



# A comparison of invasive arterial blood pressure measurement with oscillometric non-invasive blood pressure measurement in patients with sepsis

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## Abstract

**Purpose** This study aimed to compare non-invasive oscillometric blood pressure (NIBP) measurement with invasive arterial blood pressure (IBP) measurement in patients with sepsis.

**Methods** We conducted a retrospective study to evaluate the agreement between IBP and NIBP using the Medical Information Mart for Intensive Care IV (MIMIC-IV) database. Paired blood pressure measurements of mean arterial pressure (MAP), systolic blood pressure (SBP), and diastolic blood pressure (DBP) were compared using Bland–Altman analysis and paired Student’s *t* test. We also focus on the effect of norepinephrine (NE) on the agreement between the two methods and the association between blood pressure and mortality during intensive care unit (ICU) stay.

**Results** A total of 96,673 paired blood pressure measurements from 6060 unique patients were analyzed in the study. In Bland–Altman analysis, the bias ( $\pm$ SD, 95% limits of agreement) was 6.21 mmHg ( $\pm$ 12.05 mmHg, –17.41 to 29.83 mmHg) for MAP, 0.39 mmHg ( $\pm$ 19.25 mmHg, –37.34 to 38.12 mmHg) for SBP, and 0.80 mmHg ( $\pm$ 12.92 mmHg, –24.52 to 26.12 mmHg) for DBP between the two techniques. Similarly, large limits of agreement were shown in different groups of NE doses. NE doses significantly affected the agreement between IBP and NIBP. SBP between the two methods gave an inconsistent assessment of patients’ risk of ICU mortality.

**Conclusion** IBP and NIBP were not interchangeable in septic patients. Clinicians should be aware that non-invasive MAP was clinically and significantly underestimated invasive MAP.

**Keywords** Invasive blood pressure measurement · Non-invasive blood pressure measurement · Sepsis

## Abbreviations

IBP	Invasive arterial blood pressure	SAPS II	Simplified Acute Physiology Score II
NIBP	Non-invasive oscillometric blood pressure	CVP	Central venous pressure
NE	Norepinephrine	IMAP	Invasive mean arterial pressure
ICU	Intensive care unit	ISBP	Invasive systolic blood pressure
MIMIC-IV	Medical Information Mart for Intensive Care IV	IDBP	Invasive diastolic blood pressure
BMI	Body mass index	NIMAP	Non-invasive mean arterial pressure
SOFA	Sequential Organ Failure Assessment	NISBP	Non-invasive systolic blood pressure
		NIDBP	Non-invasive diastolic blood pressure
		MAP	Mean arterial pressure
		SBP	Systolic blood pressure
		DBP	Diastolic blood pressure
		AAMI	Association for the Advancement of Medical Instrumentation
		SD	Standard deviation
		IQR	Interquartile range
		LOA	Limits of agreement
		AKI	Acute kidney injury

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## Introduction

In acutely or critically ill patients, both hypotension and hypertension can potentially impair the function of vital organs such as heart, brain, or kidneys [1], so thus having a reliable method of blood pressure measurement plays a vital role [2]. Invasive arterial blood pressure (IBP) monitoring using an arterial catheter is considered the clinical reference method in critically ill patients. However, complications such as bleeding, infection, and dependence on good peripheral vascular in addition to being cost-intensive and limited availability limit its use [2]. In most ICU settings, the use of IBP is recommended for invasive monitoring in patients with sepsis, but non-invasive oscillometric blood pressure (NIBP) measurement using an upper-arm cuff is a widely used alternative even though it is not reliable in acute conditions due to a wide degree of unreliability and inaccuracy [3–5]. Indeed, in clinical practice, at least in the transport to the hospital and the initial hours of healthcare management, blood pressure is measured non-invasively [6]. Hromádka M. et al. demonstrated that initial IBP of mean and systolic arterial pressures was in good agreement with NIBP [6]. On the contrary, Rebesco MR et al. indicated that NIBP had a significant difference compared to IBP [7]. Thus, the discrepancy between IBP and NIBP in patients with sepsis remains controversial.

Accuracy of blood pressure monitoring is crucial in evaluating the cardiocirculatory system and adjusting drug therapy for hemodynamic support. Norepinephrine (NE) is the first-line agent recommended during resuscitation of septic shock [8]. Recent research revealed that NIBP was a sufficient replacement for IBP in cardiogenic shock patients, except for those receiving very high doses of NE ( $> 0.6 \mu\text{g}/\text{kg}/\text{min}$ ) [6]. There are few studies on the effect of NE on blood pressure measurement. Furthermore, maintenance of blood pressure at lower or higher levels might result in different outcomes in patients with sepsis. Lee G.T. et al. revealed that mortality of MAP between 75 and 85 was significantly lower compared with those between 65 and 75 in patients with hypertension [9]. High-frequency arterial blood pressure data could be useful in predicting the clinical outcomes of patients with sepsis [10].

