

# Comparison of non-invasive cardiac output measurement and pulse-indicated continuous cardiac output monitoring for determining hemodynamic parameters in patients with critical septic shock: a prospective study

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## Research Article

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# Abstract

**Objective** To compare non-invasive cardiac output measurement (NICOM) and pulse-indicated continuous cardiac output (PiCCO) monitoring for determining hemodynamic parameters in patients with critical septic shock and to analyze the correlation between the two techniques. **Methods** Patients with critical septic shock admitted to the Department of Critical Care Medicine at Peking Union Medical College Hospital from April to December 2015 who required hemodynamic monitoring were enrolled prospectively. Cardiac output (CO) and stroke volume variation (SVV) were measured by NICOM and PiCCO in all patients and compared by Spearman's correlation and Bland–Altman analyses. Trial registration: ChiCTR-OOB-17014129. Registered 24 September 2017. retrospectively registered. **Results** Thirty-one patients were included in the study (19 males and 12 females, mean age  $\pm$  standard deviation,  $55.5 \pm 18.1$  years), with a mean Acute Physiology and Chronic Health Evaluation II (APACHE II) score of  $22.7 \pm 6.1$ . There was no significant difference in CO measured by the NICOM and PiCCO methods ( $5.10 [4.35, 6.50]$  L/min vs.  $4.89 [4.34, 6.23]$  L/min;  $P > 0.05$ ). However, SVV measured by NICOM was significantly higher than that measured by PiCCO ( $13.00 [11.00, 16.00]$  vs.  $12.00 [9.00, 15.00]$ ;  $P = 0.009$ ). CO and SVV determined by NICOM and PiCCO were significantly correlated according to Spearman's correlation analysis (CO:  $R = 0.904$ ,  $P < 0.001$ , 95% confidence interval  $0.932-1.135$ ; SVV:  $R = 0.841$ ,  $P < 0.001$ , 95% confidence interval  $0.601-0.786$ ). Bland–Altman analysis revealed a bias in mean CO of  $0.21$  L/min ( $P = 0.0032$ ) and limits of agreement of  $-1.12$  to  $1.54$  L/min; and a bias in mean SVV of  $1.56$  ( $P < 0.0001$ ) and limits of agreement of  $-2.56$  to  $5.68$ . **Conclusions** Hemodynamic parameters monitored by NICOM and PiCCO differed in patients with critical septic shock, but the correlation between the two methods was good. Use of non-invasive NICOM may therefore help to reduce complications associated with invasive procedures. **Keywords:** Septic shock; Non-invasive cardiac output measurement; Cardiac output; stroke volume variation

## Background

Severe infection and septic shock are the major causes of death in critically ill patients. Monitoring the hemodynamics and guiding treatment are crucial measures for improving the prognosis of these patients[1, 2]. Cardiac output (CO) is an index reflecting cardiac function in the clinic, and its continuous measurement and corresponding treatment adjustment are important measures in the treatment of severely ill patients. The variation in stroke output volume (SVV) reflects the volume responsiveness of patients, and monitoring this index is also necessary to improve patient mortality[3]. Pulse-indicated continuous cardiac output monitoring (PiCCO) provides continuous CO monitoring and volume responsiveness data by monitoring SVV, and has been widely used in clinical settings[4, 5]. However, PiCCO requires invasive arteriovenous catheterization and is associated with certain clinical complications. According to Belda[6], 86.4% of 544 PiCCO catheters obtained arterial access in the first attempt, 3.3% exuded after insertion, 3.5% exuded after extraction, 4.5% inserted catheter, and 1.2% removed catheter . Local hematoma occurred , while site inflammation occurred in 2% of patients,

catheter-related infection in 0.78%, ischemia in 0.4%, disappearance of pulse in 0.4%, and femoral artery thrombosis in 0.2%.

