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Hemodynamic Assessment of Patients With Septic Shock Using Transpulmonary Thermodilution and Critical Care Echocardiography

A Comparative Study

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BACKGROUND: To assess the agreement between transpulmonary thermodilution (TPT) and critical care echocardiography (CCE) in ventilated patients with septic shock.

METHODS: Ventilated patients in sinus rhythm requiring advanced hemodynamic assessment for septic shock were included in this prospective multicenter descriptive study. Patients were assessed successively using TPT and CCE in random order. Data were interpreted independently at bedside by two investigators who proposed therapeutic changes on the basis of predefined algorithms. TPT and CCE hemodynamic assessments were reviewed offline by two independent experts who identified potential sources of discrepant results by consensus. Lactate clearance and outcome were studied.

RESULTS: A total of 137 patients were studied (71 men; age, 61 ± 15 years; Simplified Acute Physiologic Score, 58 ± 18; Sequential Organ Failure Assessment, 10 ± 3). TPT and CCE interpretations at bedside were concordant in 87/132 patients (66%) without acute cor pulmonale (ACP), resulting in a moderate agreement (kappa, 0.48; 95% CI, 0.37-0.60). Experts' adjudications were concordant in 100/129 patients without ACP (77.5%), resulting in a good intertechnique agreement (kappa, 0.66; 95% CI, 0.55-0.77). In addition to ACP (n = 8), CCE depicted a potential source of TPT inaccuracy in 8/29 patients (28%). Lactate clearance at H6 was similar irrespective of the concordance of online interpretations of TPT and CCE (55/84 [65%] vs 32/45 [71%], $P = .55$). ICU and day 28 mortality rates were similar between patients with concordant and discordant interpretations (29/87 [36%] vs 13/45 [29%], $P = .60$; and 31/87 [36%] vs 16/45 [36%], $P = .99$, respectively).

CONCLUSIONS: Agreement between TPT and CCE was moderate when interpreted at bedside and good when adjudicated offline by experts, but without impact on lactate clearance and mortality.

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KEY WORDS: doppler ultrasonography; echocardiography; hemodynamic; thermodilution

ABBREVIATIONS: ACP = acute cor pulmonale; CCE = critical care echocardiography; TEE = transesophageal echocardiography; TPT = transpulmonary thermodilution; TTE = transthoracic echocardiography

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Septic shock constitutes the leading cause of acute circulatory failure in the ICU.[1] Sepsis-induced circulatory failure may diversely combine distinct mechanisms over time, including hypovolemia, vasoplegia, and cardiac dysfunction.[2] International guidelines have been implemented for prompt resuscitation of patients presenting with septic shock on the basis of predefined therapeutic goals.[3] After ICU admission, hemodynamic assessment and monitoring are recommended to help guide subsequent resuscitation aimed at improving tissue perfusion and oxygen delivery.[4] Transpulmonary thermodilution (TPT) and critical care echocardiography (CCE) are widely used for the hemodynamic assessment of ICU patients sustaining shock,[5] but have not yet been compared on clinical grounds. CCE combines transthoracic (TTE) and transesophageal echocardiography (TEE) according to image quality, required information, and local standards of care.[6] TPT is based on the analysis of a thermodilution curve that provides the measurement of cardiac output, volumetric parameters of preload, extravascular lung water, and derived parameters of myocardial performance and pulmonary vascular permeability. Incorporated pulse-contour technology provides continuous cardiac output and indices of fluid responsiveness.[7] In the present study, we sought to evaluate the agreement between the interpretation of quantitative parameters derived from TPT and CCE when performed in ventilated patients requiring a comprehensive hemodynamic assessment for septic shock.

Methods

Study Design

This descriptive, prospective study was conducted over a 36-month period in five French ICUs. This study was in keeping with the standards of care of participating ICUs, which all followed Surviving Sepsis Campaign guidelines available at the time of patient enrollment[8] and systematically assessed hemodynamics serially to guide therapeutic management.[9] Accordingly, the study was approved by our institutional review board (2010-A00616-33), which waived the need for informed consent.

