Transpulmonary Thermodilution-Based Management of Neurogenic Pulmonary Edema After Subarachnoid Hemorrhage

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Abstract: Neurogenic pulmonary edema (NPE) is a potentially catastrophic but treatable systemic event after subarachnoid hemorrhage (SAH). The development of NPE most frequently occurs immediately after SAH, and the severity is usually self-limiting. Despite extensive research efforts and a breadth of collective clinical experience, accurate diagnosis of NPE can be difficult, and effective hemodynamic treatment options are limited. Recently, a bedside transpulmonary thermodilution device has been introduced that traces physiological patterns consistent with current theories regarding the mechanism (hydrostatic or permeability PE) of NPE. This article provides an overview of the clinical usefulness of the advanced technique for use in the neurointensive care unit for the diagnosis and management of post-SAH NPE.

Key Indexing Terms: Hemodynamic monitoring; Neurogenic pulmonary edema; Subarachnoid hemorrhage. **[Am J Med Sci 2015;350 (5):415–419.]**

Neurogenic pulmonary edema (NPE) is a potentially devastating but treatable systemic event associated with many forms of central nervous system (CNS) injury.[1] NPE after subarachnoid hemorrhage (SAH) occurs in 8% of patients in which the clinical grade and the extent of subarachnoid clotting may contribute to poor outcomes.[2] The development of NPE occurs most frequently immediately after SAH, and the severity is usually self-limiting or reversible after resolution of the CNS insult.[3] Although the precise mechanism underlying the development of NPE is not fully understood, the proposed etiology involves massive sympathetic hyperactivity (catecholamine surge) triggered in the hypothalamus and medulla after a sudden increase in intracranial pressure at the site of the aneurysm rupture, leading to interstitial and alveolar accumulation of protein-rich edema fluid and hemorrhage.[4] Recent studies suggest that NPE associated with SAH may contribute to a global decrease in cerebral perfusion or localized ischemia, especially when combined with severe hypoxemia or hypotension,[5] thereby complicating post-SAH fluid management and increasing the risk of delayed cerebral ischemia (DCI) and poor outcomes.[6,7] Despite extensive research efforts and a breadth of collective clinical experience, accurate diagnosis of NPE can be difficult, and effective hemodynamic treatment options are limited.

Hemodynamic monitoring is essential for the diagnosis and therapeutic management of critically ill patients.[8] Several different methods and techniques are used to monitor patients with cardiopulmonary complications, although none are ideal (ie, noninvasive, safe, reproducible, assessing both preload and lung edema volumes, as well as cardiac function).[9] Unfortunately, the use of such monitoring devices has been limited in neurocritical care, presumably due to inexperience and complexity of handling multiple hemodynamic parameters (eg, pulmonary artery catheter).[10] Recently, several studies examined acute hemodynamic changes after SAH using an advanced bedside transpulmonary thermodilution (TPTD) device.[6,11–17] The practical usefulness of early goal-directed hemodynamic management with this technique has also been proposed in postoperative patients with SAH.[18–20] This technique is very attractive for the management of NPE and related neurogenic cardiac disorders because it enables the repeated detection of small short-term changes in indexed extravascular lung water (EVLW) and pulmonary vascular permeability for the diagnosis and characterization of the mechanism of cardiac (hydrostatic) or noncardiac (permeability) PE. This technique also allows hemodynamic optimization for preventing and treating DCI, the most critical complication that impacts clinical outcomes.

This mini review provides an overview of the ability of the TPTD device in the neurointensive care unit to demonstrate real-time physiological patterns consistent with current theories regarding the mechanism and therapeutic course of post-SAH NPE.

