Arterial Pulse Cardiac Output Agreement With Thermodilution in Patients in Hyperdynamic Conditions

Giorgio Della Rocca, MD,* Maria Gabriella Costa, MD,* Paolo Chiarandini, MD,* Gaia Bertossi, MD,* Manuela Lugano, MD,* Livia Pompei, MD,* Cecilia Coccia, MD,* Mauricio Sainz-Barriga, MD,† and Paolo Pietropaoli, MD‡

Objective: This study aimed to compare continuous cardiac output (CCO) obtained using the arterial pulse wave (APCO) measurement with a simultaneous measurement of the intermittent cardiac output (ICO) and CCO obtained with a pulmonary artery catheter (PAC) in liver transplant patients.

Design: A prospective, single-center evaluation.

Setting: A university hospital intensive care unit.

Patients: Eighteen patients after liver transplantation.

Interventions: Pulmonary artery catheters were placed in all patients, and ICO and CCO were determined using thermodilution. APCO measurements were made with the Vigileo System (Edwards Lifesciences, Irvine, CA).

Measurements and Main Results: The authors obtained 126 data pairs of ICO and APCO and 864 pairs of CCO and APCO. ICO data were collected after intensive care unit admission and every 8 hours until the 48th postoperative hour. CCO and APCO data were collected every hour from admission until the 48th postoperative hour. Bias and precision were 0.95 ± 1.41 L/min for ICO versus APCO and 1.29 ± 1.28 L/min for CCO and APCO. Bias and precision for cardiac output (CO) data pairs less than 8 L/min were 0.32 ± 1.14 L/min between ICO and APCO and 0.71 ± 0.98 L/min between CCO and APCO. For CO data pairs higher than 8 L/min, bias and precision were 1.79 ± 1.54 L/min between ICO and APCO and 2.25 ± 1.14 L/min between CCO and APCO.

Conclusions: APCO enables the assessment of CO with clinically acceptable bias and precision. At higher CO levels, APCO underestimates PAC measurements and it is not as reliable as thermodilution in hyperdynamic liver transplant patients.

KEY WORDS: cardiac output, measurement techniques, arterial pulse contour analysis, thermodilution, pulmonary artery catheter, liver transplantation

DIRECT MEASUREMENT OF cardiac output (CO) is an important component of the perioperative management of high-risk patients undergoing major surgery, partly because physicians cannot reliably estimate CO by physical examination and routine clinical assessment alone.[1,2] The most common method of measuring hemodynamic status is with a pulmonary artery catheter (PAC), which is also considered to be the clinical gold standard for cardiac output monitoring[3,4] and is routinely used during orthotopic liver transplantation (OLT). However, the PAC is an invasive instrument, and this limits its use. The development of less invasive continuous measurement technologies[5,6] combined with a series of reports suggesting an increases in morbidity and mortality associated with pulmonary artery catheterization have refocused attention on alternatives.[7,8] The method behind the calculation of stroke volume from the contour of an arterial pressure curve dates from 1899, but it was not until 1980 that advances in computer technology allowed this to take place.[9,10] Recently, a device offering uncalibrated CO measurement by arterial waveform analysis using standard radial artery catheterization (APCO) (FloTrac/Vigileo; Edwards Lifesciences, Irvine, CA) has been introduced.[11-16] It does not require calibration by thermodilution but bases its calculations on arterial waveform characteristics in conjunction with patient anthropometric data. So far, this new device has been tested mainly during cardiac surgery and has shown different levels of agreement between APCO and PAC.[11-16] The authors selected liver transplant patients to test APCO in patients with a hyperdynamic circulation.

This study aimed to determine the agreement of APCO with intermittent (ICO) and continuous cardiac output (CCO) measurements performed with a PAC in cirrhotic patients after OLT.

METHODS AND MATERIALS

After ethics committee approval and written informed consent was obtained, 18 consecutive patients undergoing OLT were enrolled in this clinical trial. Patients with pre-existing pulmonary and/or cardiac diseases, other than the common symptoms of end-stage liver dysfunction, and patients with fulminant hepatic failure, hepatopulmonary syndrome, or pulmonary hypertension were excluded from the study.[17] These features were evaluated during the preoperative clinical assessment of the liver transplant candidates. Other exclusion criteria were cardiac valve disease, left ventricular ejection fraction <50%, and symptomatic peripheral artery disease.