Study Population

Patients were eligible if mechanically ventilated, perfectly adapted to the ventilator, in sinus rhythm, had an inserted arterial and central venous catheter, and if they required advanced hemodynamic assessment for septic shock. Septic shock was defined as a suspected infection responsible for a sustained hypotension despite adequate fluid loading that required vasopressors, with associated clinical signs of tissue hypoperfusion (mottled skin, encephalopathy, oliguria for more than 2 h) that were biologically confirmed (pH $<$ 7.38 and base deficit $>$ -5 mmol/L or lactate $>$ 2 mmol/L or central venous oxygen saturation $<$ 70%).[8,10] All patients were studied before the new Sepsis-3 definition of septic shock.[11] Exclusion criteria included age $<$ 18 years, pregnancy, non-sinus rhythm, contraindication to the insertion of a femoral arterial catheter, TEE contraindication, moribund status, and previous participation in the study.

Hemodynamic Assessment

A comprehensive hemodynamic assessment was successively performed by two investigators who were not in charge of the patient, using either TPT (Picco plus, Pulsion France) or a full-feature ultrasound system (CX50, Philips Healthcare France). Each investigator independently interpreted online the hemodynamic profile at bedside and proposed a therapeutic strategy according to a predefined algorithm (Fig 1). Importantly, threshold values were proposed to guide investigators but not strictly required to establish diagnoses (eg, fluid responsiveness, left ventricular dysfunction) because the interpretation of hemodynamic profiles were left at the discretion of operators. Acute cor pulmonale (ACP) was conventionally defined echocardiographically,[12] because its diagnosis is not accessible to TPT.[13] Both investigators had access to the same information, including medical history, physical examination, first-line hemodynamic monitoring (ie, invasive blood pressure, pulse pressure variation, central venous pressure), and biological results, including central venous oxygen saturation and lactate, but not to the results of the hemodynamic assessment performed by their counterpart. Investigators who performed echocardiographic examinations had an advanced level in CCE.[6] The order of TPT and CCE hemodynamic assessment was determined using a centralized randomization with blocks of various sizes and was stratified on participating centers. Investigators were urged to perform their respective hemodynamic assessment consecutively; no change in ongoing therapy was performed during this time frame. Patients were hemodynamically assessed in the semirecumbent position (e-Appendix 1), and performance of passive leg raise was left at the discretion of investigators.[14] This baseline hemodynamic assessment defined H0. The attending physician in charge of the patient was provided with bedside interpretation of both hemodynamic assessments and associated therapeutic proposals. In the presence of discordant interpretations, the choice of the therapeutic strategy was left at the discretion of the front-line intensivist.

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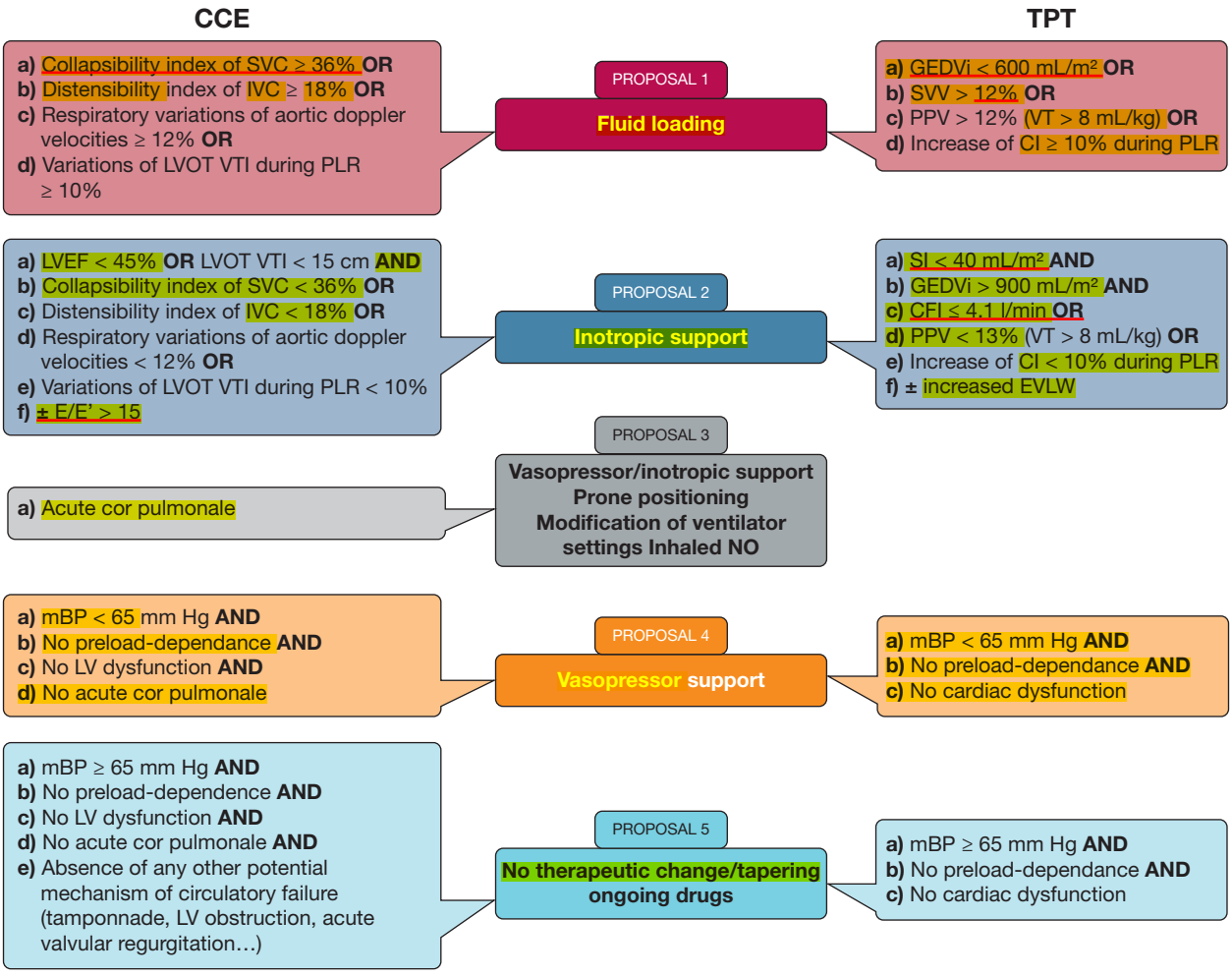