Clinical data comparing the two techniques in septic patients are sparse. Therefore, we examined the following hypotheses using a large-scale database. The hypotheses of this study were as follows: (1) there are differences in the accuracy of IBP measurement and oscillometric non-invasive blood pressure measurement; (2) NE doses significantly affect the agreement between the two techniques; (3) the two methods give an inconsistent assessment of patients' risk of ICU mortality.

## Materials and methods

### Data source

All data in our study were extracted from the Medical Information Mart for Intensive Care IV (MIMIC-IV) v1.0, a freely accessible public database constructed by the Massachusetts Institute of Technology Computational Physiology Laboratory. Patient information was collected from patients admitted to ICU at the Beth Israel Deaconess Medical Center between 2008 and 2019, including vital signs, medications, laboratory results, diagnosis, and so on [11]. The author who had finished the online training for the Collaborative Institutional Training Initiative Program can access the database (Record ID 40486481). The MIMIC-IV data contain no identifiers and are publicly available for studies of critical medical research. Therefore, the current study was deemed to be exempt from Institutional Review Board approval and the need for informed consent was waived.

### Study population and study design

This is a consistency analysis of repeated IBP and NIBP measurements based on the single-center database MIMIC-IV v1.0. Patients (age  $\geq 18$  years) admitted to the ICU with sepsis (Defined by sepsis-3.0 criteria [12]) were included. Sepsis-3.0 code package which was available on Github (<https://github.com/MIT-LCP/mimic-iv>) was used, including 32,753 patients diagnosed with sepsis-3.0. Those whose death of date that less than the time of ICU admission were excluded. The exclusion criteria were as follows: (1) patients received extracorporeal membrane oxygenation; (2) patients received intra-aortic balloon counter pulsation; (3) patients with arterial dissection (Defined by ICD-9 codes of 44,100 dissection of aorta, unspecified site, 44,101 dissection of aorta, thoracic, 44,102 dissection of aorta, abdominal, 44,103 dissection of aorta, thoracoabdominal; or ICD-10 codes of I71 aortic aneurysm and dissection, I710 dissection of aorta, I7100 dissection of unspecified site of aorta, I7101 dissection of thoracic aorta, I7102 dissection of abdominal aorta, I7103 dissection of thoracoabdominal aorta) (4) patients without paired IBP and NIBP measurements at the same minute.

### Variables extraction

Data extraction was performed using PostgreSQL14.0 (PostgreSQL Global Development Group, Santa Barbara, USA)  $< \text{https://www.postgresql.org/ftp/source/v14.0/} > .$  PostgreSQL 14.0 is an open-source object-relational database management system known for its reliability, scalability, and advanced features. It is originated in 1986 as part of

the Postgres project at the University of California, Berkeley. Its robustness and support for complex data types make it suitable for storing and managing a wide variety of medical data, and is widely used in medical industry.

In our study, the patient characteristics were extracted as follows: age, sex, body mass index (BMI), lactate, the first 24-h Sequential Organ Failure Assessment (SOFA) score, Simplified Acute Physiology Score II (SAPS II) score, comorbidities (myocardial infarction, congestive heart failure, peripheral vascular disease, renal disease, hypertension), central venous pressure (CVP), invasive and non-invasive mechanical ventilation, vasoactive drugs (NE infusion dose, the use of vasopressin, epinephrine, dopamine, and dobutamine), IBP (invasive mean arterial pressure[IMAP], invasive systolic blood pressure[ISBP], invasive diastolic blood pressure[IDBP]), NIBP (non-invasive mean arterial pressure[NIMAP], non-invasive systolic blood pressure[NISBP], non-invasive diastolic blood pressure[NIDBP]), and ICU mortality.

### Measurement and criteria for selection of IBP and NIBP

In the database, NIBP was measured by the oscillometric method with a brachial sphygmomanometer cuff, and IBP was measured by radial artery intubation. Blood pressure measurements that exceeded the boundaries of reasonable physiological signals and damped waveforms were excluded. Both IBP and NIBP were limited to the following range: mean arterial pressure (MAP) [20, 200] mmHg, systolic blood pressure (SBP) [40, 250] mmHg, and diastolic blood pressure (DBP) [10, 150] mmHg. In addition, measurements with MAP higher than SBP or lower than DBP were excluded. The absolute difference between estimated and recorded MAP that was greater than 30% of the measured MAP was excluded, where estimated MAP was defined with the formula  $MAP = (2 * DBP + SBP) / 3$  [13]. Finally, patients with less than two pairs of concurrently measured IBP and NIBP pairs were excluded.

### Objectives

The primary objective was to evaluate the agreement between IBP and NIBP, which was defined according to the Association for the Advancement of Medical Instrumentation (AAMI) standard. The AAMI definition of an acceptable agreement in adults between IBP and NIBP is a mean difference of  $\leq 5$  mmHg with a standard deviation (SD) of  $\leq 8$  mmHg [14].

