The authors provide us with two "supporting" references, one by Wyffels (5), and the other by Lansdorp (6). The first of these two papers included 15 patients, 10 of whom exhibited dynamic indices (DynI) that were less than 10% or were within the gray zone (7, 8). DynI within these ranges are unlikely to be associated with FR. Of note, all patients demonstrated physiologic concordance with the passive leg raising (PLR) maneuver: Stroke volume variation (SVV) and pulse pressure variation (PPV) decreased and the cardiac index (CI) rose, even during open chest conditions, though the rise in CI was not statistically significant in this small sample. The second paper by Lansdorp investigated FR in *post*-cardiac surgical patients within the Intensive Care Unit (ICU) and does not address the use of dynamic indices during open chest conditions. The idea that DynI lose their predictive ability during open chest surgery is also supported by de Waal who demonstrated that DynI were no more useful than static indicators for predicting FR during open chest conditions (9). Contrary to these findings, Reuter (10), Suehiro (11), Lee (12), Kang (13), and Rex (14) have all demonstrated that DynI can be used to predict FR during cardiothoracic surgery. *How is the practicing anesthesiologist to reconcile these contradictory conclusions?* This question was best answered by Jean Louis Teboul, who not only described a plausible physiologic mechanism based on transpulmonary pressure changes generating meaningful DynI during open chest conditions, but also provides us with a solid understanding of how DynI should be interpreted during open chest conditions. Assuming that appropriate clinical conditions are met for using DynI (15), Teboul states "the presence of high PPV (or SVV) is indicative of fluid responsiveness under both closed and open chest conditions. However, under open conditions, other tools are still required to diagnose the origin of hemodynamic instability because the presence of low PPV and SVV cannot preclude a positive hemodynamic response to fluid." (16). *As with any hemodynamic parameter, the clinician must be aware of its underlying physiologic mechanism, its clinical meaning, and the pitfalls that may derail its interpretation.*

Second, Goal-Directed Hemodynamic Therapy (GDHT) is a term that describes the protocolled use of cardiac output and related parameters as end-points for the administration of fluids and/or inotropic therapies with the objective of optimizing organ perfusion and thus improving surgical outcomes. Optimum hemodynamic management represents the cornerstone of perioperative GDHT, and it includes rational fluid management (17). In this context, the "zero-balance" approach is a form of Goal-Directed Fluid Therapy (GDFT). Although the concept of GDFT was first suggested more than 30 years ago (18), there remains no consensus about the most effective goals for fluid therapy or the most appropriate monitoring methods. As such, despite evidence demonstrating the potential benefit of this technique in several disease states (19), GDFT remains a well-accepted concept that has yet to translate into an established standard of care (20). One of the many reasons that explain this incongruity is the fact that GDFT is based on fluid challenges and the patient's response to them. Accordingly,

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as pointed out by Della Rocca and Vetrugno (4), based on the editorial by Takala (21), the crucial issue concerning FR testing is what to do with the information gleaned from it. As pointed out, FR should be considered a normal physiologic response for an individual with a healthy cardiovascular system; on the other hand, patients with heart failure, who most certainly can be FR, may easily suffer iatrogenic fluid overload if given fluids until they lack responsiveness thus generating undesirable outcomes. Among these negative outcomes, we highlight pulmonary complications. Licker et al. commented that high fluid rates during thoracic surgery may produce lung injury and pulmonary complications. Likewise, a more restrictive fluid management is important to prevent such complications in other high risk surgical and non-surgical patients. Corcoran et al. (22) showed that GDFT reduces the incidence of pneumonia, and a restrictive strategy of fluid delivery also reduces pulmonary edema. In critically ill patients, extra-vascular lung water (EVLW) monitoring may represent a valuable safety parameter to predict fluid overload (23), which is associated with prolonged mechanical ventilation and increased mortality in critically ill patients, and, more specifically, in patients with sepsis (24, 25). A study in acute respiratory distress syndrome (ARDS) patients suggests that high EVLW is an independent risk factor for mortality in ARDS (26). Accordingly, in patients where acute circulatory failure and ARDS coexist, fluid administration should be limited even in cases of preload responsiveness because of the severity of lung injury (27), as assessed by increased lung water and by alteration of pulmonary vascular permeability (28). *In this regard, rational fluid administration should include restriction of fluids especially in patients at high risk for developing pulmonary complications.*

Third, we wish to comment on two points in the Editorial comments made by Dr. Mert Senturk, that accompany Licker et al. (*Fluid therapy in thoracic surgery: A zero balance target is always the best!"*). Dr. Senturk raises the concept of the glycocalyx in fluid management and suggests that we have to "revise all the knowledge we have, such as the Frank-Starling Curve". Dr. Senturk must mean that our understanding of the glycocalyx requires a revision of the *Starling Principle,* not the Frank-Starling curve. Indeed, JR Levick and Michel CC presented a historical treatise that explained in great detail the role of the intact glycocalyx on transcapillary fluid balance entitled *Microvascular Fluid Exchange and the Revised Starling Principle* (29). Drawing upon a history of data from Papenheimer, Soto-Rivera, Landis, Zweifach and Michel, the authors propose how the intact glycocalyx, by creating a low-protein filtrate in the sub-glycocalyx space, prevents reabsorption of fluid from the tissue space back into the vascular compartment. The absence of reabsorption means that edema fluid must return to the vascular compartment by way of the lymphatic system and this is a slow process. *The take home message for anesthesiologists and intensivists is that edema can be induced quickly but resolves slowly.*

In his concluding statement Dr. Senturk asks about the existence of the "3rd space". The history of the "3rd space" concept has been thoroughly reviewed by Jacobs (30), and can be summarized as an issue of precision, or lack thereof, in measurement techniques *and* terminology. Early studies designed to assess volume changes of the intra-vascular and extra-vascular compartments required measuring changes in tracer concentrations that were assumed to be specific for their intended compartment. Frequently, however, at the end of the observation period, the total quantities of injected tracer could not be accounted for. It is likely that tracer equilibrium had not been reached and that non-specific binding of the various tracers was higher than expected. Therefore, the "missing tracer" was not in some un-measurable 3rd space that was "consuming fluid", but rather, was simply not accounted for due to measurement errors.

From a nomenclature standpoint, "the 3rd space" has occasionally been used to mean a fluid compartment that has very slow turnover and therefore has very different kinetic parameters compared to interstitial fluid and is not available to "refill" the vascular space. For example, ascites and pleural effusions are examples of such pathological fluid collections. From a terminology standpoint, calling this slow turnover compartment a "3rd space" lacks precision and has, historically, created confusion. *From a clinical perspective, there is no rationale to use the term "3rd space".*

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