Comparison of Esophageal Doppler, Pulse Contour Analysis, and Real-Time Pulmonary Artery Thermodilution for the Continuous Measurement of Cardiac Output

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Objective: **Continuous measurement of cardiac output (CCO) is of great importance in the critically ill. However, pulmonary artery thermodilution has been questioned for possible complications associated with right heart catheterization. Furthermore, measurements are delayed in the continuous mode during rapid hemodynamic changes. A new pulmonary artery catheter CCO device (Aortech, Bellshill, Scotland) enabling real-time update of cardiac output was compared with 2 different, less-invasive methods of CCO determination, esophageal Doppler and pulse contour analysis.**

Design: **Prospective, observational study.**

Setting: **University hospital, single institution.**

Participants: **Patients scheduled for elective coronary artery bypass grafting (CABG).**

Interventions: **None.**

Measurements and Main Results: **CCO measurements were analyzed using a Bland-Altman plot. Bias between CCO and pulse contour cardiac output (PCCO), and Doppler-derived cardiac output (UCCO) was (mean ± 1 SD) −0.71 ± 1 L/min versus −0.15 ± 1.09 L/min, and between UCCO and PCCO −0.58 ± 1.06 L/min. Bias was not significantly different among methods, nor were comparative values before and after cardiopulmonary bypass ($p > 0.05$).**

Conclusions: **Agreement between the CCO method and both less-invasive measurements was clinically acceptable. There were no adverse events associated with the use of either device.**

KEY WORDS: continuous cardiac output, esophageal Doppler, pulmonary artery catheter, pulse contour analysis

THE MEASUREMENT of cardiac output (CO) is a parameter often used to assess the hemodynamic status and efficacy of therapy in critically ill patients.[1] In past decades, intermittent bolus thermodilution cardiac output (ICO) with ice cold saline via a pulmonary artery catheter (PAC) was the gold standard for the calculation of cardiac output according to the Fick principle in the clinical setting.[2] Over the years, interest in continuous monitoring of cardiac output (CCO) increased because the assessment of changes in the hemodynamic status of patients over time can facilitate adequate therapy. As a result, among other devices, PACs with integrated heating filaments were developed. Intermittently, this filament heats the blood up to 4°C over baseline temperature and an attached computer calculates the resulting cardiac output.[3] However, the heating filament-based CCO measurements show a lack of agreement with ICO during rapid hemodynamic changes because of the time constant of the calculation algorithm.[3,4]

Recently, the value of PACs has been questioned. In a large study the PAC was found to increase mortality, hospital stay, and costs.[5] Ramsey et al[6] also found that PAC measurements had no impact on clinical decision making. Therefore, alternative measurement methods have been developed that are less invasive and/or allow the real-time calculation of CO.

A new PAC with an alternative calculation principle was compared with pulse contour analysis and ultrasound-based measurements for the continuous measurement of CO. In previous studies, good-to-excellent agreement of the methods under investigation was shown with the gold standard of pulmonary arterial bolus thermodilution.[7-25] Therefore, the authors did not use pulmonary arterial thermodilution as the reference for these measurements, but instead compared the continuous methods with each other in the setting of a cardiac surgical unit.

METHODS

After approval of the institutional review board committee and after written informed consent, 10 American Society of Anesthesiologists physical status IV patients with impaired left ventricular function (ejection fraction <50%) scheduled for elective cardiac surgery (coronary artery bypass grafting) were enrolled in the study. Patients with valvular heart disease, intracardiac shunts, or peripheral vascular disease, as well as emergency cases, were excluded. Only patients with sinus rhythm in the preoperative electrocardiogram were included.

Patients received 0.1 to 0.2 mg/kg of midazolam and 2 μg/kg of clonidine, orally, 30 minutes before the induction of anesthesia. After local anesthesia, a 5F introducer was inserted into the right femoral artery and a 4F thermodilution catheter (Pulsion Medical Systems, Munich, Germany) was placed and connected to the pressure transducer for continuous arterial pressure recording. Anesthesia was subsequently induced with propofol (2 mg/kg) and sufentanil (0.5 μg/kg). Tracheal intubation was facilitated with rocuronium (0.6 mg/kg) and the patient ventilated with an air/oxygen mixture (F_IO_2 0.5). Ventilation was adjusted to a $PetCO_2$ of 35 mmHg. A PAC (Aortech, Bellshill, Scotland) was inserted via an 8.5F introducer in the right internal jugular vein and advanced under continuous pressure recording into the wedge position. A monitor (Aortech, Bellshill, Scotland) was attached to the PAC and calibrated according to patient height and weight. This new system uses a thermistor in a small heating coil and measures the energy required to maintain the coil surface at 1°C differential above the blood temperature. This mechanism of action enables a beat-to-beat update of the CO for CCO measurement.