Figure 1 – *Predefined therapeutic algorithm according to hemodynamic profiles. The presence of one or more of listed parameters (rather than all of them) allowed the diagnosis of fluid responsiveness and left ventricular failure and suggested fluid loading or initiation of inotropic support, respectively. In these cases, optional parameters of each hemodynamic profile ("OR") are not listed in descending order of importance because no hierarchy in their respective diagnostic capacity was respected. In contrast, the diagnosis of vasoplegia suggested the need of further vasopressor support and the confirmation of stabilized hemodynamics triggered no therapeutic changes or tapering ongoing vasoactive drugs; both required the presence of all listed hemodynamic parameters ("AND"). In all cases, threshold values were informative rather than fully required to suggest a therapeutic change since the interpretation of hemodynamic profiles were left at the discretion of operators. Abbreviations: CCE = critical care echocardiography; CFI = cardiac function index; CI = cardiac index; E/E' = ratio of maximal mitral E wave velocity and maximal tissue Doppler imaging E' wave velocity recorded at the lateral aspect of the mitral ring; EVLW = extravascular lung water; GEDVi = indexed global end-diastolic volume; IVC = inferior vena cava; LVEF = left ventricular ejection fraction; LVOT = left ventricular outflow tract; mBP = mean blood pressure; NO = nitric oxide; PLR = passive leg raise; PPV = pulse pressure variation; SI = stroke index; SVC = superior vena cava; SVV = stroke volume variation; TPT = transpulmonary thermodilution; VT = tidal volume; VTI = velocity time integral.*

Patient Follow-up

In each patient, lactate was measured at H0 and H6 and adverse events potentially related to the initiated therapy following hemodynamic assessment (bradycardia < 70 beats/min, supraventricular or ventricular arrhythmias, acute pulmonary edema) were recorded during the same period. Lactate clearance was considered achieved when arterial blood lactate level decreased of at least 10% between H0 and H6, or when initially increased lactate level decreased to a value < 2 mmol/L at H6.[15] This low threshold value was chosen to increase the chance of detecting a potential difference according to the concordance or discordance of hemodynamic assessments.

