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Change in cardiac index during Trendelenburg maneuver as a predictor of fluid responsiveness among patients under mechanical ventilation with spontaneous breathing activity: A protocol for prospective observational study

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ABSTRACT:

Background: Optimal fluid management in surgical intensive care units (SICUs) is challenging, with under or over-resuscitations linked to increased mortality and extended ICU stays. Dynamic parameters like stroke volume variation and pulse pressure variation are unreliable in intubated patients with spontaneous breathing activity. The passive leg raise (PLR), which relies on translocation of the patient's intravascular volume, is effective in identifying fluid responsiveness, but it still has some limitations. Regarding limitations, another potential method, using the same principle, known as the Trendelenburg maneuver (TM), has been introduced. This study aims to assess the diagnostic performance of TM in mechanically ventilated patients with spontaneous breathing activity, focusing on changes in cardiac index in relation to fluid administration.

Methods: In this single-center, prospective observational study conducted in a surgical ICU, we enrolled 68 patients with inadequate tissue perfusion who had spontaneous breathing while receiving mechanical ventilation to evaluate the diagnostic ability of TM in fluid responsiveness prediction. The patients were classified as fluid responders when the change in cardiac index, measured by the FloTrac™ sensor with the HemoSphere™ advanced monitoring platform, increased by more than 10% after fluid administration.

Hypothesis: We hypothesize that TM has the ability to predict fluid responsiveness in mechanically ventilated patients with spontaneous breathing activity.

Ethics and dissemination: This trial received approval from the Siriraj Institutional Review Board. We plan to present the result in peer-reviewed publications in critical care medicine.

Trial registration: TCTR20230704005

Keywords: Trendelenburg maneuver; Fluid responsiveness; Spontaneous breathing activity; Cardiac index

INTRODUCTION

Fluid management plays a pivotal role in the care of patients in surgical intensive care units (SICUs). Both under-resuscitations and over-resuscitations in critically ill patients can lead to increased mortality, prolonged mechanical ventilation (MV), and extended ICU stays.[1-3] Although appropriate fluid administration can enhance cardiac output in fluid-responsive patients and thereby increase oxygen delivery and improve outcomes, the challenge lies in the ability to accurately identify these individuals. Several dynamic parameters, such as stroke volume variation (SVV) and pulse pressure variation (PPV), have been developed. These parameters are based on the effects of cardio-pulmonary interactions during controlled MV. Although some studies have demonstrated that fluid management guided by these dynamic parameters can minimize fluid accumulation, their reliability is debatable, especially in intubated patients who exhibit spontaneous breathing activity.

Given the limitations previously mentioned, passive leg raise (PLR) has emerged as a prominent method for predicting fluid responsiveness in certain patient groups. The fundamental principle of PLR is the translocation of a patient's intravascular fluid, pooled in the lower extremities while upright, into the thoracic compartment upon lying down, acting as a transient fluid expansion. Despite the widespread adoption of PLR, there are concerns regarding patient discomfort, and its feasibility in patients who have undergone abdominal, pelvic, or spinal surgeries.

The Trendelenburg maneuver (TM) is a technique based on the same principle and is used to evaluate fluid responsiveness. Initially, the patient is placed in a neutral position, followed by an upward and downward bed angulation. Yonis, et al. demonstrated the effectiveness of TM in predicting fluid responsiveness among patients undergoing mechanical ventilation (MV) in the prone position. A cardiac output increase of at least 8%induced by the maneuver suggests fluid responsiveness, with an area under the receiver operating characteristic (ROC) curve (AUROC) of 0.90, with a 95% confidence interval (CI) ranging from 0.80-1.00, a sensitivity of 0.87, 95%CI 0.67-1.00, and a specificity of 0.89, 95%CI 0.72-1.00 [4]. Another study performed in patients undergoing veno-arterial extracorporeal membrane oxygenation (VA-ECMO) reported TM's effectiveness in predicting volume status, noting a cardiac output change over 10% as indicative of fluid responsiveness (AUROC 0.93, 95%CI 0.81-0.98, sensitivity 0.82, 95%CI 60-95%, specificity 0.88, 95%CI 0.64-0.99) [5]. Besides its promising accuracy, further potential benefits include decreased patient agitation and discomfort, reduced procedural complexity, and the ability to apply its use in patients limited by position.