However, novel, non-invasive hemodynamic monitoring technologies have developed rapidly in recent years, and non-invasive cardiac output monitoring (NICOM) based on bioelectrical impedance has attracted increasing attention[7, 8].

The current study aimed to compare the accuracies of NICOM and PiCCO for monitoring CO and SVV in patients with septic shock, and to determine the correlation between the two techniques. The results support the use of NICOM for non-invasive hemodynamic monitoring, to reduce the risk of invasive procedures in patients with septic shock.

## Patients And Methods

### Patients

We conducted a prospective, observational, self-controlled study to select patients with infectious shock who received hemodynamic monitoring from April 2015 to December 2015 in the Department of Critical Medicine, Peking Union Medical College Hospital. The inclusion criteria were patients  $\geq 18$  years old with septic shock according to the International Guidelines for Serious Infectious and Septic Shock 2012 [9], who required hemodynamic monitoring. Patients aged  $< 18$  years, or with contraindications for central venous and arterial catheter placement, arrhythmia or abnormal cardiac anatomy, or any other factors that might affect the monitoring and evaluation of the related indicators were excluded.

### Hemodynamic monitoring

All patients received an intra-cervical or subclavian venous catheter connected to a pressure-measuring device, which was in turn connected to a monitor (Philips, the Netherlands). A 4F arterial catheter was placed in the femoral artery (Pulsion Medical Systems, Germany). Hemodynamics were monitored by PiCCO using the thermal dilution method and by NICOM immediately (0 h) and at 24 and 48 h. All measurements were made and recorded by the same investigator.

PiCCO monitoring: Using the thermal dilution method, 15 mL ice-cold normal saline was injected through the central venous catheter. CO and SVV values were measured three times continuously and the mean values were calculated and recorded.

NICOM measurement: Measurements were made using the NICOM monitoring system (Cheetah, USA) with the patient in the decubitus position. Four electrodes were attached to the patient's chest, abdomen, or back, symmetrical upper and lower, around the heart, and connected to the instrument. Data were acquired three times at 5 minute intervals, and the average values were calculated.

### Statistical methods

The data were analyzed using SPSS 20 (SPSS Inc., Chicago, USA) and Medcalc software (MedCalc Software, Ostend,Belgium). Normally distributed variables were expressed as mean  $\pm$  standard deviation and non-normally distributed variables as median (25th, 75th percentile). The results for the two measurement systems were compared by paired *t*-tests. The correlation between the methods was analyzed by Spearman's correlation, and the consistency was evaluated by Bland–Altman analysis. A value of *P* < 0.05 was considered significant.

## Results

### Patient characteristics

A total of 31 patients with septic shock were included in the study. There were 19 males and 12 females, aged 19–84 years (mean age 55.5  $\pm$  18.1 years). The median of body mass index was 21.3 (20.9, 21.4) and the mean Acute Physiology and Chronic Health Score II (APACHE II) score was 22.7 ( $\pm$  6.1). In terms of the type of infection, 19 patients had pneumonia, 11 had abdominal infection, and one had a bloodstream infection. Eleven patients had a previous history of cardiovascular disease, 12 had chronic obstructive pulmonary disease, and eight had chronic renal insufficiency. All 31 patients required continuous ventilator-assisted ventilation. Twenty-five patients received norepinephrine (median 0.5 (0.2, 0.8))  $\mu$ g/kg/min to maintain blood pressure, and 12 patients needed continuous renal replacement therapy.

### Comparison of hemodynamic parameters measured by two methods

A total of 93 hemodynamic monitoring data values were obtained in 31 patients. The median of CO values measured by PiCCO and NICOM were 4.89 (4.34, 6.23) L/min and 5.10 (4.35, 6.50), respectively, with no significant difference between the two groups. However, the SVV measured by NICOM (13.00 [11.00, 16.00]) was significantly higher than that measured by PiCCO (12.00 [9.00, 15.00]) (*P* = 0.009) (Table 1).