The arterial catheter was connected to a monitor for pulse contour analysis of CO (PCCO) (Pulsion Systems) and the resulting signal processed for determination of hemodynamic variables (left ventricular stroke volume and derived parameters). To calibrate the system for the individual vascular impedance, pulse contour analysis was performed

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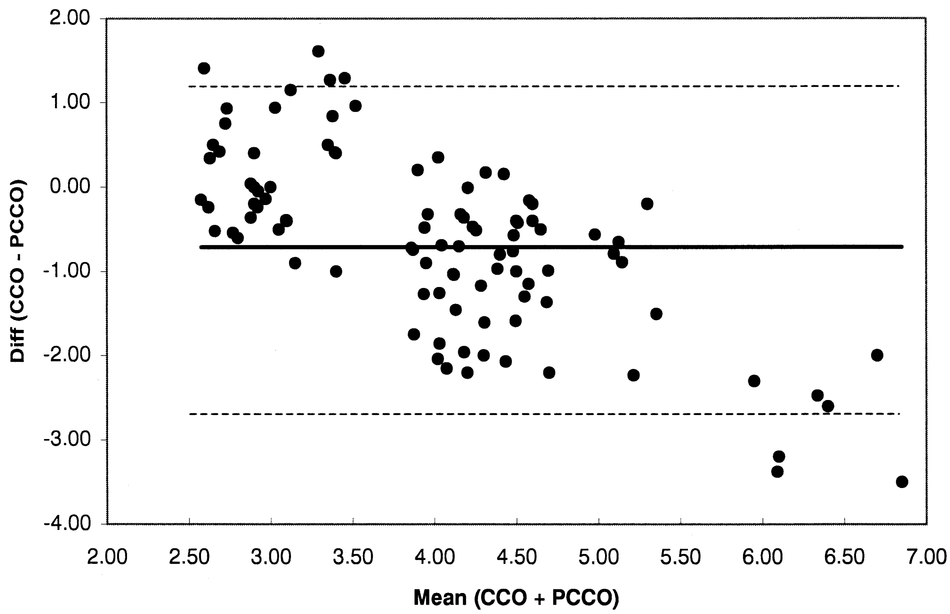

Fig 1. Bland-Altman plot between CCO and PCCO. The solid line represents the mean difference (bias); the dotted line represents the 2SD limits of agreement.

while simultaneously injecting 10 mL of ice cold saline in the proximal port of the PAC and registration of the resulting arterial thermodilution curve via the catheter in the femoral artery. The mean of three consecutive measurements randomly assigned to the respiratory cycle was used for calibration. The PCCO was not recalibrated during the surgical procedure.

An esophageal echo probe (Hemosonic, Arrows International, Everett, MA) was inserted nasally and advanced into the esophagus approximately up to the sixth thoracic vertebra for measurement of ultrasound Doppler cardiac outputs (UCCOs). Depth of probe insertion in each patient was chosen to obtain the best signal quality, and, therefore, the position may have varied in the individual patient. Two acoustic transducers are located at the tip of the flexible esophageal probe. The echo signal was adjusted to the maximum signal height and the probe positioned until both the anterior and the posterior wall of the aorta were visible on the screen. The echo probe was readjusted if necessary (loss of the aortic wall detected by M-mode ultrasound).

Before and after cardiopulmonary bypass (CPB), 6 measurements were performed. Timing of data acquisition was assigned to 12 different time points, which were defined as follows: (1) baseline after induction of anesthesia, (2) skin incision, (3) sternotomy, (4) start harvesting of the mammary graft, (5) end harvesting of the mammary graft, (6) before initiation of CPB, (7) directly after termination of CPB, (8) 15 minutes after termination of CPB, (9) start thoracic closure, (10) end of thoracic closure, (11) end of surgery, and (12) before discharge to the intensive care unit. These time points were at least 15 minutes apart and were chosen to achieve a high within-subject variability in cardiac output. CO was measured during stable hemodynamic conditions. All coronary artery bypass grafting operations were performed uniformly using a standard CPB technique (pump flow rate of 2.5 L/min/m^2), with mild hypothermia (rectal temperature 32-33°C).