The aim of this study was to investigate the association between changes in cardiac index prompted by the Trendelenburg maneuver and fluid administration, with the objective of assessing the diagnostic effectiveness of this maneuver in mechanically ventilated patients who exhibit spontaneous breathing activity in a surgical ICU setting.

KEY MESSAGE:

- Appropriate fluid management based on fluid responsiveness in surgical ICUs is challenging, especially in patients with spontaneous breathing during mechanical ventilation. We hypothesize that the Trendelenburg maneuver can differentiate fluid responsiveness in these patients. Further benefits include decreased patient agitation and discomfort, reduced procedural complexity, and application in patients with positioning limitations.

OBJECTIVES

Primary objective

The primary objective of this study was to evaluate the efficacy of the Trendelenburg maneuver as a predictor of fluid responsiveness in surgical ICU patients requiring mechanical ventilation and exhibiting spontaneous breathing activity. This was achieved by monitoring changes in the cardiac index using the uncalibrated continuous pulse contour analysis provided by the FloTrac™ and the HemoSphere™ advanced monitoring platforms.

Secondary objective

The secondary objective of this research was to evaluate the diagnostic accuracy of alterations in hemodynamic parameters, including pulse pressure variation (PPV), velocity time integral (VTI) of the left ventricular outflow tract, and central venous pressure (CVP) during the Trendelenburg maneuver, as indicators of fluid responsiveness in patients.

MATERIALS AND METHODS

Trial design and setting

This study was a single-center, prospective observational study conducted in the surgical ICU of a tertiary care hospital. The Institutional Review Board of Siriraj Hospital, Mahidol University, Bangkok, Thailand, approved the study protocol (COA number si 386/2023). It was also registered with the Thai Clinical Trial Registry (TCTR20230704005). Patient enrollment began in July 2023, after obtaining informed consent from the patients' next of kin.

Study population

Eligible participants for this study included all adult patients aged above 18 years receiving invasive mechanical ventilation with spontaneous breathing activity in the surgical ICU. The subjects also fulfilled the following criteria: ability to cooperate during the maneuver, either awake or under sedation, with a Richmond Agitation Sedation Scale (RASS) lower than +2, and signs of inadequate tissue perfusion, including mean arterial pressure < 65 mmHg, pulse rate > 100 min^{-1}, urine output < 0.5

ml.kg^{-1}.h^{-1}, skin mottling, capillary refill time > 2 seconds, and serum lactate > 2 mmol.L^{-1}.

Patients with at least one of the following criteria led to exclusion: patient or patient's representative refused participation, contraindications to the Trendelenburg position due to intracranial or intraocular pressure, contraindications to peripheral arterial cannulation, cardiogenic pulmonary edema, cardiac dysfunction characterized by a left ventricular ejection fraction (LVEF) <30%, severe aortic or mitral valves disease, persistent arrhythmias, pulmonary artery hypertension, intraabdominal pressure >12 mmHg, use of muscle relaxants, evidence of thrombosis of the Inferior Vena Cava or any great veins of the lower extremities, amputation above the ankle level in the lower limbs, contraindication of human albumin (either a history of its allergic reactions or refusal of human albumin), or pregnancy.

Protocol description and hemodynamic measurement

After enrollment, a radial arterial cannulation was placed and connected to the FloTrac™ sensor together with the HemoSphere™advanced monitoring platform (Edwards Lifesciences, Irvine, CA, USA) to measure hemodynamics using the uncalibrated pulse contour analysis method. The pressure transducer was secured to the bed at the phlebostatic axis to ensure accurate readings. Prior to initiating the study, several preparatory measures were undertaken; the intraabdominal pressure was measured, the endotracheal cuff pressure was maintained between 20-30 cmH_2O, and the nasogastric tube was suctioned to prevent the risk of regurgitation and aspiration. The specifics of these preparatory steps are illustrated in Figure 1.

First, the patient was positioned in the supine position for 1 minute to establish baseline measurements (T_0). During this phase, ventilatory variables of interest were mode of MV, tidal volume, respiratory rate, minute ventilation, pulse oximetry, and end-tidal carbon dioxide levels. Concurrently, the hemodynamic variables, obtained from the FloTrac™ sensor/HemoSphere™ monitoring and transthoracic echocardiogram, were also measured. These included the mean arterial pressure (MAP), pulse rate (PR), cardiac index (CI), stroke volume index (SVI), SVV, PPV, CVP, LVEF, and VTI. The patient's level of sedation was also assessed.

