Cardiac Output Assessed by the Fourth-Generation Arterial Waveform Analysis System Is Unreliable in Liver Transplant Recipients

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ABSTRACT

Background. Liver transplant recipients often have violent hemodynamic fluctuation during surgery that may be related to perioperative and postoperative morbidity. Because there are some considerations for the risk of the pulmonary arterial catheter (PAC), the conventional invasive device for cardiac output (CO) measurement, a reliable and minimally invasive alternative is required. We validated the reliability of CO measurements with the use of a minimally invasive FloTrac system with the latest fourth-generation algorithm in liver transplant recipients.

Methods. Forty liver transplant recipients without atrial fibrillation, valvular pathology, or intracardiac shunt were recruited in this prospective, observational study. CO values measured by use of PAC with continuous thermodilution method (CO_{Th}) and FloTrac devices (CO_{FT}) were collected simultaneously throughout the operation for reliability validation.

Results. Four hundred pairs of CO data points were collected in total. The linear regression analysis showed a high correlation coefficient (73%, $P < .001$). However, the percent error between CO_{Th} and CO_{FT} was 42.2%, which is worse than the established interchangeability criterion of 30%. The concordance rates were calculated at 89% and 59% by 4-quadrant plot and polar plot analysis, respectively. Neither met the preset validation criteria (>92% for the 4-quadrant plot and >90% for polar plot analyses).

Conclusions. Our study demonstrates that the CO measurements in liver transplant recipients by the latest FloTrac system and the PAC do not meet the recognized interchangeability criterion. Although the result showed improvement in linear regression analysis, it failed to display a qualified trending ability.

DURING liver transplant surgery, fluctuating hemodynamics have always been a challenge for anesthesiologists to address, and poorly controlled hemodynamics are implicated in subsequent morbidity and mortality in perioperative and postoperative care. Conventional intervention with a pulmonary arterial catheter (PAC) is not only applied in clinical hemodynamic monitoring for pulmonary artery pressure and central venous oxygen saturation but also is generally recognized as the gold-standard method for assessing cardiac output (CO) values. However, the lack of solid evidence to demonstrate favorable post-transplant outcomes and potential risks of seriously lethal complications, such as infection, pulmonary vascular rupture, valvular damage, and severe arrhythmia, have driven the development of non- or less-invasive CO measurement techniques.

The FloTrac system (Edwards Life Sciences, Irvine, Calif, United States) was developed in 2005 and analyzes the peripheral arterial waveform and references the database

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0041-1345/16
http://dx.doi.org/10.1016/j.transproceed.2015.12.070

to estimate stroke volume (SV) and thereby the presumed CO values [1]. The early algorithm had some limitations when applied in liver transplant recipients because of its long interval (10 minutes) of adaptation to vascular compliance and the limited demographic database, which only recruited healthy volunteers or patients with cardiac diseases. For the purpose of refinement, an updated shorter interval of adaptation, auto-switching model for different hemodynamic status [2], and the inclusion of more surgical patients in the database were programmed into the newer algorithm.

There are several possible explanations for the inaccuracy of the FloTrac-derived CO values in liver transplant recipients. First, recipients who are indicated for liver transplant surgeries usually have low systemic vascular resistance (SVR). Low SVR may result from chronic cirrhotic pathogenesis, such as hyperdynamic circulation, cirrhotic cardiomyopathy, and pulmonary vascular abnormalities [1]. Second, the transplant procedures include clamping of major vessels, organ reperfusion, vasopressor administration, and massive fluid resuscitation, and these procedures may reduce the reliability of arterial waveform analysis. Because of these factors, accurate assessment of CO is a challenge for this minimally invasive device in liver transplant surgery [3–8]. Compared with previous versions, the latest fourth-generation algorithm introduced new correction factors with a short adaption interval (20 seconds) to enhance the ability to address rapid changes in vascular compliance and further broaden the database to include a greater variety of patient conditions [8].

The aim of the present study was to validate the reliability of CO measurements with the use of the upgraded minimally invasive FloTrac system with the newer algorithm (Version 4.0) in liver transplant recipients.