Standard monitoring consisted of 2-lead electrocardiography (II/V_5), pulse oximetry, invasive systemic arterial pressure (AP) monitoring, and multigas analysis. A radial artery catheter was placed in all patients prior to induction of anesthesia to obtain invasive AP. Anesthetic management was standardized and consisted of propofol (0.5 mg/kg) for the induction, cisatracurium besylate (0.15 mg/kg) as the muscle relaxant, and alfentanil (7-10 μg/kg) for analgesia. Anesthesia was maintained with sevoflurane (end-tidal 0.8%) or desflurane (end-tidal 4%) and a continuous infusion of remifentanil (0.1-0.5 μg/kg/min). Mechanical ventilation with a volumetric anesthesia ventilator included a positive end-expiratory pressure of 5 cmH_2O. After the induction of anesthesia, an 8.0F PAC (Swan-Ganz Catheter CCOmbo CCO/SvO_2/CEDV/VIP catheter 777HF8, Edwards Lifesciences) was placed via an 8.5F introducer (AVA 3Xi, Edwards Lifesciences) inserted into the right internal jugular vein.

A FloTrac sensor kit was connected to the arterial catheter and to the Vigileo monitor programmed with the software version V0.1.10, PIC V1.0 for this device (Edwards Lifesciences). Patient data (age, sex, body weight, and height) were entered, and the system was zeroed and CO measurements initiated. The system consists of a specialized blood pressure sensor and monitor that collect and analyze arterial pressure

*From the Departments of *Anesthesia and Intensive Care Medicine and †Surgery-Transplant Unit, University of Udine, Udine, Italy; and ‡Department of Anesthesia and Intensive Care Medicine, University of Rome "La Sapienza," Rome, Italy.*

Address reprint requests to Maria Gabriella Costa, MD, Department of Anesthesia and Intensive Care Medicine, Azienda Ospedaliero Universitaria di Udine, P.le S.M. della Misericordia, 15, 33100 Udine, Italy. E-mail: gabriella.costa@med.uniud.it

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data in real time. The FloTrac/Vigileo system does not require calibration by thermodilution, and it uses an algorithm to derive APCO from the arterial pressure wave. Each arterial waveform is analyzed with a frequency of 100 Hz over 20 seconds. The arterial waveform is also analyzed for 8 different characteristics, such as upstroke and downslope of the curve. Each curve is analyzed separately, and additional curves are analyzed and compared with former and next curves. From this analysis, which takes 20 seconds, the average curve is given by means of the standard deviation of the given characteristics of the curves. From the given stroke volume (SV) and heart rate (HR), the cardiac output is determined and updated every 20 seconds.

The algorithm uses the basic equation for measuring CO, with HR being determined from the pressure waveform, through conventional methods as follows: $CO = HR \times SV$.

The calculation of SV can be divided into 2 parts based on manually entered patients' data (age, sex, body length, and weight): (1) the contribution of pulse pressure to SV, which is proportional to the standard deviation of arterial pressure (SD_{AP}), and (2) the influence of vascular resistance and compliance on SV integrated into a single variable (χ). Thus, CO is calculated as follows: $CO = HR \times SD_{AP} \times \chi$ as previously reported by Breukers et al.[15] Different characteristics of the blood pressure[10] are used in the equation for the derivation of χ from a multivariate regression model (M) as follows: $\chi = M$ (HR, SD_{AP}, Cp, BSA, mAP, μ3AP, μ4AP), where M is the multivariate approximating function, mAP is the mean arterial pressure, Cp is a function for arterial compliance, BSA is the body surface area calculated from the weight and height, μ3AP is the skewness of the arterial pressure data, and μ4AP is the kurtosis of the arterial pressure data. Cp is derived from Langewouters et al[18] using sex and age and modified using weight, height, and BSA.

The Langewouters' model is an arctangent (sigmoidal, not exponential) model to determine static and dynamic elastic properties of the thoracic and abdominal aortas in vitro.[18] Pressure and area data are simultaneously fitted to the so-called "arctangent model" to obtain the mechanical characteristics of "in vitro" aortas. The Langewouters' method involves, by using aortic compliance, data generated from cadaver studies as a "starting point" for the χ value. Arterial waveform characteristics (eg, skewness and kurtosis of individual waves) are then used to "fine tune" the value.[14] For example, a wave skewed to the left indicates noncompliance of the vascular tree as does a wave with pronounced kurtosis (shortness). A large, rounded arterial wave shifted to the right is more indicative of a compliant arterial tree. Pulse pressure is recorded at a frequency of 100 Hz, and SD_{AP} is determined during a window of 20 seconds. The calibration constant χ is automatically recalculated every 10 minutes.

