Accuracy, Precision, and Trending Ability of Uncalibrated Arterial Pressure Waveform Analysis of Cardiac Output in Patients With Impaired Left Ventricular Function: A Prospective, Observational Study

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Objectives: **Uncalibrated arterial waveform analysis provides minimally invasive and continuous measurement of cardiac output (CO). This technique could be of great value in patients with impaired left ventricular function, but the validity in these patients is not well established. The aim of this study was to investigate the accuracy, precision, and trending ability of uncalibrated arterial waveform analysis of cardiac output in patients with impaired left ventricular function.**

Design: **Prospective, observational, method-comparison study.**

Setting: **Nonuniversity teaching hospital, single center.**

Participants: **The study included 22 patients with a left ventricular ejection fraction of 40% or less undergoing elective coronary artery bypass grafting.**

Interventions: **In the period between induction of anesthesia and sternotomy, CO was measured using the FloTrac/Vigileo system (third-generation software) and intermittent pulmonary artery thermodilution before and after volume loading.**

Measurements and Main Results: **Accuracy and precision as determined using Bland-Altman analysis revealed a bias of –0.7 L/min, limits of agreement of –2.9 to 1.5 L/min, and a mean error of 55% for pooled data. Proportional bias and spread were present, indicating that bias and limits of agreement were underestimated for high CO values. Trending ability was assessed using 4-quadrant analysis, which revealed a concordance of 86%. Concordance from a clinical perspective was 36%. Polar plot analysis showed an angular bias of 13° degrees, with radial limits of agreement of –55° to 51°. Polar concordance at ±30° was 50%.**

Conclusions: **Arterial waveform analysis of cardiac output and pulmonary artery thermodilution cardiac output were not interchangeable in patients with impaired left ventricular function.**

KEY WORDS: cardiac output, heart failure, hemodynamics, intraoperative monitoring, pulmonary artery catheterization, pulsed-wave analysis

UNCALIBRATED ARTERIAL PRESSURE waveform analysis enables continuous measurement of cardiac output (CO) from an arterial line, which almost routinely is inserted in critically ill patients.[1,2] The reliability of the technique has been investigated thoroughly in a variety of patients and clinical settings.[1–3] The evidence in patients with impaired left ventricular function (LVF) is, however, limited and conflicting, and the ability to track changes in CO has not yet been investigated.[4–6] Continuous CO monitoring would be extremely valuable in this patient group, to guide fluid administration and the use of inotropic support in the operating room and intensive care unit. Baseline CO may be low, and further reductions in CO induced by blood loss, fluid shifts, or anesthetic agents may have deleterious consequences. The trending ability of arterial waveform analysis-based CO monitoring devices may, therefore, be even more important than measuring the absolute value of CO in clinical practice.[7,8]

In patients with impaired LVF, the upstroke in the arterial waveform may be decreased. Moreover, these patients have an increased risk of vascular disease, which influences the elastic properties of the vascular tree. The modeling of the waveform and vessel compliance for CO calculation may, therefore, be hindered in patients with impaired LVF. The aim of this prospective, observational, method-comparison study was to investigate the accuracy and precision of uncalibrated arterial pressure waveform analysis of CO measured using the FloTrac sensor and Vigileo monitoring system (software version 3.02; Edwards Lifesciences, Irvine, CA) in patients with impaired LVF undergoing coronary artery bypass grafting (CABG). In addition, the ability to track changes in CO induced by volume loading was assessed using 4-quadrant analysis, polar plot methodology, and concordance from a clinical perspective. The results from this study may contribute to the implementation of continuous CO monitoring in patients with impaired LVF.

METHODS

This study was approved by the institutional review board of the University Medical Centre Utrecht, The Netherlands (file number: 10/099). Written informed consent was obtained from each participating patient. Patients with a left ventricular ejection fraction (LVEF) $\leq$40%, determined using preoperative transthoracic echocardiography (TTE) or magnetic resonance imaging (MRI), were eligible for inclusion into the study.[9] Exclusion criteria were significant valvular heart disease (tricuspid, pulmonary, mitral and/or aortic valve stenosis and/or insufficiency grade $\geq$2), right ventricular dysfunction, intracardiac shunts, cardiac arrhythmias, age younger than 18 years, and patients undergoing emergency surgery. Intraoperatively, transesophageal

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echocardiography (TEE) was performed to verify the LVEF (≤40%) and the absence of exclusion criteria.

A radial artery catheter was inserted and connected to the FloTrac sensor and Vigileo monitor for continuous measurement of arterial pressure waveform CO (APCO).[10] General anesthesia was induced using sufentanil and midazolam. Endotracheal intubation was facilitated using rocuronium. After induction of anesthesia, a pulmonary artery catheter (PAC) was introduced via the internal jugular vein, guided by typical pressure waveform changes (Swan-Ganz CCOmbo catheter type 744HF75; Edwards Lifesciences, Irvine, CA).

