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Comparing Cardiac Output Measurements Using a Wearable, Wireless, Noninvasive Photoplethysmography-Based Device to Pulse Contour Cardiac Output in the General ICU: A Brief Report

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OBJECTIVES: Cardiac output (CO) measurements in the ICU are usually based on invasive techniques, which are technically complex and associated with clinical complications. This study aimed to compare CO measurements obtained from a noninvasive photoplethysmography-based device to a pulse contour cardiac output device in ICU patients.

DESIGN: Observational, prospective, comparative clinical trial.

SETTING: Single-center general ICU.

PATIENTS: Patients admitted to the general ICU monitored using a pulse contour cardiac output device as per the decision of the attending physician.

INTERVENTIONS: Parallel monitoring of CO using a photoplethysmography-based chest patch device and pulse contour cardiac output while the medical team was blinded to the values obtained by the noninvasive device.

MEASUREMENTS AND MAIN RESULTS: Seven patients (69 measurements) were included in the final analysis. Mean CO were 7.3±2.0 L/m and 7.0±1.5 L/m for thermodilution and photoplethysmography, respectively. Bland-Altman showed that the photoplethysmography has a bias of 0.3 L/m with −1.6 and 2.2 L/m 95% limit of agreement (LOA) and a bias of 2.4% with 95% LOA between −25.7% and 30.5% when calculating the percentage of difference from thermodilution. The values obtained by thermodilution and photoplethysmography were highly correlated ($r = 0.906$).

CONCLUSIONS: The tested chest patch device offers a high accuracy for CO compared to data obtained by the pulse contour cardiac output and the thermodilution method in ICU patients. Such devices could offer advanced monitoring capabilities in a variety of clinical settings, without the complications of invasive devices.

KEY WORDS: cardiac output; cardiovascular; intensive care; noninvasive monitoring; pulse contour cardiac output; remote patient monitoring

The ability to accurately measure vital signs is important for patient assessment (1). Invasive arterial and pulmonary artery occlusion pressure monitoring, considered the gold standard of hemodynamic monitoring, may be required in ICU patients, providing important indications and early recognition of patient deterioration, yet they are associated with inherent risks (1, 2).

In this report, we focus on cardiac output (CO) measurements, comparing a noninvasive photoplethysmography-based chest patch wearable monitor (BB-613P; Biobeat Technologies, Petah Tikva, Israel) to pulse contour cardiac output (PiCCO), including both its thermodilution- and pulse contour analysis-based measurements, in hemodynamically unstable ICU patients.

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MATERIALS AND METHODS

Ethical Considerations

This prospective, comparative clinical trial was approved by the Institutional Review Board of the Assaf Harofeh Medical Center, Zerifin, Israel (0184-19-ASF; NCT04215627). All participants or their family members signed an informed consent form.

Patients

ICU patients with PiCCO were recruited for the study. All patients were hemodynamically unstable and on a noradrenaline dose of at least 0.2 mcg/kg/min. Monitoring started immediately upon signing an informed consent form. The research team received coded numbers of the devices only, without any personally identifiable information.

Study Protocol

In all subjects, a PiCCO device (PULSION Medical Systems AG, Munich, Germany) was inserted as part of the ICU monitoring as defined by the attending physicians, allowing spot measurements of CO. Monitoring was conducted in parallel using the invasive and noninvasive monitoring devices. The medical team was blinded in real-time to the values obtained by the noninvasive devices, with medical decisions and treatment provided based on the accepted invasive devices only. The comparison was performed retrospectively after completion of the measurement phase. Calibration of the PiCCO was performed following the manufacturers' instructions for use throughout the study period.

The PiCCO Device

The PiCCO technology is based on transpulmonary thermodilution and pulse contour analysis, both allowing to calculate of hemodynamic parameters (**Fig. 1**). When using the transpulmonary thermodilution measurement, a defined bolus of a cold solution is injected via a central venous catheter. When the cold bolus passes through the right heart, the lungs, and the left heart, it is detected by the PiCCO Catheter, placed either in the femoral or the axillary arteries. This procedure is repeated three times in under 10 minutes to ensure the average used to calibrate the device and to calculate the thermodilution parameters is accurate. The thermodilution parameters should be evaluated whenever there is a substantial change in the patients' condition or therapy, and it is recommended to recalibrate at least three times per day. The transpulmonary thermodilution is used to calibrate the pulse contour parameters, and from that moment on the pulse contour analysis provides continuous information, while transpulmonary thermodilution provides static measurements.