Statistical analysis was performed according to the method of Bland and Altman.[7] Bias between methods was calculated as the mean difference (±SD) between CCO and PCCO, between CCO and UCCO, and between PCCO and UCCO. The limits of agreement were defined as bias ± 2 SD and as the range in which 95% of the differences between the methods were expected. Data points from each individual were averaged; resulting mean values were then compared for between-method differences with analysis of variance for repeated measures with Bonferroni correction. Bias before and after the cardiopulmonary bypass was analyzed with paired student *t* test. Statistical significance was assumed at a value of $p < 0.05$.

RESULTS

Ten patients (aged 56-78 years; 6 male, 4 female) were enrolled in the study. A total of 113 PCCO, 107 UCCO, and 113 CCO measurements were analyzed. CO measurements ranged from 1.89 to 8.6 L/min for PCCO, 1.5 to 8.2 L/min for UCCO, and 2.4 to 5.7 L/min for CCO.

The Bland-Altman plot for CCO and PCCO is shown in Figure 1, for UCCO and CCO in Figure 2, and for PCCO and UCCO in Figure 3. Bias between CCO and PCCO was −0.71 L/min (precision 1 L/min), between CCO and UCCO −0.15 L/min (precision 1.09 L/min), and between UCCO and PCCO −0.58 L/min (precision 1.06 L/min). Linear regression analysis of the CCO/PCCO and CCO/UCCO Bland-Altman plot yielded a negative slope representing an overestimation of low COs and an underestimation of high COs compared with PCCO and UCCO ($r^2 = 0.48$ and 0.27, respectively). Bias between methods showed no significant differences ($p > 0.05$, Fig 4). Comparing values before and after CPB, bias of UCCO, PCCO, and CCO measurements did not differ significantly ($p > 0.05$, Fig 5).

There were no adverse effects related to either the PCCO/PAC catheter or the echo probe.

DISCUSSION

Perioperative determination of cardiac output is of great interest in the critically ill. Since 1970, PAC thermodilution has become the clinical "gold standard" in the field of anesthesia and intensive care. However, right heart catheterization for CO monitoring has been questioned for various reasons. First, ICO shows remarkable variance and has proved to be no real reference method in comparison studies.[8,9] Second, until recently,

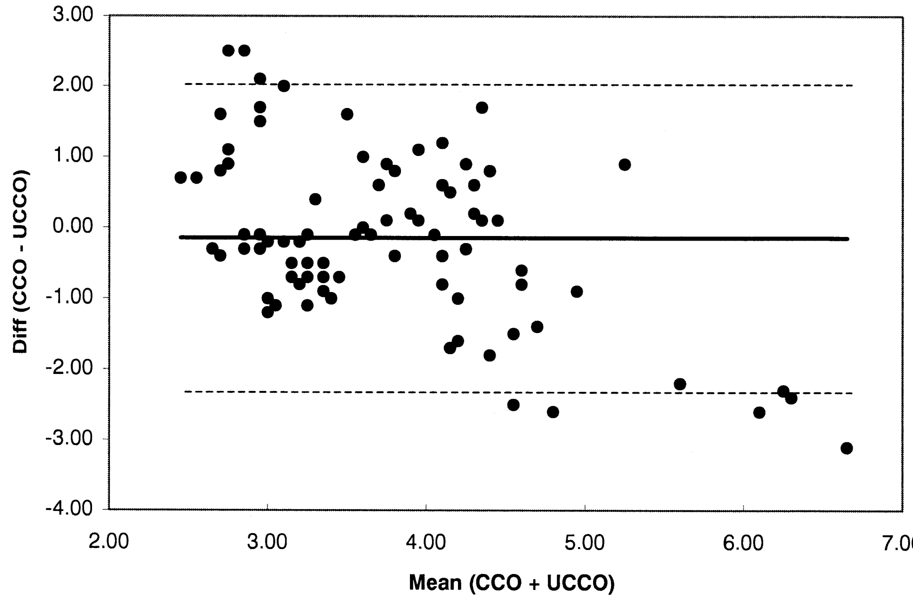

Fig 2. Bland-Altman plot between CCO and UCCO. The solid line represents the mean difference (bias); the dotted represents the 2SD limits of agreement.

there was no real CCO measurement by PA thermodilution. The PAC with integrated heating filament was able to perform semicontinuous determinations at best. The time constant of the measurement algorithm led to a delayed time response in cases of rapid hemodynamic changes.[3,4]

Unfortunately, there is no clear evidence in the literature for the need for CO determinations. Treating patients with the goal of augmenting CO has given inconsistent results with some authors reporting no improvement in survival rates and others finding reduced mortality and duration of hospital stay.[10,11] Reviewing the current literature, it seems that at least in a subset of patients, measurement of CO is still indicated for guiding adequate therapy.[12] Because invasiveness of right heart catheterization is under debate, alternative measurement methods were developed that are less invasive and/or allow the real-time calculation of CO. Impedance cardiography, partial CO_2 rebreathing, esophageal Doppler, and pulse contour analysis are newly developed or enhanced, each having specific drawbacks and advantages.