The secondary objective was to analyze the discrepancy between the two techniques in different NE groups. The association between blood pressure and ICU mortality was also explored.

### NE in different dose groups

To explore the role of NE in blood pressure measurement in septic patients, we categorized the IBP and NIBP pairs according to the doses of NE: (1) no NE, (2) low dose of NE ( $< 0.1 \mu\text{g}/\text{kg}/\text{min}$ ), (3) high dose of NE ( $\geq 0.1 \mu\text{g}/\text{kg}/\text{min}$ ). To avoid the effect of other vasoactive drugs (vasopressin, epinephrine, dopamine, and dobutamine) on blood pressure measurements, IBP and NIBP pairs of patients who received other vasoactive drugs during NE infusion were excluded before classifying into the above three catalogs. This was a longitudinal study in which each patient had at least two blood pressure measurements. We directly analyzed the blood pressure pairs of patients rather than all the blood pressure measurements of each individual patient as some patients whose dose of NE had been changed during the measurement of blood pressure.

### Statistical analysis

Normally distributed variables are presented as mean  $\pm$  SD, and nonnormally distributed variables are presented as median with interquartile range (IQR). Frequency and percentage were used in categorical variables. The agreement of IBP and NIBP was assessed using the Bland–Altman analysis, by calculating the bias (mean difference), precision (SD of the bias), and 95% limits of agreement (LOA) ( $= \text{bias} \pm 1.96 \times \text{SD}$ ) of the IBP and NIBP.

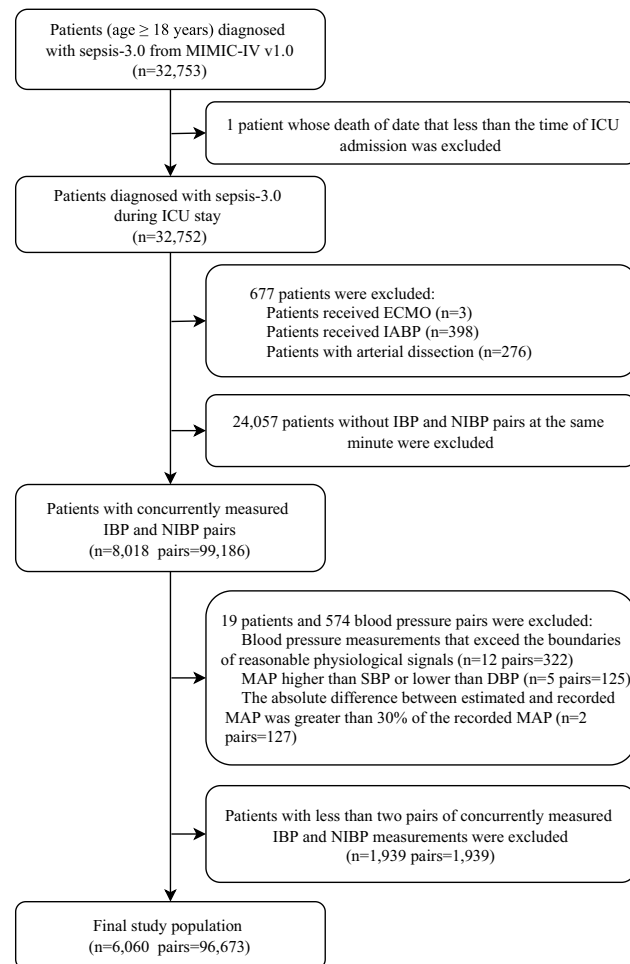
The paired Student's *t* test was used to compare the IBP and NIBP pairs in the study population. Two-tailed Pearson bivariate correlation analysis was applied to explore the correlation coefficients, and simple linear regression was performed to calculate the linear regression equations. Analysis of variance (ANOVA) was applied to explore the difference between IBP and NIBP in different NE groups. If Levene's test showed homogeneity of variance, one-way ANOVA was used for population mean comparison, and then Bonferroni was used for pairwise comparison. If not, the Welch test was used for the population mean comparison, and then the Tamhane T2 test was used for pairwise comparison. Line charts with errors were used to display the correlations between blood pressure measurement and ICU mortality. A Chi-square test was conducted to compare the difference of ICU mortality between the two methods.

Statistical analyses were carried out using IBM SPSS 25.0 software (IBM Corp., Armonk, NY, USA), and a two-tailed *p* value  $< 0.05$  was considered significant.