The PiCCO technique has several limitations. It requires intra-arterial and central venous access, pulmonary artery pressures cannot be measured, and the pulse contour analysis is unreliable in patients with arrhythmia, mechanical circulatory assist devices, aortic valve pathology, and possibly dependent on arterial line site (3).

The Photoplethysmography-Based Wearable Device

Photoplethysmography is a noninvasive optical technique used to detect volumetric changes in blood at the surface of the skin, employing several wavelengths. Since the light is more absorbed by blood than the surrounding tissues, the changes in blood flow can be detected as changes in the intensity of light. The volumetric changes of the signal in arterial blood are associated with cardiac activity.

The photoplethysmography-based chest patch monitor device (Fig. 1, sections 1–4) was previously described (4). Shortly, it includes a reflective photoplethysmography sensor providing multiple vital signs using the pulse wave transit time approach combined with pulse wave analysis. Monitoring starts following a single trimonthly offset baseline calibration process. Calibration could be performed using either a cuff-based device or an arterial line, depending on the specific monitor used on the patient. In this case, the average of the first three blood pressure (BP) measurements obtained by an arterial line was considered as a baseline calibration measurement for the photoplethysmography-based devices. After obtaining the calibration value, it was entered into a web application, and from this moment onwards, the study continued with parallel measurements. The vital signs collected by the wearable monitor include blood oxygen saturation (Spo_2), respiratory rate, pulse rate (PR), cuff-less noninvasive BP, stroke volume, CO, cardiac index, systemic vascular resistance, temperature, and more. There was no need for further calibration of the