Recently, a new PAC was introduced into clinical practice. Bias was found to be acceptable under clinical conditions compared with pulse contour and Doppler-derived values, (-0.71 ± 1 L/min and -0.15 ± 1.09 L/min, respectively), in the present study.

Esophageal Doppler-derived CO measurements have given inconsistent results in the literature. Initial studies showed significant variability between Doppler-derived and thermodilution measurements, and the technique was found to be clin-

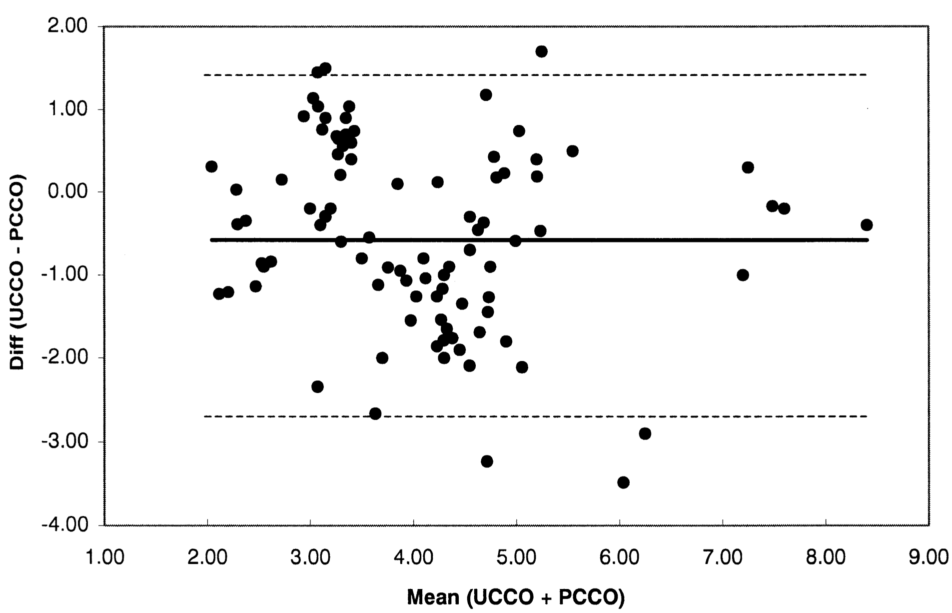

Fig 3. Bland-Altman plot between UCCO and PCCO. The solid line represents the mean difference (bias); the dotted line represents the 2SD limits of agreement.

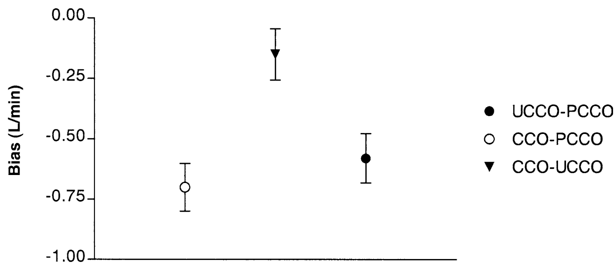

Fig 4. Bias between methods (mean ± standard error of the mean).

ically unacceptable because of operator dependency and the frequently necessary readjustment of the echo probe.[13,14] In this study, a newly developed echo probe (Hemosonic; Arrow International) was used, offering the advantage of determining the true aortic diameter by M-mode ultrasound, thus avoiding errors introduced by nomogram-derived calculations. Measurements performed with this device are in good agreement with PA thermodilution CO in preliminary investigations.[15] The authors confirmed good agreement of Doppler-derived measurements with both CCO and PCCO. However, readjustment of the echo probe was commonly necessary after CPB, although the same experienced investigator positioned the echo probe. The authors cannot completely exclude the influence of a learning curve on these results. Lefrant et al[16] found a remarkable training effect using the device in intensive care unit patients. The operator dependency remains a problem, particularly in the case of readjustment. The echo probe measures aortic blood flow, which is closely correlated with CO ($r = 0.89$).[17] This derived cardiac output was used in the study calculations to facilitate between-method comparisons. There are various other parameters derived from the aortic blood flow (eg, peak ejection velocity and left ventricular ejection time), which give additional information on left ventricular performance and may help to guide optimal therapy.