TECHNIQUE TO DIAGNOSE AND TREAT NPE

Single-Indicator Thermal TPTD Technique

The TPTD device is available for use with PiCCO (Pulsion, Munich, Germany) or EV-1000 (Edwards Lifesciences, Irvine, CA) monitoring. The TPTD device is based on the bolus injection of normal saline into a central vein, and the thermodilution curve is measured with a thermistor-tipped catheter. This TPTD approach provides a measurement of cardiac output (CO), global end-diastolic volume (GEDV) and intrathoracic blood volume, both volumetric parameters of the preload and the EVLW, as well as additional parameters of pulmonary vascular permeability and global cardiac function. The CO, GEDV and EVLW are normalized to body surface area to obtain the cardiac index (CI) (manufacturer's reference range for the PiCCO device: 3.0–5.0 $L \cdot min^{-1} \cdot m^{-2}$), GEDV index (GEDI) (680–800 mL/m^2) and EVLW index (ELWI) (3–7 mL/kg), respectively. The pulmonary vascular permeability index (PVPI) (reference range: <3.0) is calculated as the ratio between EVLW and pulmonary blood volume. The cardiac function index (CFI) (4.5–6.5 minutes) is defined as the ratio

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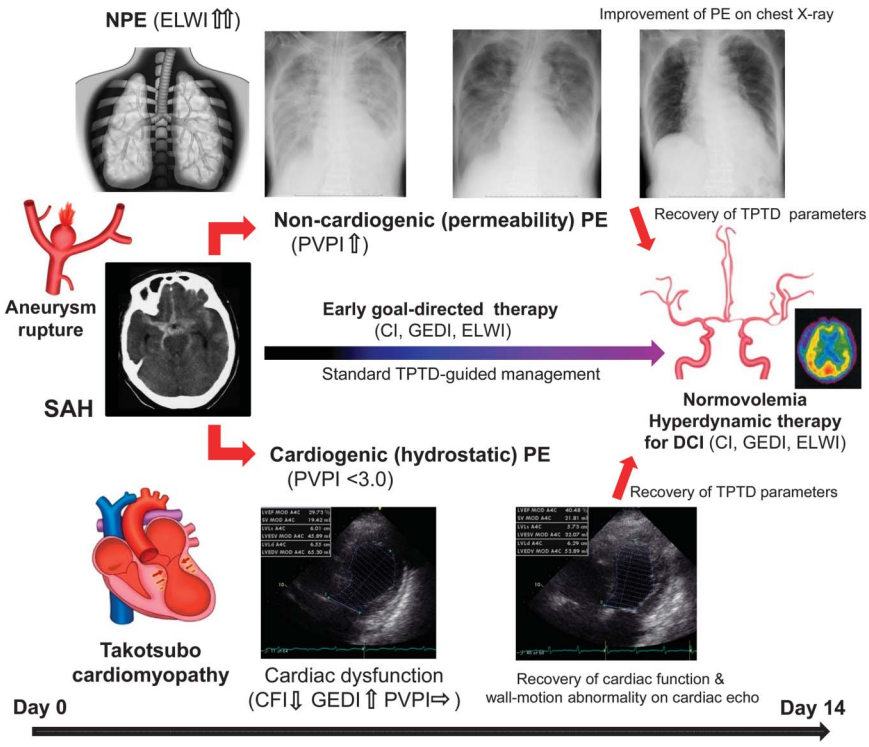

FIGURE 1. Schematic illustration of TPTD-based differentiation of non-cardiogenic and cardiogenic PE. NPE and cardiac dysfunction that are attributable to stress-induced (Takotsubo) cardiomyopathy can manifest clinically as separate entities[28] but can induce cardiogenic PE when they occur together early after SAH. In most cases, recovery or improvement in TPTD-derived parameters (in particular, CFI, ELWI and PVPI) may lead to a promising shift to standard TPTD-based hemodynamic management unless they are complicated by prolonged or other secondary cardiopulmonary disorders. TPTD, transpulmonary thermodilution; PE, pulmonary edema; NPE, neurogenic pulmonary edema; SAH, subarachnoid hemorrhage; CFI, cardiac function index; ELWI, extravascular lung water index; PVPI, pulmonary vascular permeability index.