Second, to alleviate potential anxiety, the patient was briefed on the next steps of the procedure to prevent agitation. The Trendelenburg maneuver was then performed by tilting the entire bed to a head-up position (+10°) for 1 minute (T_1), followed by adjusting the bed to a head-down position (-13°) for 1 minute (T_2). The parameters were recorded after each step of the procedure.

Last, the patient was repositioned to the supine position for an additional one minute, during which parameters were recorded (T_3). Subsequently, an infusion of 4 ml/kg of 5%human albumin was administered for over 15 minutes while the patient was kept in the supine position. Post fluid administration, the parameters were measured again (T_4).

During the study period, no alterations to additional fluids, vasopressors, sedative agents, or mechanical ventilation settings were allowed. Fluid responsiveness was determined to be positive if there was an increase in the CI of more than 10%, as measured by the FloTrac™ sensor/HemoSphere™ monitoring system, following fluid administration.

The protocol required early termination for any patient who experienced severe hypotension or collapse requiring immediate resuscitation, new persistent arrhythmias, oxygen desaturation (SpO_2 < 90%), severe agitation (RASS ≥ +2), or regurgitation, which were considered complications of the Trendelenburg maneuver.

DATA ANALYSIS PLAN

Sample size estimation

We calculated the sample size using MedCalc version 22.009 (MedCalc Software, Ostend, Belgium) to ensure an 80% power to detect a significant difference between two groups, with a two-sided alpha level of 0.05. This calculation was based on an assumed 50% incidence of fluid responsiveness [4,5] and an AUROC of at least 0.7. As a result, 68 patients were enrolled, accounting for a 10% dropout rate.

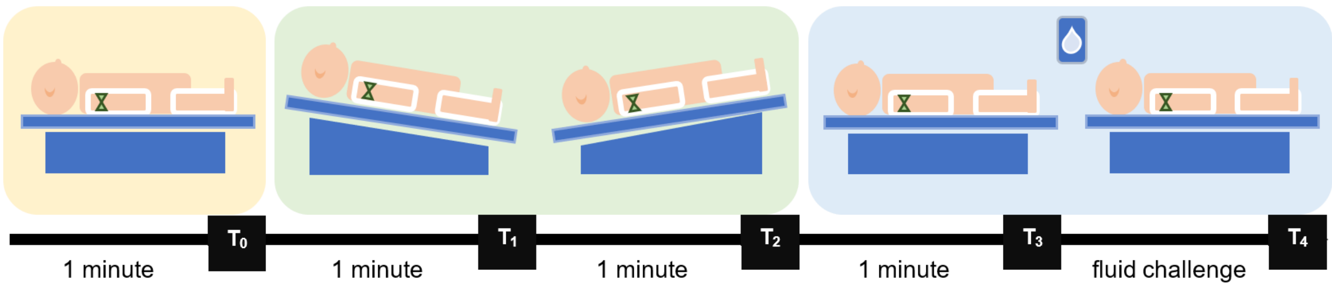

Figure 1. Demonstrates the study protocol.

The patient is placed in the supine position, and the sensor is attached to the patient's bed at the phlebostatic reference point for one minute for baseline measurement (T_0). The focus parameters are assessed. After informing the patient, the TM is performed by increasing bed angulation to head up +10° position for 1 minute (T_1), followed by decreasing the bed angulation to head down -13° position for one minute (T_2). Then, the patient is placed in the supine position for one minute (T_3). Last, 4 ml/kg of 5% human albumin is infused for 15 minutes while the patient is maintained in the supine position (T_4). The parameters are re-assessed and recorded after finishing each step.

OUTCOME ANALYSIS PLAN

Statistical analysis

Patient baseline characteristics and hemodynamic parameters induced by TM will be evaluated and presented as frequencies with percentages (%) for categorical variables, means with standard deviation (SD), or medians with interquartile range (IQR) for continuous variables, depending on the distribution. Comparative analyses between groups will be performed with the Fisher's exact test for categorical data and with the unpaired t-test or Mann-Whitney U test for continuous data, where appropriate. The planned analytic data are demonstrated in the Supplement Table.