## Results

### Patient demographics

A total of 96,673 paired blood pressure measurements from 6060 unique patients were analyzed in the study (Fig. 1). There were more males than females (59.79% versus 40.21%) and the median age of all patients was 67.15 years (IQR 56.09–77.27 years). More patients were overweight with the median of BMI 28.29 kg/m<sup>2</sup> (IQR 24.49–32.99 kg/m<sup>2</sup>). There were 1079 patients with myocardial infarct (17.81%), 1,838 patients with congestive heart failure (30.33%), 887 patients with peripheral vascular disease (14.64%), 1352 patients with renal disease (22.31%), and 2,674 patients with hypertension (44.13%). The median



**Fig. 1** Flowchart. Estimated MAP was defined with the formula  $MAP = (2 \times DBP + SBP) / 3$ . *MIMIC-IV*, Medical Information Mart for Intensive Care IV, *ECMO* extracorporeal membrane oxygenation, *IABP* intra-aortic balloon counter pulsation, *IBP* invasive blood pressure, *NIBP* non-invasive blood pressure, *SBP* systolic blood pressure, *DBP* diastolic blood pressure, *MAP* mean arterial pressure

SOFA score was 3.00 (IQR 2.00–4.00) and SAPS II score was 37.00 (IQR 28.00–47.00). Invasive ventilation was administered in 5138(84.79%) of the patients, while non-invasive ventilation in 450 (7.43%) of the patients. The means values were  $79.15 \pm 17.37$  mmHg for the *IMAP*,  $72.94 \pm 14.06$  mmHg for *NIMAP*,  $115.62 \pm 27.39$  mmHg for *ISBP*,  $114.96 \pm 21.48$  mmHg for *NISBP*,  $60.76 \pm 15.42$  mmHg for *IDBP*, and  $59.97 \pm 14.11$  mmHg for *NIDBP*. The clinical characteristics of the study population were shown in Table 1.

### Analysis of the entire sample

The agreement of all paired measurements between *IBP* and *NIBP* in the study population was shown by Bland–Altman analysis (Table 2; Fig. 2). The bias ( $\pm$  SD, LOA) was 6.21 mmHg ( $\pm$  12.05 mmHg, – 17.41 to 29.83 mmHg) for *MAP*, 0.39 mmHg ( $\pm$  19.25 mmHg, – 37.34 to 38.12 mmHg) for *SBP*, and 0.80 mmHg ( $\pm$  12.92 mmHg,

**Table 1** Clinical characteristics of the study population

Variables	Total (n=6060)
Age (years)	67.15 (56.09, 77.27)
Male	3623 (59.79)
BMI (kg/m <sup>2</sup> )*	28.29 (24.49, 32.99)
Myocardial infarct	1079 (17.81)
Congestive heart failure	1838 (30.33)
Peripheral vascular disease	887 (14.64)
Renal disease	1352 (22.31)
Hypertension	2674 (44.13)
SOFA score	3.00 (2.00, 4.00)
SAPS II score	37.00 (28.00, 47.00)
Lactate (mmol/L)*	1.60 (1.10, 2.50)
CVP (mmHg)*	11.00 (8.00, 15.00)
Invasive ventilation	5138 (84.79)
Non-invasive ventilation	450 (7.43)
<i>IMAP</i> (mmHg)	$79.15 \pm 17.37$
<i>NIMAP</i> (mmHg)	$72.94 \pm 14.06$
<i>ISBP</i> (mmHg)	$115.34 \pm 27.39$
<i>NISBP</i> (mmHg)	$114.96 \pm 21.48$
<i>IDBP</i> (mmHg)	$60.76 \pm 15.42$
<i>NIDBP</i> (mmHg)	$59.97 \pm 14.11$

Categorical variables are presented as frequency and percentage, and nonnormally distributed variables are presented as median with interquartile range

*BMI* body mass index, *CVP* central venous pressure, *IMAP* invasive mean arterial pressure, *NIMAP* non-invasive mean arterial pressure, *ISBP* invasive systolic blood pressure, *NISBP* non-invasive systolic blood pressure, *IDBP* invasive diastolic blood pressure, *NIDBP* non-invasive diastolic blood pressure

\*Missing data were 1719 (28.37%) for BMI, 2300 (37.95%) for CVP and 212 (3.50%) for lactate

**Table 2** Bias, precision, and limits of agreement between invasive and non-invasive measurements of the study population ( $n=6060$ , pairs=96,673)

Variable	Bias (Mean difference, mmHg)	Precision (SD of bias, mmHg)	LOA (bias $\pm$ 1.96 SD, mmHg)	$t$	$p$
IMAP-NIMAP	6.21(6.14–6.29)	$\pm$ 12.05	(– 17.41–29.83)	160.24	<0.001
ISBP-NISBP	0.39(0.27–0.51)	$\pm$ 19.25	(– 37.34–38.12)	6.30	<0.001
IDBP-NIDBP	0.80(0.71–0.88)	$\pm$ 12.92	(– 24.52–26.12)	19.13	<0.001

SD standard deviation, LOA limits of agreement, IMAP invasive mean arterial pressure, NIMAP non-invasive mean arterial pressure, ISBP invasive systolic blood pressure, NISBP non-invasive systolic blood pressure, IDBP invasive diastolic blood pressure, NIDBP non-invasive diastolic blood pressure

– 24.52 to 26.12 mmHg) for DBP between the two techniques. There were significant differences between IMAP and NIMAP, ISBP and NISBP, and IDBP and NIDBP (all  $p < 0.001$ ) in Bland–Altman analysis. There were 5058/96,673 (5.23%) blood pressure measurements out of LOA in MAP, 5444/96,673 (5.63%) out of LOA in SBP, and 4917/96,673 (5.09%) out of LOA in DBP.