Table 1 Hemodynamic parameters in patients with septic shock monitored by different methods

Monitoring method	Number of cases	Sample number	Monitoring index(median (Q1,Q3))	
			CO(L/min)	SVV
PiCCO	31	93	4.89(4.34, 6.23)	12.00(9.00, 15.00)
NICOM	31	93	5.10(4.35, 6.50) <sup>a</sup>	13.00(11.00, 16.00) <sup>b</sup>

Abbreviations: PiCCO, pulse-indicated continuous cardiac output monitoring; NICOM, bioelectrical impedance non-invasive cardiac output monitoring; CO, cardiac output; SVV, stroke output variation rate. *aP* > 0.05, *bP* < 0.01

Regarding CO, there was a significant positive correlation between CO measured by PiCCO and NICOM (Spearman's correlation coefficient = 0.904;  $P < 0.001$ ; 95% confidence interval [CI] 0.932, 1.135) (Figure 1). Bland–Altman analysis showed high consistency of CO between PiCCO and NICOM, except in three cases, with a mean deviation of 0.21 ( $\pm 0.68$ ; 95% CI  $-1.12$  to  $1.54$ ;  $P < 0.001$ ) (Figure 2). The coefficient of variation of repeated measurements was 9.13%.

In terms of SVV, there was a significant positive correlation between SVV measured by PiCCO and NICOM (Spearman's correlation coefficient = 0.841;  $P < 0.001$ ; 95% confidence interval [CI] 0.601, 0.786) (Figure 3). Bland–Altman analysis showed high consistency of SVV between PiCCO and NICOM, except in three cases, with a mean deviation of 0.56 ( $\pm 2.1$ ; 95% CI  $-2.56$  to  $5.68$ ;  $P < 0.001$ ) (Figure 4). The coefficient of variation of repeated measurements was 14.71%.

## Discussion

Active fluid resuscitation is an important aspect of hemodynamic therapy in patients with septic shock. If tissue perfusion remains unsatisfactory, CO output needs to be measured and additional interventions implemented to improve it[2]. Commonly used methods for monitoring hemodynamics, including pulmonary artery catheterization and PiCCO, are accurate but require invasive procedures. Furthermore, catheter placement requires the cooperation of nurses, representing an aseptic barrier[10]. In addition, the measurement of CO is complex, requiring the preparation of ice saline, which is then placed in saline at 0°C and used for rapid injection. To ensure the accuracy of the results, each procedure requires nurses to prepare and care for the patient. The daily care and maintenance routine involves checking the central venous and PiCCO arterial catheters at least once a day, and replacing catheter dressings every 5–7 days[10] to prevent catheter thrombosis and infection. Nursing of patients with central venous catheters is particularly important and strict aseptic procedures are required to prevent catheter infection. The catheters required by PiCCO may also cause patient discomfort. The use of non-invasive hemodynamic monitoring methods has gradually increased in recent years, including methods utilizing ultrasound and bioelectrical impedance, such as NICOM[11]. The current study found a significant correlation between NICOM and PiCCO measurements of CO and SVV in patients with septic shock, and conformity analysis also showed that the two measurements were highly consistent. These observations suggest that non-invasive hemodynamic monitoring could replace invasive monitoring to a certain extent.

The human chest is a conductive cylinder, and the change in blood flow in the chest cavity when the heart pumps blood is the main factor affecting conductivity. When a fixed frequency of alternating current passes through the thorax, the impedance is proportional to the voltage at both ends of the thorax, causing a displacement between the released current and the induced voltage. Cardiac pulsation can cause changes in the voltage at both ends of the thorax, as well as changes in the displacement between the released current and the induced voltage. Bioreactance methods can then be used to measure the displacement between the current and voltage curves to measure the output of each stroke and other hemodynamic parameters. The NICOM system designed by Keren and others[7] based on this principle has demonstrated high accuracy for measuring stroke volume and CO.