Good waveform fidelity is mandatory to obtain accurate APCO values. A dampened arterial waveform may result in an underestimation of the APCO values, whereas an increase in signal oscillations may result in an overestimation of these values. In normal conditions, this technical interference should be minimal because all systems conform to strict guidelines with respect to gain and damping coefficients and the presence of continuous flushing devices.[19] After calibration and zeroing to atmospheric pressure and before each comparison with thermodilution, the arterial waveform quality was visually inspected and assessed in terms of damping. To ensure a stable hemodynamic condition, the infusion of large volumes of colloids or crystalloids or the bolus administration of vasopressors was not permitted during the measurements. In the Vigileo computer, a filter is embedded to filter out excessively high systolic blood pressure and high-frequency atrial fibrillation. If arrhythmias occurred during the measurements, the results were discarded and measurements were repeated.

Intermittent CO measurements were made by the manual injection of 10 mL of cold saline solution into the superior vena cava through the atrial port. Three consecutive measurements were obtained randomly during the entire respiratory cycle over a 2-minute period, and the plausibility of every temperature curve was judged visually on the monitor.[20] In case of a deviation of $>$10% between the highest and lowest of these measurements, 2 more measurements were performed, and the highest and lowest of the 5 measurements were rejected. To avoid variation between operators, the injection was always performed by the same person. In the case of patients mechanically ventilated, the ventilator setting was kept the same during the measurements. The correct position was confirmed by pressure tracings and by a routine chest radiograph immediately after admission to the intensive care unit. All intravascular pressure measurements were performed to the midchest level.

ICO was measured after intensive care unit admission (T0), 2 hours after completion of surgery when the patients were hemodynamically stable, and every 8 hours until the 48th postoperative hour (T8, T16, T24, T32, T40, and T48). APCO and CCO data were collected at T0 and every hour until T48. APCO measurement was performed by operators who were blinded to the corresponding ICO or CCO measurements. APCO values were obtained as the mean of 3 values read from the Vigileo monitor before each injection performed to obtain ICO. At each time point, CCO measurement was recorded immediately before and after ICO measurements, and the mean of these CCO data pairs was recorded. The mean CCO was compared with the corresponding mean APCO value collected every hour, and ICO was compared with APCO collected at predefined steps (T0-T48).

Data are presented as mean and standard deviation (SD), unless otherwise stated. Hemodynamic measurements and mean CO values derived from ICO and CCO versus APCO were analyzed by using analysis of variance for repeated measurements and the paired Student *t* test with Bonferroni correction; $p < 0.05$ was considered statistically significant.

The measurement methods were compared by using the analysis described by Bland and Altman[21] in terms of bias and limits of agreement. Bias is the mean difference between the 2 methods of measurement and represents the systematic error, precision is represented by single SD, and the limit of agreement (LOA) is defined as the upper and the lower LOA calculated as the mean $\pm$ 2 SD and defining the range in which 95% of the differences between methods were expected to lie (mean bias $\pm$ 2 SD).

In 1999, Critchley and Critchley[22] provided a comprehensive mathematically derived method for the assessment of observed variability between measurement methods. They recommended that in comparative studies the percentage error (PE) should be presented as well as the limits of agreement, putting the magnitude of the latter in the context of the absolute values found in the specific patient group being studied. Given an inherent variability of $\pm$20% for each method under comparison, the combined variability (ie, limits of agreement) should not exceed $\pm$30% of the mean CO according to the suggested criteria.[22] It has been suggested in a recent discussion of methodologies for assessing agreement between different methods of clinical measurement that this 30% cutoff value is an "arbitrary limit."[23]

In the present study also, the PE was calculated as the limit of agreement (ie, 2 SD from the bias) divided by the CO (calculated as the mean of both methods) per 100, as proposed by Critchley and Critchley.[22] Bias, limit of agreement, and Spearman coefficient of correlation were calculated for the entire dataset and also separately for datasets with CO below and above 8 L/min.

For statistical calculations, the software package, SPSS for Windows (Version 12.0; SPSS Institute, Chicago, IL), was used, and for Bland-Altman plots, the software package GraphPad for Windows (Version 5.01; GraphPad Software, Inc, San Diego, CA) was used.

RESULTS

Eighteen consecutive patients (14 men and 4 women) receiving OLT were enrolled in the study. The mean age was 50.5 (8.1) years (range, 36-67 years), and the mean BSA was 1.8