IBP showed good correlation with NIBP, with the correlation coefficients 0.72, 0.72 and 0.62 in MAP, SBP and DBP, respectively. The regression equations between IBP ( $y$ ) and NIBP ( $x$ ) were  $y = 0.90x + 13.81$  for MAP ( $R^2 = 0.53$ ) and  $y = 0.91x + 10.52$  for SBP ( $R^2 = 0.51$ ) and  $y = 0.68x + 20.08$  for DBP ( $R^2 = 0.39$ ).

### NE groups in different dose

Of 96,673 paired measurements from 6060 patients, 86,788 pairs from 5750 patients without other vasoactive drugs (vasopressin, epinephrine, dopamine, and dobutamine) were divided into three predefined groups according to NE dose: no NE (72,644 pairs), low dose (7719 pairs), and high dose (6425 pairs). Bias, precision, and LOA in Bland–Altman analysis were shown in Table 3. Significant discrepancies were observed between IMAP and NIMAP in septic patients with and without receiving NE. In different NE groups, IMAP and IDBP were higher than NIMAP and NIDBP in all categories. ISBP was lower in low and high doses of NE but higher in no NE compared to NISBP, with the bias of – 1.46 mmHg in low dose of NE, – 5.07 mmHg in high dose of NE, and 1.95 mmHg in no NE. The blood pressure measurements out of LOA of MAP, SBP, and DBP were 5.20%, 5.78%, and 5.26% in patients without receiving NE, 4.55%, 5.52%, and 4.55% in patients with low dose of NE, and 5.71%, 5.93% and 5.28% in patients with high dose of NE.

In ANOVA, there were significant differences between IBP and NIBP of MAP ( $F = 287.22$ ,  $p < 0.001$ ), SBP ( $F = 500.71$ ,  $p < 0.001$ ), and DBP ( $F = 17.64$ ,  $p < 0.001$ ) in different groups of NE. The agreement between the two techniques was influenced by NE catalogs. In the pairwise comparison of MAP, SBP and DBP, there were significant differences between low dose versus high dose of NE (all

$p < 0.001$ ), low dose of NE versus no NE (all  $p < 0.001$ ), and high dose of NE versus no NE (all  $p < 0.001$ ).

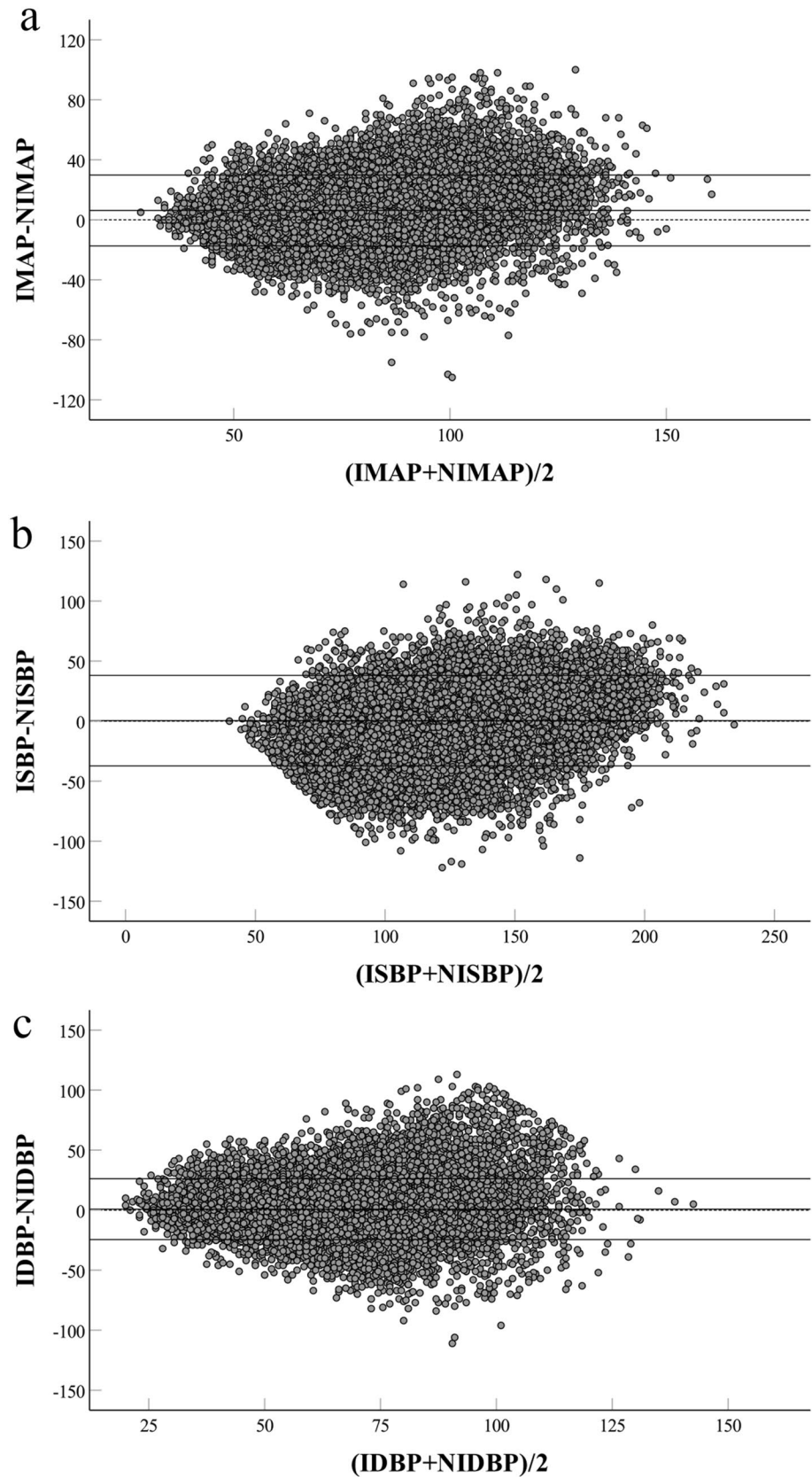
### Association between blood pressure measurements and ICU mortality