CO data for 110 patients were measured by NICOM and pulmonary artery catheter thermodilution methods, respectively, with a sensitivity and specificity of NICOM of 93% and patient acceptability of 85% [12]. Raval et al. further confirmed a good correlation between bioimpedance and CO measured by pulmonary artery catheterization ( $r = 0.78$ ,  $P < 0.0001$ )[8]. A pulmonary artery floating catheter is an invasive hemodynamic monitoring technique, which has been replaced in the clinic by PiCCO because of its complex placement technique and short indwelling time. Hemodynamic monitoring during lung recruitment in patients with acute respiratory distress syndrome revealed that NICOM and PiCCO were comparable in terms of CO measurements, and that the changes in CO were also accurate[13].

Fluid management is difficult in patients with septic shock, and early fluid therapy can increase effective blood volume, and improve CO and tissue perfusion. However, hemodynamic monitoring through PiCCO to adjust volume load and improve tissue perfusion requires invasive arteriovenous operations, with risks of catheter infection, bleeding, thrombosis, catheter displacement, and other factors that can affect patient prognosis. Although one previous study showed that a passive leg-lift test combined with NICOM could effectively judge the volume responsiveness in sepsis patients[14], another group suggested that this result was not credible[13]. Both NICOM and PiCCO can continuously monitor SVV. We previously found that cardiac function was inhibited in patients with septic shock who received mechanical ventilation, even if vasoactive drugs were used. However, SVV measured by PiCCO can still be used as an indicator of volume responsiveness in patients with septic shock[3]. In the current study, SVV measured by the two methods was highly consistent, suggesting that SVV measurements obtained by non-invasive NICOM can be used as an indicator of responsiveness for capacity management in patients with infectious shock.

This study had some limitations. It was a single-center study with a small number of cases. Furthermore, although the consistency of SVV was compared, no infusion liquid was used to verify the volume reactivity. The results showed that the SVV value measured by NICOM was larger than that measured by PiCCO, and the threshold values of the two methods may thus differ when using SVV value to judge the volume reactivity. In addition, some PiCCO monitoring data cannot be measured by NICOM, and PiCCO therefore cannot be completely replaced by NICOM.

## Conclusions

NICOM is a non-invasive and continuous hemodynamic monitoring technique that can quickly and accurately measure hemodynamic parameters such as CO and SVV, producing results that are highly consistent with those obtained by invasive PiCCO monitoring. Non-invasive hemodynamic monitoring with NICOM may thus significantly reduce invasive arteriovenous puncture in patients with septic shock and help to reduce invasive operation-related complications, with potentially high value and good prospects for the treatment of patients with septic shock.

## Abbreviations

NICOM: non-invasive cardiac output measurement, PiCCO: pulse-indicated continuous cardiac output, CO: Cardiac output, SVV: stroke volume variation, APACHE II: Acute Physiology and Chronic Health Evaluation II

## Declarations

### Ethics approval and consent to participate

The study conformed to medical ethics standards and was approved by the Medical Ethics Committee of Peking Union Medical College Hospital. Informed consent was obtained from the patients' family members. Patients received verbal and written information about the study and provided written consent to participate. For patients with reduced cognitive function (e.g. because of sedation), their contact person gave consent. All data were kept confidential and processed anonymously.

### Consent for publication

Not applicable

### Availability of data and material

The details including all figures and raw data used to support the findings of this study are available from the corresponding author upon request.

### Competing interests

All authors declare that they have no conflicts of interest.