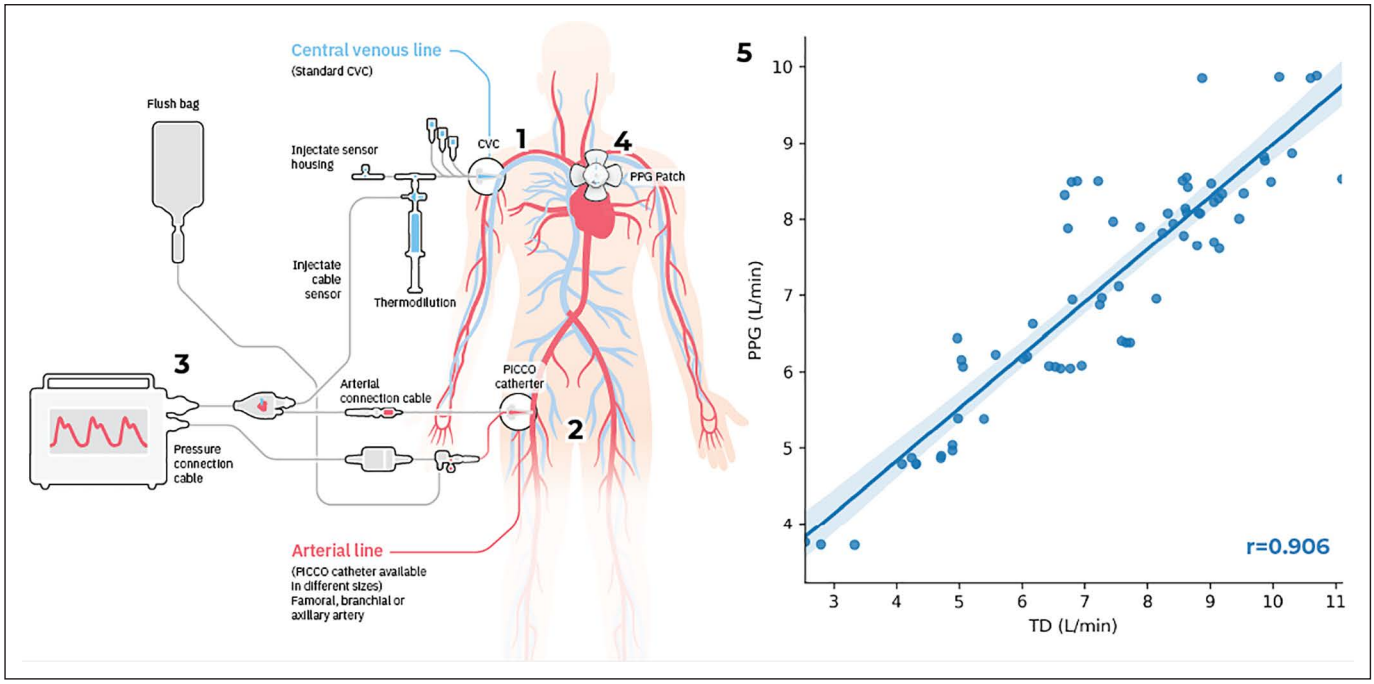

Figure 1. The photoplethysmogram (PPG)-based device and the pulse contour cardiac output (PiCCO) device. 1) Central venous catheter (CVC) with the thermodilution (TD) solution; 2) arterial line connected to the PiCCO catheter; 3) the PiCCO pulse contour analysis device; 4) the PPG-based chest patch device; 5) Pearson's correlation analysis between TD and the PPG-based device measurements.

photoplethysmography-based devices following the initial baseline measurements. Designated gateways were deployed and installed in the ICU to ensure continuous monitoring, data transmission, and automatic data collection of all measurements. The device has Food and Drug Administration clearance for BP, PR, and Spo_2.

Statistical Analysis

Bland-Altman was used to compare the two methods (PiCCO and photoplethysmography) and thermodilution for CO measurements. Bias and 95% limit of the agreement were calculated for each comparison. Pearson's correlation was used to assess the relation between thermodilution and the photoplethysmography measurements of CO.

RESULTS

Seven patients were recruited and included in the final analysis. All received positive pressure ventilation at the time measurements were taken. Demographic data are provided in **Table 1**. Sixty-nine measurements were obtained from the three methods (thermodilution, PiCCO, and photoplethysmography). The mean values were 7.3 ± 2.0 L/m and 7.0 ± 1.5 L/m for thermodilution and photoplethysmography, respectively. When using the mean of three sequential measurements using the photoplethysmography-based sensor, the values were 7.1 ± 1.5, which was not different from the measurements obtained by the thermodilution. The Bland-Altman analysis showed that the photoplethysmography has a bias of 0.3 L/m with –1.6 and 2.2 L/m 95% limit of agreement (LOA) and a bias of 2.4% with 95% LOA between –25.7% and 30.5% when calculating the percentage of difference (**Supplementary Fig. 1**, http://links.lww.com/CCX/A904). The bias was even smaller when using the mean of three sequential measurements by the photoplethysmography-based device (bias: 0.2 L/m, 95% LOA: –1.6 to 1.9 L/m; bias: 0.7%, 95% LOA: –25.4% to 26.8%) (**Supplementary Fig. 2**, http://links.lww.com/CCX/A904). Measurements obtained by the PiCCO are discussed in the **Supplemental File** (http://links.lww.com/CCX/A904) and **Supplementary Figure 3** (http://links.lww.com/CCX/A904). The values obtained by thermodilution and photoplethysmography were highly correlated (r = 0.906) (Fig. 1, section 5).

DISCUSSION

Invasive cardiopulmonary monitoring devices are prone to complications and are inconvenient (5). Thus, advanced