Pulse contour analysis has gained widespread attention recently. Arterial pulse pressure waveform analysis according to the method by Wesseling consists of measuring the area under the systolic portion of the arterial pulse wave from the end of diastole to the end of the ejection phase.[19] Numerous studies have shown good agreement with arterial and pulmonary arterial thermodilution.[20,21] Arterial cannulation is less invasive and has proven to have no severe complications during its use over a longer period of time.[18] Pulse contour enables a beat-to-beat update of the instantaneous CO. Transpulmonary thermodilution also gives important information concerning the patient's volume status and left ventricular loading conditions (eg, intrathoracic blood volume, extravascular lung water). Some authors postulated an influence of changes in systemic vascular resistance (eg, after vasopressor administration) on PCCO.[21,22] In contrast, Della Rocca et al[23] found no influence on the accuracy of PCCO even after substantial changes of SVR. The authors did not control for changes in the tone of the vascular bed because the PCCO device was not recalibrated during the study.

In conclusion, by comparing a new CCO PAC and an esophageal UCCO probe with PCCO for the continuous measurement of CO in cardiac surgical patients, a clinically acceptable agreement was found between methods. However, judgment of bias and precision is subjective and not yet standardized. Critchley[19] recommended that limits of agreement between methods should not exceed ± 30%. Zöllner et al[20] postulated limits of agreement of ± 0.5 L/min between methods and rejected the interchangeability of continuous and intermittent PA thermodilution using IntelliCath (Baxter, Irvine, CA) and Opti-Q (Abbott Laboratories, Morgan Hill, CA) catheters. In a recently published study comparing PCCO and ICO, however, the same authors found limits of agreement of ±2.5 L/min to be acceptable.[21] When reviewing recently published large studies comparing PCCO and ICO, bias varied between 0.003 and 0.31 L/min.[21-30] These studies, however, compared PCCO with ICO, whereas the present study compared CCO with PCCO. Della Rocca et al[23] reported a bias of −0.03 L/min with limits of agreement of −1.78 to 1.72 L/min comparing PCCO versus CCO. With CCO, measurements show a tendency of underestimation of CO compared with ICO, possibly because of the temperature shift in the PA after CPB.[29] This may explain the negative bias between CCO and both PCCO and UCCO because PCCO and UCCO measurements are not affected by temperature. Comparison of CCO and PCCO, as well as CCO and UCCO, in the present study showed a negative slope of the Bland-Altman plot. An overestimation of low CO was also shown for the bolus thermodilution technique, probably caused

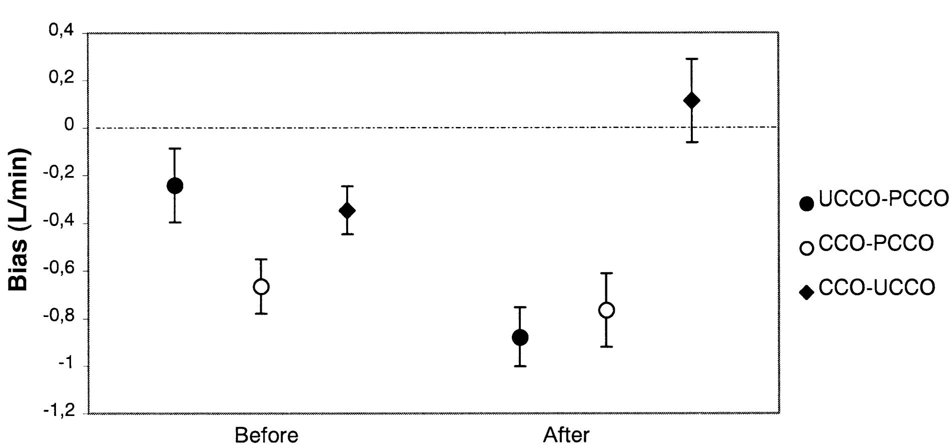

Fig 5. UCCO-PCCO, CCO-PCCO, and CCO-UCCO bias (± standard error of the mean) before and after cardiopulmonary bypass. Dotted line represents an ideal bias of zero.

by the cold saline bolus.[31] During continuous measurement with the heating coil technique, temperature shifts in the PA commonly seen after CPB may have caused this error. This systematic deviation of the new CCO catheter has to be verified in larger study populations.

Taking into account the recent discussion on the safety of PACs, several alternatives exist when CO needs to be monitored. The results of this study show that accuracy of CO measurements is clinically acceptable for all methods. Therefore, it seems unjustified to perform right-heart catheterization simply for the determination of cardiac output. The less-invasive esophageal probe and the PCCO system offer specific additional information concerning important parameters of the cardiovascular system. Hence, the choice of the equipment for CO measurement should be made according to individual patient needs.

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