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## Figures



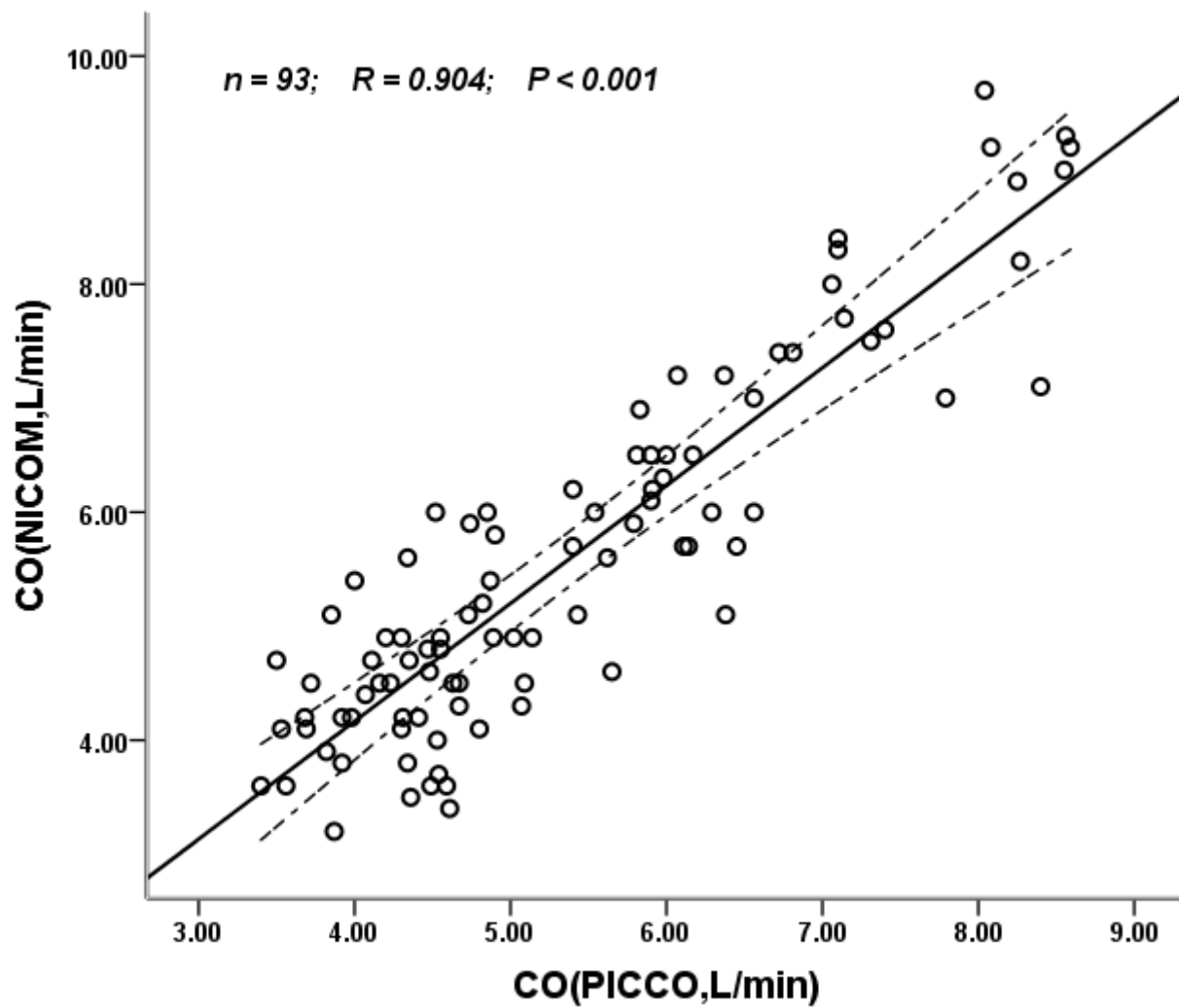


Figure 1

Correlation between cardiac output (CO) determined by PiCCO and NICOM in patients