The association between ICU mortality and paired blood pressure measurements was assessed in 6060 patients, in which 994 (16.40%) died during ICU stay. ISBP and NISBP gave an inconsistent assessment of patients' risk of ICU mortality (Fig. 3). ICU mortality associated with NISBP diverged from that of ISBP in a lower threshold of hypotensive patients, and an increasing discrepancy was found as the blood pressure threshold decreased. The Fig. 3 showed the following information: the ICU mortality associated with SBP less than 65 mmHg was 35.21% (144/409 patients expired) for IBP and 44.83% (78/174 expired) for the NIBP; the ICU mortality associated with SBP less than 70 mmHg was 33.90% (219/646 patients expired) for IBP and 41.89% (124/296 expired) for the NIBP; the ICU mortality associated with SBP less than 75 mmHg was 30.51% (310/1016 patients expired) for IBP and 36.20% (181/500 expired) for the NIBP. There was a significant difference between ISBP and NISBP in assessing patients' risk of ICU mortality with thresholds of 65 mmHg ( $p = 0.029$ ), 70 mmHg ( $p = 0.018$ ), and 75 mmHg ( $p = 0.026$ ). No significant difference was found in the association between MAP and DBP and ICU mortality (Figure S1 and Figure S2 in supplementary materials).

### Discussion

In our study, NIBP of MAP, SBP, and DBP showed large LOA compared to IBP. It had been pointed out that the discrepancies greater than 10 mmHg should be regarded as clinically relevant and that they became clinically unacceptable in excess of 20 mmHg in critically ill patients [15]. Thus, we concluded that NIBP was not a substitute for IBP in sepsis patients. Clinically relevant differences between IBP and NIBP were frequent [16]. Kaufmann T. et al. revealed that NIBP using brachial cuff oscillometry showed large LOA compared to invasive radial arterial catheter-derived

**Fig. 2** Bland–Altman plot for mean arterial pressure (a), systolic blood pressure (b) and diastolic blood pressure (c). Comparison between measurements of non-invasive oscillometric blood pressure and invasive arterial blood pressure was shown. *IMAP* invasive mean arterial pressure, *NIMAP* non-invasive mean arterial pressure, *ISBP* invasive systolic blood pressure, *NISBP* non-invasive systolic blood pressure, *IDBP* invasive diastolic blood pressure, *NIDBP* non-invasive diastolic blood pressure