Statistics

Enrollment of 139 patients was deemed necessary to achieve good agreement between TPT and CCE reflected by a Cohen kappa coefficient of 0.80 with a precision of 10% and an alpha risk of 5% using a two-tailed approach. Continuous variables were expressed as means ± SDs and qualitative variables were expressed as frequencies and percentages. Quantitative parameters were compared using the Student *t* test and proportions using the χ^2 or Fisher exact test, when necessary. A *P* value < .05 was considered statistically significant. Contingency tables were built to assess the agreement of bedside interpretations by the two independent investigators of hemodynamic profiles derived from TPT and CCE at

H0, and offline adjudication by two experts who were not involved in the study (BL, MS). Concordance between the two hemodynamic assessments was evaluated using the Cohen kappa coefficient and its 95% CI, while excluding patients with ACP.[13]

Results

Among 234 consecutively screened patients, 85 (36%) had an exclusion criterion and 12 of the 149 remaining eligible patients were not included in the study (Fig 2). Finally, 137 patients were studied (71 men; age: 61 ± 15 years; Simplified Acute Physiologic Score, 58 ± 18; Sequential Organ Failure Assessment, 10 ± 3). Pneumonia and intra-abdominal infections were most frequently identified at the origin of septic shock and the causative micro-organism was documented in 122 patients (89%). All patients received catecholamines at inclusion (Table 1).

A comprehensive hemodynamic assessment was successfully performed in all randomized patients and CCE was performed first in 70 patients (Fig 2). Mean time lag between the two hemodynamic assessments was 19 ± 17 min. No complication related to either TPT or TEE was observed. ACP was identified at bedside using CCE in 5 patients (4%). Hemodynamic parameters measured using TPT and CCE are summarized in e-Tables 1 and 2. All CCE and TPT criteria to suggest fluid loading were present in only four and 11 patients, respectively, and to suggest inotropic support in 10 and eight patients, respectively (Fig 1). Hemodynamic profiles resulting from independent online interpretation of TPT and CCE assessment were concordant in 87/132 patients without ACP (66%). When the two independent investigators agreed, they proposed a fluid loading in 47 patients (54%), inotropes in 16 patients (18%), vasopressors in one patient (1%), and no therapeutic changes or tapering ongoing catecholamines infusion in 23 patients (27%). Agreement between TPT and CCE interpretations was moderate (kappa, 0.48; 95% CI, 0.37-0.60). Discordances were relatively uniformly distributed among hemodynamic profiles (Table 2). Overall, bedside clinicians adhered to the treatment proposed by investigators in 85/87 patients (98%). In the presence of discordant therapeutic proposals