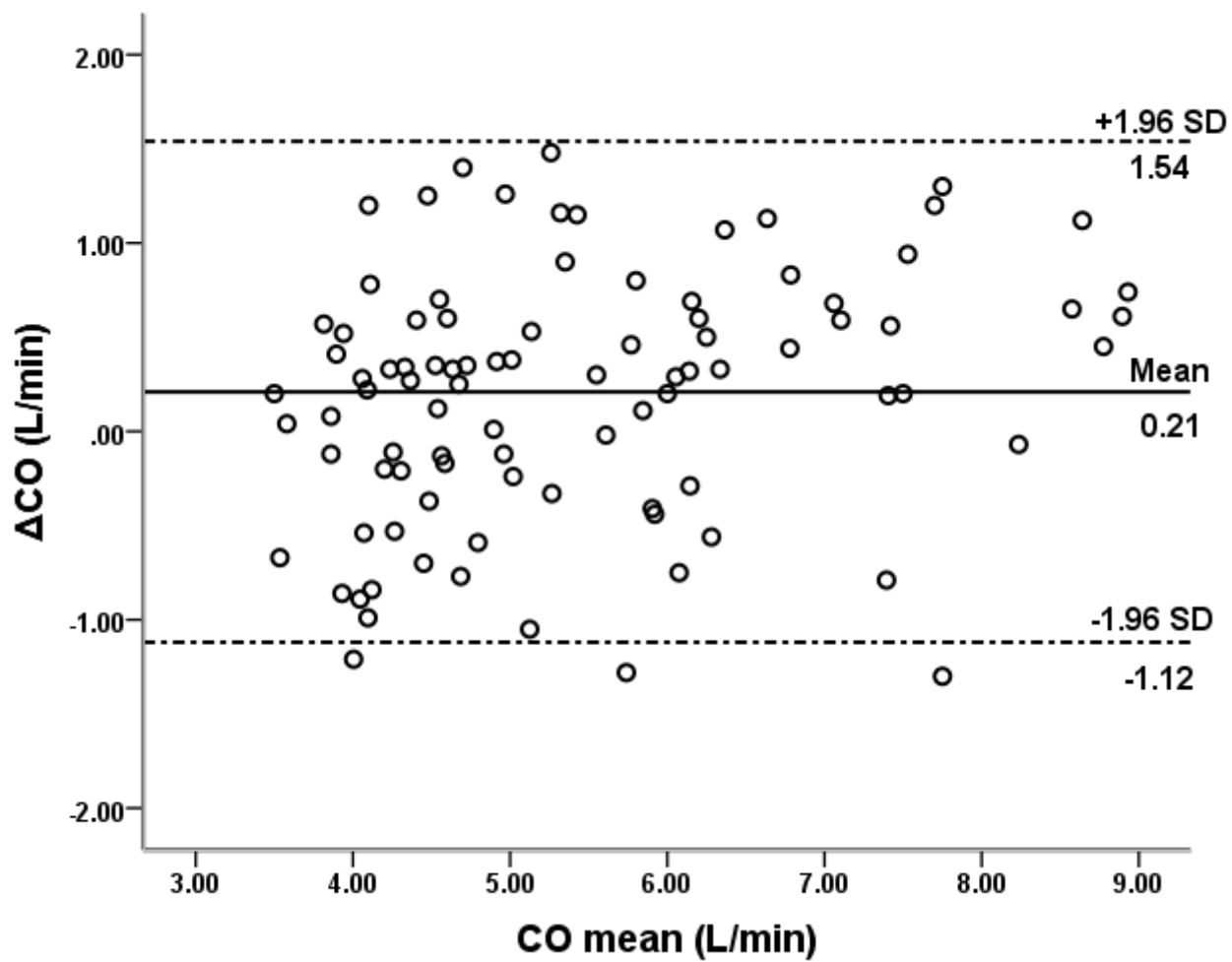


Figure 2

Bland–Altman analysis of PiCCO and NICOM for determining consistency of cardiac output (CO) in patients with septic shock