METHODS

After Institutional Review Board approval (103-3452B), our prospective study enrolled 40 patients ages 20 to 70 years who received liver transplant surgeries in Chang-Gung Memorial Hospital between September 2014 and August 2015. The exclusion criteria were preoperative atrial fibrillation, significant valvular pathology, and intracardiac shunt.

Every patient received anesthetic induction as per routine protocol with propofol, 1 to 2 mg/kg; fentanyl, 1 to 2 μg/kg; and cisatracurium, 0.2 mg/kg. For CO measurement, a FloTrac sensor kit was connected to left radial artery catheter, and a PAC (Opti-Q SvO2/CCO, Abbott Laboratories, North Chicago, Ill, United States) was placed through the right internal jugular vein catheter. The adequate position of the PAC was confirmed by tracing the continuous changes in waveform. All recipients then received the standard surgical procedures performed by a single surgical team, and all patients were sent to the intensive care unit for postoperative care.

The clock time of the FloTrac system and the thermodilution monitor were synchronized with the standard time of the operation room before surgery. The values of CO were then simultaneously measured with the use of the continuous thermodilution method via PAC (CO_{Th}) and arterial waveform analysis via the fourth-generation algorithm of the FloTrac system (Version 4.0) (CO_{FT}). The continuous thermodilution method was considered the reference measurement because it had demonstrated interchangeability with the gold standard, the intermittent thermodilution method, and attenuated the bias from different operators in previous studies [9,10]. Both sets of data were recorded automatically in the devices and then were extracted for subsequent analysis. Ten predefined time points were chosen, based on previous literature [6]. These time points were (1) immediately after PAC placement, T1; (2) 30 minutes after incision, T2; (3) 10 to 15 minutes before inferior vena cava (IVC) clamping, T3; (4) 10 to 15 minutes after IVC clamping, T4; (5) 10 to 15 minutes before portal venous reperfusion, T5; (6) within 3 minutes of portal venous reperfusion, T6; (7) 10 to 15 minutes after portal venous reperfusion, T7; (8) 10 to 15 minutes after hepatic artery reperfusion, T8; (9) within 5 minutes of biliary reconstruction, T9; and (10) the end of the surgery, T10.

Subgroups

Subgroup analysis was performed according to the different surgical phases (dissecting phase, anhepatic phase, or reperfusion phase), disease severities (model for end-stage liver disease scoring system [MELD] score $\geq$20 or <20), vascular compliance (SVR <800 and $\geq$800 dyne·cm^{-5}) [11], and norepinephrine administration. Bland-Altman analysis was applied for agreement validation.

Statistical Analysis

Statistical analysis was performed with the use of SPSS version 17.0 (SPSS Inc, Chicago, Ill, United States) and R 3.2.0 for windows (Free Software Foundation Inc, Boston, Mass, United States). Descriptive statistics were applied for demographic, clinical, and hemodynamic data. Linear regression analysis was used to determine the correlation between continuous parameters, and the result was considered significant only when the P value was <.05. These parameters can be considered very highly correlated when the correlation coefficients (γ) are between 0.9 and 1.0, highly correlated when γ is between 0.7 and 0.9, moderately correlated when γ is between 0.5 and 0.7, and weakly correlated when γ is <0.5. Bland-Altman analysis was applied to evaluate CO agreement by calculating percent error (1.96 standard deviations of the bias divided by mean CO) between 2 different assessments. When the percent error was <30%, the tested method (CO_{FT}) was regarded as interchangeable with the CO_{Th} [12]. Four-quadrant plots and polar plots were analyzed to evaluate trending ability. Concordance in a 4-quadrant plot is defined when the ratio of the measurements fall in the first and third quadrants. The validation criterion was set at a concordance rate >92% [10,12]. Concordance in a polar plot is defined when the ratio of the measurements fall within the −30° to 30° area. The validation criterion was a concordance rate >90% [13].

RESULTS

We recruited 40 patients, and 2 other patients with atrial fibrillation were precluded. The group included 34 men and 6 woman, 29 cases of viral hepatitis, 14 cases of alcohol-related disease, and 17 cases of hepatocellular carcinoma. Other etiologies for end-stage liver diseases included 1 patient with autoimmune hepatitis and 2 with Wilson disease. All patients were diagnosed with liver cirrhosis, and 8, 12,