Validity of Corrected Flow Time (FTc) as a Predictor of Fluid Responsiveness in Patients with Sepsis-induced Hypotension

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Purpose: To determine the validity of corrected flow time (FTc) as a predictor of fluid responsiveness for patients with sepsis-induced hypotension in the emergency department.

Methods: A total of 26 adult patients, who presented in the emergency department with sepsis-induced hypotension with spontaneous breathing, were enrolled in this prospective, interventional study. These patients were monitored by Esophageal Doppler (ED); FTc, central venous pressure (CVP), stroke volume index (SVI), and inferior vena cava diameter (IVCD) were measured before and after fluid challenge. Responsiveness to fluid challenge was defined as an SVI increase ≥10%. Receiver operating characteristic (ROC) curves were constructed and compared to evaluate the overall performance of preload indices (CVP, FTc, IVCD) in terms of predicting fluid responsiveness.

Results: Of the hemodynamic parameters initially measured, there were statistically significant differences in FTc and CVP between the responsive and unresponsive groups. Before and after fluid challenge, noticeable changes were observed in mean arterial pressure (MAP), CVP and IVCD between the two groups. Only the responsive group demonstrated statistical difference in FTc. The areas under the curves for FTc (0.870; 95% CIs, 0.708–0.979; p=0.009) were significantly greater than those for CVP and IVCD.

Conclusion: The corrected flow time (FTc) method may be a good predictor of fluid responsiveness relative to sepsis-induced hypotension for patients in the emergency department.

Key Words: Esophageal Doppler, Corrected flow time, Sepsis, Emergency department

Introduction

Solid evidence exists that fluid therapy must be started as a first-line treatment in all patients with septic shock as soon as hypotension is detected, with the goal of rapidly restoring tissue perfusion1). However, accurate evaluation is important to avoid unnecessary volume replacement, which can be deleterious in critically ill patients2). Therefore the prediction of fluid responsiveness is a major issue in optimizing hemodynamic therapy. Fluid responsiveness is defined as an increase in a patient’s stroke volume in response to fluid challenge3,4). Consequently, a number of technologies have been developed with indexes of cardiovascular function to assist in therapeutic decision making5). Pulmonary artery wedge pressure and central venous pressure are invasive techniques that are poor predictors of fluid responsiveness6,7). Therefore, recently continuous and noninvasive esophageal Doppler (ED) monitoring has emerged as an alternative to pulmonary artery catheterization. ED is a non-invasive technique for monitoring cardiac function. The technique and clinical use were first described in 1971, subsequently refined by Singer and colleagues9) in 1989, and recently have been easily utilized in the emergency department with less likelihood of causing complications compared to other monitor devices8,10-12). Information is obtained from the size, shape, and changes in shape of the velocity waveforms of descending aortic blood flow. Minute distance, the product of waveform area (stroke distance) and heart rate, provides a measure of cardiac output8). Previous studies demonstrated a good correlation in the cardiac output measured by thermodilution with Swan-ganz pulmonary artery...
catheterization when using the ED for measurements\(^{13-15}\). Of the ED variables, the left ventricular ejection time (flow time) corrected for heart rate provides an index of preload and is reflected by the waveform base\(^{16}\). When used as an intravascular volume index during the surgery, fewer post-operative complications and a shorter hospitalization time were reported\(^{17,18}\). However, most patients enrolled in those studies were monitored in an operation room or intensive care unit with mechanical ventilation, and few studies were performed to clarify whether the corrected flow time (FTc) can be used as a predictor of fluid responsiveness in conditions such as sepsis-induced hypotension with spontaneous breathing among patients in the emergency department.

The objective of the study is to determine whether FTc can be used for patients with sepsis-induced hypotension as a predictor of fluid responsiveness in the emergency department. We compared use of this technique to other indexes, such as CVP, IVCD, and stroke volume index (SVI).

**Materials and Methods**

This prospective, interventional study was reviewed and approved by the Institutional Review Board of the study institution (IRB no.1007-D-07). The study was conducted at the emergency department of a tertiary academic medical center with annual census of 35,000.

This study included 26 spontaneously ventilated patients with sepsis-induced hypotension requiring cardiac output (CO) measurement in the emergency department over a six-month period (October 2010 to April 2011). Sepsis-induced hypotension is defined as systolic blood pressure (SBP) <90 mmHg, mean arterial pressure <70 mmHg or an SBP decrease >40 mmHg in the absence of other causes of hypotension\(^{19}\).

Patients with cardiac disease (except for those with hypertension), arrhythmias, upper gastrointestinal bleeding, and other contraindications to ED monitoring probe insertion (i.e., esophageal stent, carcinoma of the esophagus or pharynx, a previous esophageal surgery, esophageal stricture, pharyngeal pouch, intra-aortic balloon pump, coarctation of the aorta, and severe coagulopathy) were excluded. Patients already taking vasoressors were also excluded.

All patients were monitored with a Cardio-Q ED 7 mm probe (Deltex, West Sussex, UK), which was also inserted into the esophagus through the nasal cavity. The probe was rotated as needed to obtain the best Doppler signal of blood flow in the midstream of the descending aorta. Correct placement was assumed when reproducible, sharply defined waveforms appeared on the screen of the monitor and crisp sound was heard through the loudspeaker. Any other medications like sedative or anesthetic agents were not used to facilitate insertion of the probe, except lidocaine jelly for local anesthesia and lubrication. The position of the probe was confirmed by portable chest X-ray and by continuously measuring descending thoracic aorta blood velocity (Doppler transducer). After positioning, the ED probe continuously measured and displayed cardiac output, SVI, and FTc. A central venous catheter was inserted into a right subclavian or internal jugular vein. Pressure transducers were set to zero at the midaxillary level to ambient pressure (Arrow\(^{®}\) International, Everett, USA). Transabdominal ultrasonography was performed to measure the IVCD using a 2.0-5.0 MHz phased-array probe (MicroMaxx, Sonosite, USA); IVCD was measured at the level of 1 cm below the hepatic vein and IVC junction.

Hemodynamic data such as heart rate (HR), mean arterial pressure (MAP), CVP, IVCD, FTc, and SVI were measured immediately before and after fluid challenge. Fluid therapy was performed by the infusion of 6% hetastarch in lactated electrolyte solution (Hextend\(^{®}\); Biotime Inc, Alameda, USA) at 7 ml/kg. It was administered over 30 minutes by infusion pump. A favorable response to fluid challenge was defined by an increase in SVI of ≥10%; these patients were regarded as a responsive group.

Categorical variables are presented as counts and percentages. These data were statistically analyzed by Fisher’s exact tests. Continuous data are presented as median and interquartile range (IQR). Comparisons of hemodynamic variables before and after fluid loading were performed using the Wilcoxon signed ranks test; comparisons between the responsive group and the unresponsive group were made using the Mann-Whitney U-test. The receiver operating characteristic (ROC) curves were generated for FTc, IVCD, CVP of fluid loading by varying the discriminating threshold of each hemodynamic parameter. The significance level was set at \(p\) value < 0.05. Statistical analyses in this study were per-