To assess the diagnostic performance of the test, a ROC curve analysis will be conducted to evaluate the change in CI derived from uncalibrated pulse contour analysis, as well as VTI, PPV, and CVP induced by the TM. The AUROCs for these parameters will be compared using the DeLong test. The optimal cutoff value for each parameter, together with sensitivity, specificity, and positive and negative predictive values (PPV and NPV), will be calculated by maximizing the Youden index.

All statistical tests are two-tailed, and a value of $p<0.05$ indicated statistical significance.

The planned study flow and the diagnostic performance of each test are, respectively, illustrated in Figure 2 and Table 1.

DISCUSSION

This study sought to determine the diagnostic performance of the Trendelenburg maneuver in predicting fluid responsiveness among mechanically ventilated patients with spontaneous breathing activity in a surgical ICU. Prior research highlights the significance of using dynamic indices, based on the concept of circulatory-respiratory interaction, to predict fluid responsiveness in critically ill patients with acute circulatory failure. This practice is associated with reduced mortality, a shorter ICU stay, and less time on mechanical ventilation [6]. The principal benefits of dynamic indices like stroke volume variation (SVV) and pulse pressure variation (PPV) lie in their simplicity, which renders them ideal for continuous monitoring. These indices also enable the prediction of the outcomes of preload expansion without the necessity of actual fluid administration. Nevertheless, their accuracy is dependent on several conditions, including controlled mechanical ventilation with a suitably sized tidal volume, an optimal ratio between respiratory and pulse rates, and a regular cardiac rhythm. The presence of spontaneous breathing introduces variability in the patient's respiratory effort, leading to poor accuracy of fluid responsiveness predictions in such situations [7,8].

Given the constraints encountered with patients with spontaneous breathing activity, the passive leg raising (PLR) method has proven reliable in forecasting fluid responsiveness in these individuals.[9] PLR operates on the principle of augmenting cardiac preload by transferring fluids pooled in the patient's lower extremities in a semi-recumbent position and directing them to the central compartment when the individual is lying flat with passive elevation of the legs. This maneuver mimics around 300 mL of fluid challenge without external fluid administration. After PLR, an increase in cardiac output and its surrogates, or a decrease in the dynamic parameters such as PPV or SVV as reported in previous studies, is indicative of fluid responsiveness [10,11]. Similarly, the Trendelenburg maneuver (TM) uses a positional change, transitioning the patient from a whole-bed head-up to a head-downward position. A mere shift of at least 10 degrees in bed angulation has been shown to significantly increase cardiac output and cardiac preload, as evidenced by many previous studies.[12,13] Thus, it can be suggested that the TM maneuver produces an effect similar to that of the PLR, thus providing a potential means to as-

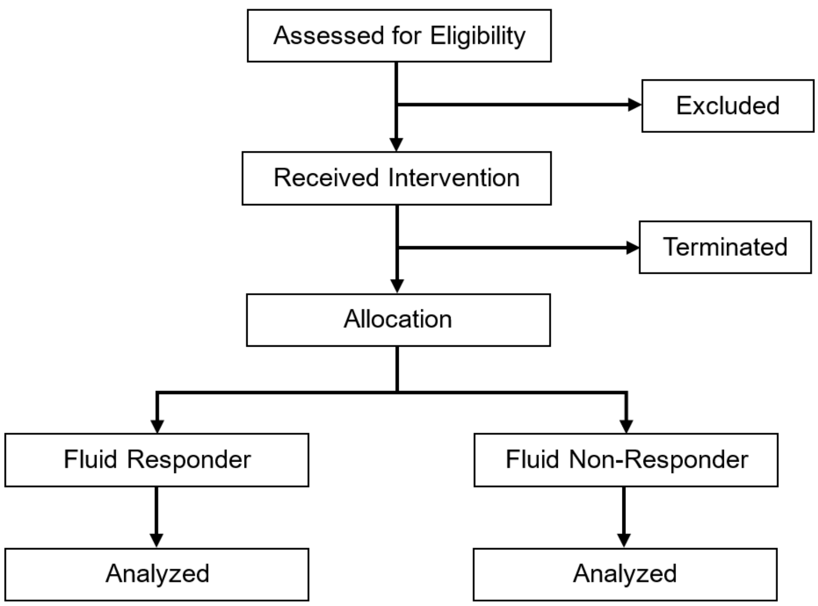

Figure 2. Demonstrates the study flow.