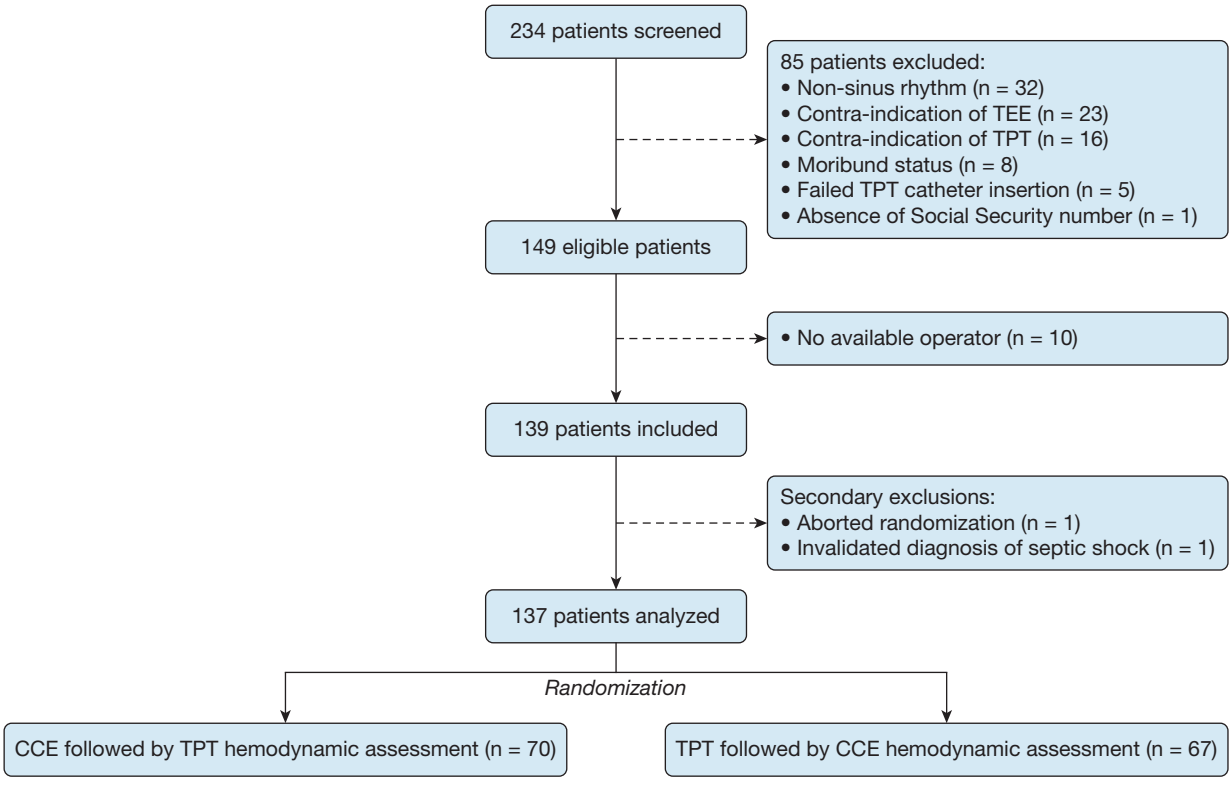

Figure 2 – *Flow chart of the study. CCE = critical care echocardiography; TEE = transesophageal echocardiography. See Figure 1 legend for expansion of other abbreviation.*

TABLE 1] Characteristics of the Study Population, According to the Concordance or Discordance of Hemodynamic Assessments When CCE and TPT Results Were Interpreted by Independent Experts

Parameters	Overall (N = 137)	Concordance (n = 100)[a]	Discordance (n = 29)[a]	*P* Value
Age, y	61 ± 14	61 ± 14	62 ± 16	.90[b]
Male	71 (52)	54 (54)	12 (41)	.23[c]
SAPS2	58 ± 18	58 ± 17	55 ± 22	.26[b]
SOFA	10 ± 3	9 ± 3	10 ± 3	.30[d]
Medical history				
Diabetes	23 (17)	17 (17)	5 (17)	1.00[e]
Cardiopathy	7 (5)	7 (7)	0 (0)	.35[e]
COPD	22 (16)	14 (14)	7 (24)	.42[e]
Chronic renal failure	4 (3)	3 (3)	1 (3)	1.00[e]
Cirrhosis	10 (7)	7 (7)	3 (10)	.76[e]
Cancer/hemopathy	22 (16)	15 (15)	7 (24)	.27[e]
Immunosuppression	18 (13)	11 (11)	7 (24)	.12[e]
Site of infection				
Lung	55 (40)	37 (37)	15 (52)	.60[e]
Abdominal	49 (36)	39 (39)	8 (28)	
Urinary tract	17 (12)	13 (13)	2 (7)	
Skin	8 (6)	6 (6)	2 (7)	
Other	8 (6)	5 (5)	2 (7)	
Hemodynamic parameters				
Heart rate, beats/min	110 ± 24	112 ± 23	106 ± 26	.19[b]
Systolic BP, mm Hg	115 ± 22	114 ± 23	115 ± 18	.68[b]
Diastolic BP, mm Hg	61 ± 14	62 ± 14	61 ± 13	.77[d]
Mean BP, mm Hg	78 ± 16	79 ± 16	75 ± 16	.28[d]
Pulse pressure variation, %	11 ± 6	12 ± 7	11 ± 5	.99[b]
Central venous pressure, mmHg	10 ± 5	10 ± 4	11 ± 6	.83[b]
Respiratory parameters				
Respiratory rate, cycles/min	23 ± 4	23 ± 4	23 ± 4	.92[b]
V_T, mL	453 ± 58	456 ± 54	440 ± 60	.13[b]
Plateau pressure, cm H_2O	21 ± 5	21 ± 5	22 ± 5	.12[b]
Positive end-expiratory pressure, cm H_2O	7 ± 3	6 ± 3	7 ± 3	.49[b]
Biology				
pH	7.28 ± 0.11	7.28 ± 0.12	7.27 ± 0.09	.27[b]
P_{AO_2}/F_{IO_2}	189 ± 104	195 ± 111	177 ± 76	.78[b]
Hemoglobin, g/dL	11.4 ± 1.8	11.5 ± 1.6	11.2 ± 2.1	.36[d]
Creatinine, μmol/L	168 ± 116	171 ± 119	138 ± 75	.25[b]
ALAT, UI/L	183 ± 454	166 ± 430	94 ± 148	.27[b]
Bilirubin, μmol/L	20 ± 23	17 ± 18	21 ± 19	.51[b]
Prothrombin time, %	54 ± 18	55 ± 17	50 ± 20	.11[b]
Lactate, mmol/L	4.24 ± 3.83	3.92 ± 3.30	4.29 ± 3.62	.49[b]
S_{CVO_2}, %	76 ± 11	76 ± 11	76 ± 12	.74[b]