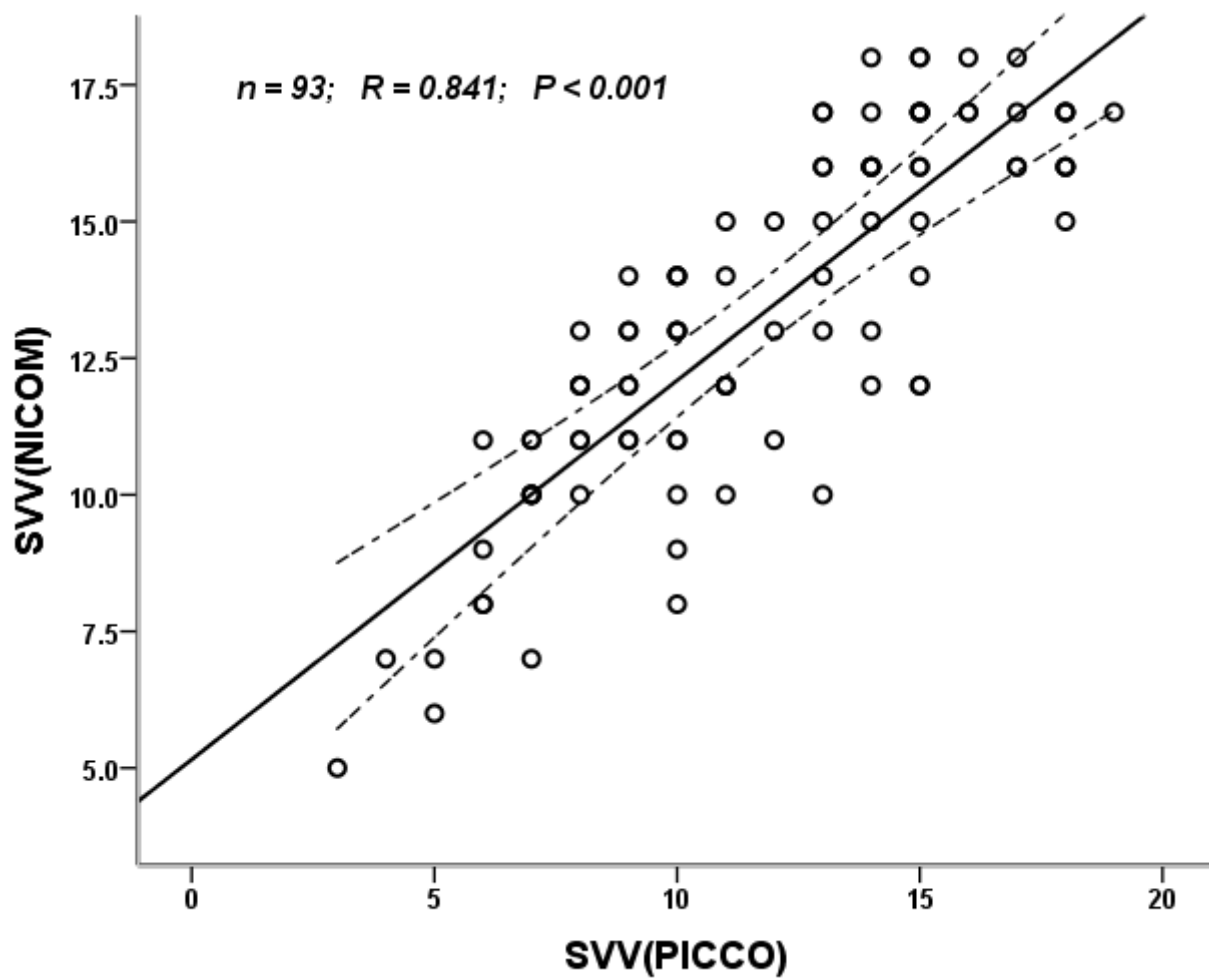
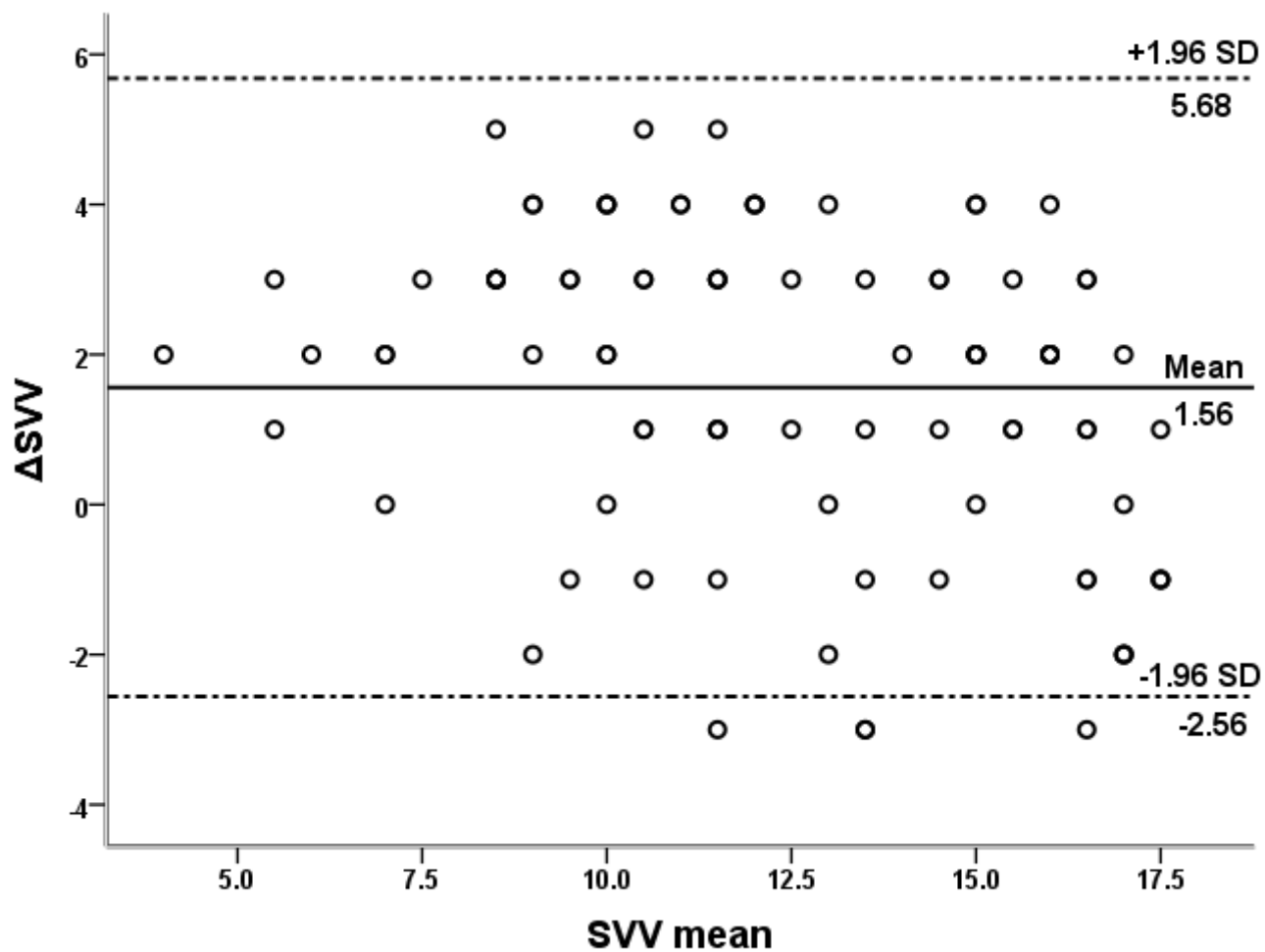


Figure 3

Correlation between stroke volume variability (SVV) determined by PiCCO and NICOM in patients with septic shock



**Figure 4**

Bland–Altman analysis of consistency between PiCCO and NICOM for measuring stroke volume variability (SVV) in patients with septic shock