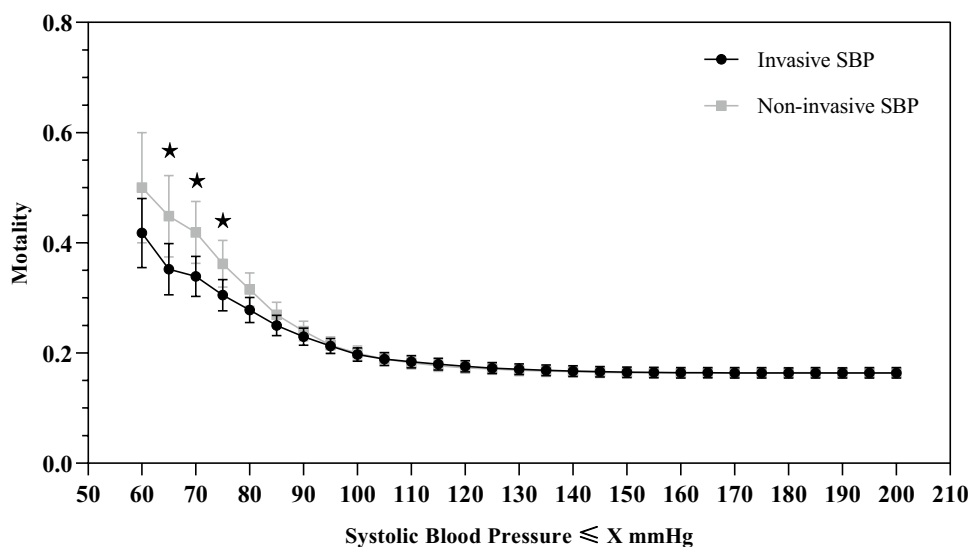


**Table 3** Invasive and non-invasive mean, systolic and diastolic blood pressure in patients with different doses of norepinephrine

Variable	Invasion (mean $\pm$ SD)	Non-invasive (mean $\pm$ SD)	Bias (95% CI) (mmHg)	SD of bias (mmHg)	LOA (mmHg)
No NE(pairs = 72,644)					
MAP	81.01 $\pm$ 17.72	73.95 $\pm$ 14.32	7.06 (6.98,7.15)	$\pm$ 12.04	(– 16.54–30.66)
SBP	119.07 $\pm$ 27.78	117.12 $\pm$ 21.81	1.95 (1.81,2.09)	$\pm$ 19.37	(– 36.02–39.92)
DBP	61.80 $\pm$ 15.86	60.68 $\pm$ 14.32	1.12 (1.02,1.21)	$\pm$ 13.06	(– 24.48–26.72)
Low dose of NE(<0.1 ug/kg/min) (pairs = 7719)					
MAP	74.54 $\pm$ 14.22	69.57 $\pm$ 12.11	4.97 (4.72,5.22)	$\pm$ 11.38	(– 17.33–27.27)
SBP	107.10 $\pm$ 21.03	108.56 $\pm$ 18.00	– 1.46 (– 1.84, – 1.08)	$\pm$ 16.99	(– 34.76–31.84)
DBP	57.88 $\pm$ 13.57	57.38 $\pm$ 12.58	0.50 (0.22,0.78)	$\pm$ 12.58	(– 24.16–25.16)
High dose of NE( $\geq$ 0.1 ug/kg/min) (pairs = 6425)					
MAP	74.32 $\pm$ 16.12	70.28 $\pm$ 13.34	4.04 (3.76,4.33)	$\pm$ 11.66	(– 18.81–26.89)
SBP	105.19 $\pm$ 24.50	110.26 $\pm$ 20.54	– 5.07 (– 5.53, – 4.61)	$\pm$ 18.88	(– 42.07–31.93)
DBP	58.18 $\pm$ 14.29	57.81 $\pm$ 13.64	0.38 (0.08,0.67)	$\pm$ 12.14	(– 23.41–24.17)

SD standard deviation, CI confidence interval, LOA limits of agreement, NE norepinephrine, MAP mean arterial pressure, SBP systolic blood pressure, DBP diastolic blood pressure

**Fig. 3** The association between ISBP and NISBP and ICU mortality. Error bars showed 95% confidence intervals of the mortality rates. \*The differences between SBP measurements in terms of their ICU mortality are statistically significant ( $p < 0.05$ ) based on the chi-square test. ICU intensive care unit, SBP systolic blood pressure



measurements in critically ill patients [14], which was similar to our main results.

The bias and precision of MAP determined by Bland–Altman analysis failed to meet the AAMI standards. NIMAP was clinically underestimated IMAP (bias of 6.21 mmHg in Bland–Altman analysis). Hohn A et al. illustrated that NIBP monitoring with Nexfin (BMEYE, Amsterdam, Netherlands) clinically underestimated intra-arterial blood pressure measurements in critically ill patients, which was consistent with our findings [17]. The oscillometric technique analyzes oscillations of the vessel during compression, transmitted through the air-filled occluding cuff. MAP corresponds to the maximum of oscillations, and an algorithm applied to the change of oscillations sets SBP and DBP, which differs between manufacturers and is often not publicly available [1]. In sepsis, vasoconstriction and low output may impair the

normal physiology of the vascular tree and therefore make reliable detection of blood pressure from oscillations in the vessel highly inaccurate [18]. Extensive use of NIMAP that underestimated IMAP in these patients may lead to excessive fluid therapy or treatment with vasoactive agents. IBP should be established as early as possible in patients with suspected sepsis. Furthermore, the relation between upper-arm circumference and cuff size may affect the accuracy of NIBP. Most of our patients were obese, which may result in the inappropriateness of the upper-arm circumference and the occluding cuff that led to the falsely high of NIBP [19, 20]. This suggests that we should pay attention to the influence of the upper-arm circumference and the occluding cuff on NIBP measurement in obese patients.