(Continued)

TABLE 1] *(Continued)*

Parameters	Overall (N = 137)	Concordance (n = 100)[a]	Discordance (n = 29)[a]	*P* Value
Treatment from ICU admission to hemodynamic assessment				
Fluid resuscitation, L	2.0 ± 1.5	2.1 ± 1.5	1.7 ± 1.1	.24[b]
Maximal dose of catecholamines				
Norepinephrine, mg/h	3.73 ± 2.26	3.81 ± 2.25	3.59 ± 2.37	.87[b]
Epinephrine, mg/h	1.77 ± 1.17	1.95 ± 1.32	1.33 ± 0.58	.74[b]
Dobutamine, μg/kg/min	5.2 ± 1.5	5.4 ± 5.1	5.0 ± 5.5	.46[b]
Treatment during ICU stay				
Duration of mechanical ventilation, d	11 ± 11	11 ± 12	9 ± 7	.83[b]
Renal replacement therapy	46 (34)	29 (29)	11 (38)	.26[c]
Mortality				
ICU	45 (33)	32 (32)	8 (28)	.65[c]
Day 28	51 (37)	34 (34)	11 (38)	.70[c]

Values are expressed as means ± standard deviations or as No. (%). ALAT = alanine amino transferase; CCE = critical care echocardiography; SAPS2 = Simplified Acute Physiologic Score; SOFA, Sequential Organ Failure Assessment; $Scvo_2$ = central venous blood oxygen saturation; TPT = transpulmonary thermodilution; V_T = tidal volume.

[a]Eight patients received a diagnosis of acute cor pulmonale and are not incorporated in the inter-technique comparison because this diagnosis is accessible to critical care echocardiography only.

[b]*P* value of a Mann-Whitney test comparing the quantitative variable according to the concordance or discordance of hemodynamic assessments.

[c]*P* value of a χ^2 test comparing the qualitative variable according to the concordance or discordance of hemodynamic assessments.

[d]*P* value of a Student *t* test comparing the quantitative variable according to the concordance or discordance of hemodynamic assessments.

[e]*P* value of a Fisher exact test comparing the qualitative variable according to the concordance or discordance of hemodynamic assessments.

derived from hemodynamic assessments, the attending physician followed predominantly CCE interpretation (30/45 patients, 67%), TPT interpretation in 13 patients (29%), and none of the two proposals in 2 patients (4%).

After offline adjudication by the two independent experts, three additional patients were echocardiographically diagnosed with ACP and the interpretation of hemodynamic profiles derived from both TPT and CCE was concordant in 100 of the 129 remaining patients (77.5%) (Table 2). This corresponded to a good agreement (kappa, 0.66; 95% CI, 0.55-0.77). Patients' characteristics were not statistically different whether experts' adjudication was concordant or not (Table 1). In addition to ACP

TABLE 2] Contingency Table Summarizing the Interpretation of Hemodynamic Assessment Using TPT and CCE in Ventilated Patients With Septic Shock, When Performed Online at Bedside by Front-Line Intensivists or Adjudicated Offline by Independent Experts[a]

TPT CCE	TPT Fluid Loading	TPT Inotropes	TPT Vasopressors	TPT No Change or Tapering Catecholamines
CCE fluid resuscitation	47/50	3/2	3/2	9/12
CCE inotropes	6/4	16/18	0/0	2/3
CCE vasopressors	2/1	4/0	1/6	0/0
CCE no change or tapering catecholamines	7/4	8/1	1/0	23/26

[a]Data are shown as interpretation of hemodynamic profiles online at beside by independent investigators (n = 132)/interpretation of hemodynamic profiles offline at the time of adjudication by experts (n = 129). Patients were excluded from analysis when acute cor pulmonale was diagnosed during CCE interpretation (bedside: n = 5; adjudication: n = 5 + 3). See Table 1 legend for expansion of abbreviations.

identified in eight patients, CCE allowed identifying a potential source of discrepant hemodynamic profiles between the two techniques in eight of 29 patients (28%), including severe left-sided valvulopathy (n = 5), dynamic left ventricular outflow tract obstruction (n = 2), or very low cardiac output (n = 2).