Between the induction of anesthesia and surgical incision, volume loading with 7 mL/kg crystalloid fluid was performed over 15 minutes. IBW was calculated as 22 × [length (m)]^2. Intermittent thermodilution CO (TDCO) was measured before and after volume loading. If short-acting vasoactive drugs were administered, measurements were postponed until hemodynamic stability was restored. TDCO represents the average of 5 bolus injections of 10 mL of saline at room temperature, randomly spread over the respiratory cycle and performed by the same observer.[11] At the moment of injection for a single TDCO measurement, APCO was recorded. APCO represents the average of 5 readings at the same time as the injections for TDCO measurement.

Statistical analysis was performed using "R" version 2.11.0 (www.r-project.org) and SPSS version 21.0 for Windows XP (IBM, Armonk, NY). A p-value of 0.05 was considered significant. A sample size calculation was performed to limit the width of the 95% confidence interval (CI) around the mean error to 20%. Based on a mean CO of 5.0 L/min and a mean error of 30%, a sample size of 22 patients was needed. All data were checked for normality using histograms and Kolmogorov-Smirnov testing. Data are expressed as mean ± standard deviation (SD) unless otherwise stated. The individual precision of APCO and TDCO was calculated using the SD of the 5 repeated CO measurements averaged as a single CO value (SD_{IND}) and was defined as: individual precision = $2 \cdot SD_{IND} / \sqrt{5} \cdot$ mean CO.[12] The combined precision of APCO and TDCO was defined as: $\sqrt{}$ ([precision APCO]^2 + [precision TDCO]^2).[12,13] Pearson correlation coefficients were calculated to investigate the relationship between LVEF and the difference between TDCO and APCO (TDCO – APCO). The bias and limits of agreement (LOA) of APCO versus TDCO were calculated using Bland-Altman analysis, with a correction for the use of paired measurements.[14–16] Before the start of the study, the authors decided to accept a percentage bias (bias / mean TDCO) of ≤10% and a mean error of ≤20% for pooled data. Linear regression was applied to check for proportional bias, which refers to an increase or decrease in bias with increasing CO.[14] The absolute values of the residuals as obtained with linear regression were plotted against mean CO. This plot enables a visual check of proportional spread, which refers to an increase or decrease in the spread of the differences around the bias with increasing CO.[14] In the presence of proportional bias, spread, or both, regression analysis was used to determine formulas for the bias and LOA as a function of mean CO.[14] Trending ability of APCO during volume loading was determined using 4-quadrant analysis, with a 15% exclusion zone.[7,8] The authors predefined a 4-quadrant concordance rate ≥90% to be clinically acceptable. In addition, concordance as defined from a clinical perspective was calculated. For this purpose, the changes in APCO (ΔAPCO) and TDCO (ΔTDCO) after volume loading were categorized as nonsignificant (0% to ± 5%), significant increase or decrease (±5%–15%), or major increase or decrease (±15% or more). Trending was considered good if the APCO and TDCO changed in the same direction and fell into the same category. For each data pair of ΔAPCO and ΔTDCO, trending was assigned "good" or "bad." "Clinical concordance" was defined as the percentage of good trending. The authors predefined a clinical concordance rate ≥90% to be

Table 1. Patient Characteristics Including Demographic Data, History, Medication, and Preoperative Left Ventricular Ejection Fraction

	Mean (SD)	Range
Age (yr)	65 (13)	42–85
Height (m)	1.75 (0.08)	1.60–1.95
Weight (kg)	85.6 (11.1)	67.0–113
BMI (kg/m^2)	27.9 (3.4)	23.8–36.5
LVEF (%)	29.8 (7.1)	17–40
	Number of patients	
Patients with		
35% > LVEF ≤40%	4	
30% > LVEF ≤35%	5	
25% > LVEF ≤30%	5	
20% > LVEF ≤25%	6	
15% > LVEF ≤20%	2	
Sex		
Male/female	18/4	
Comorbidity		
Diabetes mellitus	10	
Hypertension	20	
COPD	4	
Dyslipidemia	15	
Medication		
Beta-blocker	20	
Calcium blocker	2	
ACE or AR inhibitor	17	
Diuretics	13	
Nitrates	5	

Abbreviations: ACE, angiotensin-converting enzyme; AR, angiotensin receptor; BMI, body mass index; COPD, chronic obstructive pulmonary disease; LVEF, left ventricular ejection fraction; SD, standard deviation

Table 2. Mean and SD of Hemodynamic Variables and Precision of TDCO Before and After Volume Loading

Hemodynamic Variable	Before Volume Loading	After Volume Loading
HR (beats/min)	62 (13)	55 (13)
MAP (mmHg)	70 (13)	75 (13)
CVP (mmHg)	10 (2.9)	12 (3.2)
TDCO (L/min)	3.4 (0.8)	3.8 (1.0)
APCO (L/min)	4.0 (1.1)	4.5 (1.2)
Precision TDCO (%)	7.8	6.7
Precision APCO (%)	8.8	4.9
Combined precision (%)	11.8	8.4

Abbreviations: APCO, arterial pressure waveform cardiac output; CVP, central venous pressure; HR, heart rate; MAP, mean arterial pressure; SD, standard deviation; TDCO, pulmonary artery thermodilution cardiac output.