NE is recommended by recent guidelines as the first-line vasopressor in septic shock [21], so we explored the effect

of different NE doses on the discrepancies between the two methods. In our study, NISBP was lower than ISBP in patients treated without NE but higher than ISBP in patients treated with NE. The discrepancies between the two methods kept rising when the NE dose increased. Arterial pulse pressure results from the interaction between the blood volume ejected from the ventricle and the arterial system, which comprises several phenomena: stroke volume, arterial wave reflection, wall stiffness, total peripheral resistance [22]. Monge G. MI. et al. showed that the change of NE from low dose to high dose increased arterial characteristic impedance, pulse wave velocity, and reflection phenomena while reducing aortic compliance [23]. Recent research had shown the effect of NE infusion on central arterial stiffness increase [24]. Arterial stiffness may predict the decrease in arterial pressure in response to NE dose reduction. [22–25] The dose of NE affects arterial stiffness [26], increasing the oscillometric NISBP [27]. Thus, the NISBP elevated in high dose of NE and we observed that the discrepancies between ISBP and NISBP kept rising when the NE dose increased. For IMAP and NIMAP, the monitor measured MAP over time and then used a specific algorithm to calculate SBP and DBP. Although our findings suggested a difference between IMAP and NIMAP, the difference for MAP was less than that for SBP in those treated with high dose of NE, which is similar to Saherwala AA. et al. [16]. MAP is actually more practical and reliable when patients received high dose of NE. When monitoring blood pressure in patients with sepsis, we should be aware that there were clinical differences in MAP between the two techniques. Meanwhile, a higher NE dose usually represented higher severity of the disease. Several studies demonstrated an unacceptable measurement performance of NIBP in critically ill patients with circulatory shock [28, 29]. When patients received high dose of NE, we should pay more attention to IBP.

In terms of the prognosis of patients with sepsis, ICU mortality associated with NISBP diverged from that of ISBP in a lower threshold of hypotensive patients (< 75 mmHg), with an increasing discrepancy between the two methods as the blood pressure threshold decreased. This may be related to the overestimation of NISBP in the high-dose NE group. The overestimation of NISBP led to lower actual blood pressure than monitored, resulting in organ tissue under-perfusion and cell ischemia and hypoxia [30], which improved the risk of mortality. [31–33] Furthermore, a higher NE dose usually represented higher severity of the disease and early use of NE. One research had shown that NE appeared to have potentially adverse effects on renal function, which may increase the risk of acute kidney injury (AKI) in patients with sepsis [34]. Sepsis associated AKI is prevalent in critically ill patients and posed treatment challenges, which led to high morbidity and mortality rates. We suggested that both IBP and NIBP should be taken into consideration to

predict ICU mortality at a lower threshold of hypotensive (< 75 mmHg). MAP and DBP from both techniques can be interpreted consistently in assessing patients' prognoses.

Our study has several limitations. First, the number of paired blood pressure measurements was not uniform and varied among different patients due to the different lengths of stay of the patients in the ICU. Second, this is a single-center study, and other centers may have different criteria for maintaining and recording blood pressure for both IBP and NIBP. However, MIMIC-IV is one of the most comprehensive databases concerning intensive care, which collected detailed hospital information from more than 380,000 patients from 2008 to 2019. Third, this study was conducted only on patients with sepsis and may not be generalizable to other critically ill patient populations. The etiology of sepsis in our study population was quite broad and differences in hemodynamic responses among individual patients could have affected the results. Fourth, the ICU mortality statistics in this study were not representative of ICU-wide mortality, but rather reflected the outcome of patients with IBP monitoring, which was selected for a hemodynamically unstable cohort with a higher expected mortality rate. Finally, only the effect of NE on blood pressure was discussed. It is necessary to include a larger cohort in future studies to explore the effect of other vasoactive drugs on blood pressure.

## Conclusion

Clinically significant discrepancies were observed between IBP and NIBP in patients with sepsis. NIMAP was significantly underestimated IMAP, and the clinical difference should be considered when monitoring blood pressure. Different dose of NE significantly affected the agreement between IBP and NIBP. Invasive SBP and non-invasive SBP gave an inconsistent assessment of patients' risk of ICU mortality.

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**Data availability** All Data was extracted from the Medical Information Mart for Intensive Care IV v1.0, a freely accessible public database constructed by the Massachusetts Institute of Technology Computational Physiology Laboratory (<https://mimic.mit.edu/>).

## Declarations

**Conflict of interest** All authors declare that there is no conflict of interest.

**Ethics approval and consent to participate** The author who had finished the online training for the Collaborative Institutional Training Initiative Program can access the database (Record ID 40486481). The MIMIC-IV v1.0 contain no identifiers and are publicly available for studies of critical care. The Institutional Review Board approval and the need for informed consent was waived.

**Consent for publication** Not applicable.

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