Lactate clearance was achieved at H6 in 87/129 patients (69%) without ACP and with serial lactate measurements available. The proportion was similar, whether TPT and CCE assessments resulted in concordant therapeutic proposals or not (55/84 [65%] vs 32/45 [71%]: $P = .55$). ICU and day 28 mortality rates were also similar between patients with concordant and discordant interpretations of hemodynamic assessment at bedside (29/87 [36%] vs 13/45 [29%], $P = .60$, and 31/87 [36%] vs 16/45 [36%], $P = .99$, respectively). In the presence of discordant interpretations, lactate clearance was achieved in a similar proportion of patients, whether the attending physician followed the therapeutic proposal derived from TPT or CCE interpretation (10/13 vs 20/30: $P = .72$), and no significant difference was observed on ICU and day 28 mortality (3/13 [23%] vs 9/30 [30%]: $P = .73$, and 3/13 [23%] vs 12/30 [40%]: $P = .49$, respectively). Between H0 and H6, the frequency of complications was similar, whether hemodynamic assessments was concordant or not (4/87 [5%] vs 2/45 [4%]: $P = 1.0$): severe bradycardia (n = 3), arrhythmia (n = 3), and no case of pulmonary venous congestion.

Discussion

In our cohort, TPT and CCE resulted in concordant bedside interpretation of hemodynamic profiles by front-line intensivists in two-thirds of cases. Additional fluid loading was the most frequent therapeutic impact of hemodynamic assessment because it involved approximately 50% of patients, a similar proportion to that commonly reported in this setting.[16] Inotropes were suggested in 26% of patients on the basis of hemodynamic assessment by CCE, confirming the 30% rate previously reported.[9] Because hemodynamic assessment was performed after fluid resuscitation and under vasopressor support, the indication to increase the dose of vasopressor involved a minority of patients and no therapeutic change was proposed in one-fourth of our cohort. This latter information is clinically relevant because therapeutic strategies aimed at achieving supranormal values of cardiac index fail to improve outcome in septic patients.[17]

Experts' adjudication resulted in a substantial increase of diagnostic concordance between TPT and CCE. Adequate training is crucial to accurately measure and interpret invasive hemodynamic parameters.[18] Although TPT is not an operator-dependent technique, as opposed to CCE,[19] a heterogeneous competency of investigators in interpreting thermodilution-derived hemodynamic parameters cannot be excluded. In all cases, interpretation of individual hemodynamic profiles is based on the analysis of quantitative parameters in a specific clinical setting, and decision-making relies on convergent findings.[20] Only a small proportion of patients fulfilled predefined criteria of fluid responsiveness and left ventricular dysfunction, irrespective of the technique used for hemodynamic assessment. This illustrates the limited diagnostic value of cutoffs with their intrinsic constraint of a binary interpretation which is not adapted to complex clinical scenarios.[16] Accordingly, certain hemodynamic profiles may not be uniformly interpreted, as in 22.5% of patients with persistent discrepancy between TPT and CCE interpretations after adjudication by independent experts. Although ventilated patients were in sinus rhythm and had no inspiratory effort, other factors limiting the validity of currently proposed indices of fluid responsiveness were present in this cohort,[21] such as low tidal volume.[22] Nevertheless, factors known to potentially limit the accuracy of dynamic parameters to predict fluid responsiveness were operant for both TPT and CEE.

Potential sources of discrepancy between TPT and CCE were identified in 16 of 37 patients (43%), one-half of them being related to the echocardiographic identification of ACP. TPT fails to accurately identify right ventricular failure,[13] and ACP is the most severe presentation.[12] Although cardiac function index has been shown to accurately predict low left ventricular ejection fraction in cardiac and septic patients,[23-25] the correlation between these two parameters of cardiac function is lower in patients with right ventricular failure because cardiac function index underestimates left ventricular systolic function.[13,25] Moreover, increased pulse pressure variation or TPT-derived stroke volume variations may erroneously trigger fluid loading in these patients.[26] In contrast, CCE is ideally suited to ascribe a low flow state to an underlying ACP and to accurately identify the resulting false-positive result of pulse pressure or stroke volume variations in a ventilated patient.[26] Pneumonia as a cause of ARDS is a risk factor for the development of ACP.[27] In addition, ACP was recently observed in 8% of a large population of ventilated patients assessed using CCE for shock.[16]