Table 1. Predictive parameters of receiver operating characteristic (ROC) curves of variable changes induced by Trendelenburg position.

Parameter	AUROC	95% CI	p-value	Cut-off	Sensitivity	Specificity
Absolute ΔCI Trendelenburg						
% ΔCI Trendelenburg						
Absolute ΔPPV Trendelenburg						
% ΔPPV Trendelenburg						
Absolute ΔVTI Trendelenburg						
% ΔVTI Trendelenburg						
Absolute ΔCVP Trendelenburg						

AUROC: area under ROC; Δ: Difference of values between T1-T2; CI: Cardiac index; PPV: Pulse pressure variation; VTI: Velocity-time integral of left ventricle.

sess fluid responsiveness in patients experiencing acute circulatory failure. This concept is supported by research from 2017 and 2021, which found that the TM reliably predicted fluid responsiveness in patients positioned prone and in those undergoing veno-arterial ECMO [4,5]. By extension, we believe that in mechanically ventilated patients with spontaneous breathing activity, alterations in CI and cardiac parameters induced by the TM can be used to evaluate fluid responsiveness.

Moreover, TM may provide certain advantages to patients who breathe spontaneously. While PLR can predict fluid responsiveness, the maneuver's implementation in patients who are still conscious raises several concerns. Adjusting a patient's position may aggravate discomfort or pain, triggering an increase in sympathetic activity and cardiac output, leading to a misinterpretation of the test results. A study by Toppen W, et al. reported the incidence of patient discomfort during the procedure to be as high as 30% [14]. Moreover, PLR requires a specialized bed and well-trained personnel to manipulate the position without influencing the patient's hemodynamics [15]. Thus, we hypothesize that TM has the potential to reduce patient distress and pain during positioning and reduce personnel's hesitation and anxiety as it is simpler to perform.

The strengths of this study are multifold. First, it targets a prevalent condition in ICUs, enhancing its practical relevance. The cardiac index and other hemodynamic variables can be obtained through minimally invasive or non-invasive methods, making it relatively safe to perform. Finally, the use of pulse-contour analysis for real-time cardiac index monitoring enhances the utility of the study.

However, this study is not without limitations. First, the measurement of cardiac index by an uncalibrated pulse-contour analysis is based on the calculation of the patient's demographic data. Second, the arterial cannulas are positional and sensitive to wrist movement. This can cause either over- or under-damping, resulting in a misinterpretation of the hemodynamic values. Finally, due to the limitations of bed angulation in the ICU, the power of estimated fluid translocation may be lower than in previous studies.

CONCLUSION

In summary, we conducted a single-center, prospective observational study in a surgical ICU to evaluate the diagnostic performance of changes in cardiac index and hemodynamic parameters during the Trendelenburg maneuver as a novel method to predict fluid responsiveness in patients under invasive mechanical ventilation with spontaneous breathing activity.

CONFIDENTIALITY

The informed consents were obtained in a separate, private space in the surgical ICU. Codes were used as an alternative to patient names, hospital identification number, and admission number. The data was recorded in the research record form, which was kept in the investigators' locked cabinet and a password protected personal computer. After the research, the information was deleted from the computer and physical documents destroyed.

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AUTHORS' CONTRIBUTIONS

(I) Conceptualization: S. Kongsayreepong, N. Kitisin; (II) Data curation: N. Hemtanon; (III) Formal analysis: S. Kongsayreepong, N. Kitisin, N. Hemtanon; (IV) Funding acquisition: N. Hemtanon, N. Kitisin, S. Kongsayreepong; (V) Methodology: N. Hemtanon, N. Kitisin, S. Kongsayreepong; (IV) Project administration: N. Hemtanon, N. Kitisin; (VII) Visualization: S. Kongsayreepong; (VIII) Writing – original draft: N. Hemtanon; (IX) Writing – review & editing: N. Kitisin, S. Kongsayreepong.

SUPPLEMENTARY MATERIALS

None

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