TABLE 1.
Demographic Details of the Patients

No.	Age	Gender	Body Mass Index	Skin Color	Acute Physiology and Chronic Health Evaluation Score/Mean Airway Pressure/ Volume Status	Diagnoses	Medical History
1	97	Male	24	4	12/9/25,900	Incarcerated hernia, resection of small bowel	Congestive heart failure, atrial fibrillation, dyslipidemia
2	53	Female	24	2	16/11/15,600	Whipple, hemorrhagic shock	Obesity, suspected carcinoma of the pancreas
3	68	Female	31	1	16/13/1,485	Hemorrhagic shock, ureteral perforation, postoperative ventral hernia repair	Ulcerative colitis, dyslipidemia, status post colectomy
4	67	Female	35	2	21/13/9,130	Peritonitis, diabetic ketoacidosis	Type 2 diabetes mellitus, status post hemicolectomy
5	83	Female	39	2	34/8/5,300	Ischemic colitis, septic shock	Aortic stenosis, ischemic heart disease, congestive heart failure, hypertension, dyslipidemia
6	84	Male	28	3	13/not applicable/ 4,500	Pancreatitis, shock	Heart failure, atrial fibrillation, ischemic heart disease, hypertension, dyslipidemia, status post hemicolectomy
7	60	Female	38	4	17/13/4,250	Incarcerated hernia, septic shock	Obesity, type 2 diabetes mellitus, hypertension, dyslipidemia

Body mass index (BMI): Overweight defined as $25 \leq \text{BMI} < 30$, and obese defined as $30 \leq \text{BMI}$. Skin color based on the Fitzpatrick types: type 1—always burns, never tans, palest, can have freckles; type 2—usually burns, tans minimally, light-colored but darker than fair; type 3—sometimes mild burn, tans uniformly, golden honey or olive; type 4—burns minimally, always tans well, moderate brown; type 5—very rarely burns, tans very easily, dark brown; and type 6—never burns, deeply pigmented dark brown to darkest brown.
All patients were ventilated with positive pressure ventilation. Volume status was assessed at admission. Not applicable, the patient was not ventilated at admission.

hemodynamic monitoring by noninvasive means might enable thoughtful diagnosis and treatment of unstable patients while minimizing morbidity and mortality.

In this study, we have shown that the photoplethysmography-based device provides accurate and valid readings with marginal bias and narrow LOAs for CO when compared with thermodilution obtained from the invasive PiCCO, which is considered the gold standard for CO measurement. Since the photoplethysmography-based device provides frequent measurements, we have provided both a single measurement comparison and a comparison between the thermodilution measurements to an average of three photoplethysmography-based measurements, showing even a higher agreement.

CO is regarded as one of the most challenging hemodynamic parameters to assess accurately using noninvasive methods, especially in unstable patients. The accuracy and reliability of minimal or noninvasive CO measurement methods have been inconsistent and unsatisfactory for clinical use so far (6, 7). Despite several commercial and academic efforts, none have gained widespread acceptance or use due to cumbersome execution and inconsistent validation data (6, 7). While the clinically acceptable percentage error (i.e., LOA as a proportion of mean CO) for CO monitors is as high as 30% (8, 9), most devices have an error of ~40% (6, 7). We have previously shown that the percentage error of the photoplethysmography-based device was as low as 25%, with a small bias and relatively narrow LOA

compared with a pulmonary artery flotation catheter in a swine study (4). In this short report, when comparing the photoplethysmography-based device with PiCCO in ICU patients, we found a high correlation rate and the Bland-Altman analysis adds more to the level of accuracy of the photoplethysmography-based device. Furthermore, the photoplethysmography-based device had a percentage error of less than 30%. We also show that the device provides accurate and precise measurements in patients with various BMI values and skin color.

There are several other noninvasive CO monitors, such as a carotid Doppler patch able to capture and provide accurate trends of blood flow velocity (10). Nevertheless, there is a recent clinical trend to move away from CO monitors and embrace repeated, focused, bedside echocardiogram providing comprehensive cardiovascular assessments, with accurate and precise CO measurements when compared with invasive catheters. We assume that with more experience gained when using wearable monitoring devices, it will help clinicians decide on the better approach for their patients.

When generally looking at patients within the ICU, a noninvasive, wireless device that automatically and frequently collects advanced hemodynamic measurements would simplify and potentially improve care. This is true also for other in-hospital or out-of-hospital patients, which are usually not being monitored. The small sample size is a limitation of this study. A larger study with more patients and in different settings, across multiple clinical sites with various patient-related factors, will help to establish its relevance and see whether it improves diagnosis, treatment, and outcomes.

CONCLUSIONS

We conclude that the photoplethysmography-based device provides comparable CO measurements to the invasive PiCCO and could be used without the complications seen with invasive methods.

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