Accordingly, CCE should be the first-line imaging technique to hemodynamically assess patients with septic shock and associated ARDS to confidently rule out underlying ACP, which requires specific therapeutic interventions,[28] before initiating hemodynamic monitoring using TPT. In five of the patients, severe left-sided valvulopathies (eg, aortic or mitral regurgitation) identified using CCE may have adversely interfered with the internal algorithm of TPT for the measurement of hemodynamic parameters.[29] Dynamic left ventricular outflow tract obstruction is neither accurately identified by right heart catheterization, which discloses reduced cardiac output with elevated left filling pressures that may be erroneously interpreted as cardiac failure,[30] nor by TPT, whereas CCE clearly depicts and quantifies both the pressure gradient induced by the dynamic obstruction and frequently associated eccentric mitral regurgitation in the presence of an underlying systolic anterior mitral motion. Finally, in two of the patients with a markedly low flow state, decreased cardiac output may have been overestimated by the thermodilution technique because of the loss of thermal indicator.[31] Although echocardiography and thermodilution similarly track directional changes of cardiac output, they are not interchangeable techniques for its measurement.[32]

When compared with the sole clinical assessment, hemodynamic monitoring provides relevant additional information with a potential impact on therapeutic decisions.[33] Nevertheless, for this new information to translate into an improvement of outcome, hemodynamic assessment should be associated with a standardized therapeutic algorithm, such as that used in the present study. In the patients, early lactate clearance was not influenced by the concordance of bedside interpretation of TPT and CCE results. In addition, adverse effects potentially related to changes in acute therapy were scarcely observed and with a similar frequency, whether hemodynamic assessments yielded concordant results or not. Accordingly, no apparent short-term impact on both the efficacy and tolerance of therapeutic interventions driven by either hemodynamic assessment was evidenced. Finally, no complication related to either TPT or TEE was encountered. When respecting contraindications of TPT and TEE (7% and 10% of screened patients, respectively), both methods can be safely used on clinical grounds with a low complication rate.[34,35]

Although CCE is not yet adequately suited for continuous hemodynamic monitoring, miniaturized TEE probes have emerged that facilitate prolonged esophageal insertion for serial assessments of hemodynamics in unstable ICU patients.[36,37] TPT allows continuous monitoring of cardiac output and of derived indices, providing regular calibrations.[38] Nevertheless, the present study confirms that various cardiac conditions can invalidate TPT measurements.[29] Accordingly, TPT and CCE appear complementary rather than mutually exclusive in ventilated patients with septic shock who require advanced hemodynamic monitoring. Initial hemodynamic assessment should rely on CCE,[39] which can exclude potential source of inaccuracy of thermodilution. TPT could then be used when a continuous monitoring is required in complex and unstable patients.

The present study has several limitations. Current definition of septic shock and Surviving Sepsis Campaign recommendations are not those that were effective at the time of patient enrollment.[3,11] Because hemodynamic assessment was not consistently performed by intensivists with expertise in TPT or CCE, we may have underestimated intertechnique agreement at bedside as suggested by offline experts' adjudication. To reflect daily practice, performance of passive leg raise was not systematic, but left at the discretion of investigators.[39] This study was intrinsically not blinded, but the order of hemodynamic assessments has been randomized and their interpretation was performed by independent investigators who were not in charge of patients. Because the study duration was limited, it neither allowed evaluating the respective diagnostic value of TPT and CCE nor the potential adverse effects of derived therapy during the entire course of septic shock. Recently proposed threshold values of CCE dynamic parameters according to the clinical context were not used,[16] but rather single cutoffs previously validated in initial studies. Finally, the descriptive nature of the study precluded determining therapeutic targets and the study was not adequately powered to assess patient centered outcome parameters.[40]

Conclusions

Concordance between online interpretation of hemodynamic assessment performed in ventilated patients with septic shock using TPT and CCE was moderate. It was good after adjudication by independent experts. Nearly one-half of discrepant results were attributed to a potential limitation of TPT depicted by CCE. Lactate clearance and adverse events were not influenced by inter-technique agreement.

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Author contributions: P. V. takes the responsibility for the content of the manuscript, including the data and analysis. P. V., A. M., M. C., and B. R. designed the study. All authors contributed to patient enrollment. Offline adjudication of transpulmonary thermodilution and critical care echocardiography data were performed by B. L. and M. L., respectively. All authors contributed to the preparation of the manuscript and read and approved the final version.

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Additional information: The e-Appendix and e-Tables can be found in the Supplemental Materials section of the online article.

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