of CO to GEDV. Full details of the TPTD method have been described elsewhere.[21]

TPTD-Based Post-SAH Hemodynamic Management

Although no specific protocols have been defined regarding postoperative SAH management, early goal-directed fluid therapy established by this study group is available.[18,20] General management of aneurysmal SAH except for postoperative hemodynamic management is basically in accordance with the American Heart Association/American Stroke Association guidelines.[22]

TPTD measurements are usually performed at least twice daily starting from day 0 to 3 until day 14 or resolution of NPE and related symptoms. Hemodynamic stability is defined as CI $\geq$ 3.0 $L \cdot min^{-1} \cdot m^{-2}$, GEDI 680 to 820 mL/m^2 (normal-to-mild hypervolemia, a range that does not increase the risk of DCI and PE)[14] and ELWI $\leq$ 14 mL/kg (the upper limits chosen were the values associated with a higher risk of mortality in patients with PE[23,24]).

For baseline fluid therapy, a crystalloid infusion of 1,500 to 3,000 mL/day is generally administered postoperatively at least until day 14. Hypovolemia (GEDI <680 mL/m^2) is corrected by increasing daily intravenous fluids (or intermittent fluid infusion, as needed). In general,

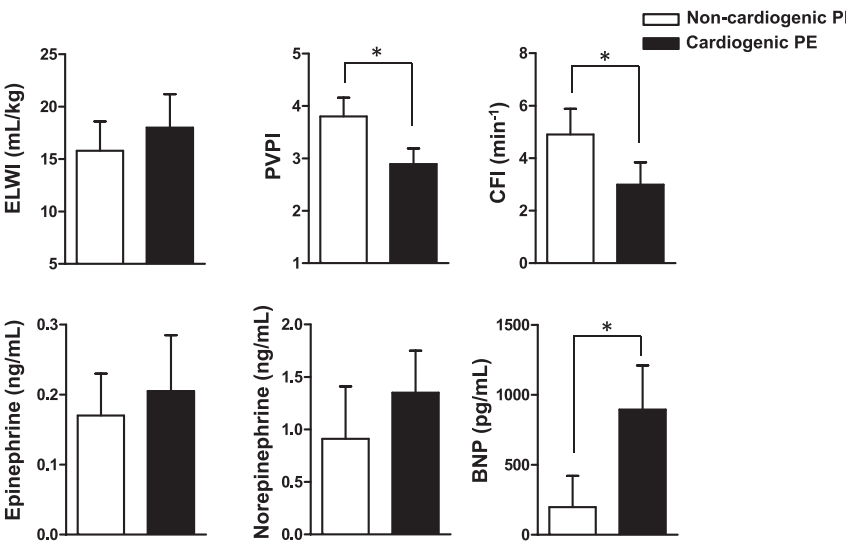

FIGURE 2. Initial values of TPTD-derived volumetric (ELWI and PVPI) and cardiac (CFI) parameters and plasma catecholamines (epinephrine [reference range: ≤0.1 ng/mL] and norepinephrine [reference range: 0.1–0.45 ng/mL]) and BNP (reference range: ≤18.4 pg/mL) in post-SAH NPE patients. Increased levels of ELWI and plasma catecholamine were observed for both cardiogenic (n = 22) and noncardiogenic (n = 15) PE. Note that elevated PVPI (≥3.0) was detected in patients with noncardiogenic PE (n = 15), whereas depressed CFI (<4.5 minutes) and increased BNP levels were notable for cardiogenic PE (n = 22). *$P < 0.05$ (unpaired t test). TPTD, transpulmonary thermodilution; PE, pulmonary edema; NPE, neurogenic pulmonary edema; SAH, subarachnoid hemorrhage; CFI, cardiac function index; EVLW, extravascular lung water index; PVPI, pulmonary vascular permeability index; BNP, brain natriuretic peptide.