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The CNAP™ Finger Cuff for Noninvasive Beat-To-Beat Monitoring of Arterial Blood Pressure: An Evaluation in Intensive Care Unit Patients and a Comparison with 2 Intermittent Devices

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BACKGROUND: Continuous and intermittent noninvasive measurements of arterial blood pressure (BP) have not been compared in the same population. In a large panel of intensive care unit patients, we assessed the agreement between CNAP™ (Continuous Noninvasive Arterial Pressure) finger cuff beat-to-beat monitoring of BP and reference intraarterial measurements. Two automated oscillometric brachial cuff devices were also tested: CNAP brachial cuff (used for CNAP finger cuff calibration) and an alternative device. The performance for detecting hypotension (intraarterial mean BP <65 mm Hg or systolic BP <90 mm Hg), response to therapy (therapy-induced increase in mean BP >10%), and hypertension (intraarterial systolic BP >140 mm Hg) was evaluated. We also assessed the between-calibration drift of CNAP finger cuff BP in specific situations: cardiovascular intervention or no intervention.

METHODS: With each device, 3 pairs of noninvasive and intraarterial measurements were prospectively collected and analyzed according to current guidelines, the International Organization for Standardization (ISO) standard. The trending ability and drift of the CNAP finger cuff BP were assessed over a 15-minute observation period.

RESULTS: In 182 patients, CNAP finger cuff and CNAP brachial cuff readings did not conform to ISO standard requirements (mean bias ± SD exceeding the maximum tolerated 5 ± 8 mm Hg), whereas the alternative automated brachial cuff succeeded for mean and diastolic BP. CNAP finger cuff trending ability was poor (concordance rate <70% over a 15-minute period) owing to a significant drift since calibration, especially if a cardiovascular intervention was performed (n = 75, −7.5 ± 10.2 mm Hg at the 14th minute, ie, before recalibration, versus −2.9 ± 7.9 mm Hg if no cardiovascular intervention occurred, n = 103, P = 0.0008). However, a similar and reliable performance was observed for the detection of hypotension with the CNAP finger cuff (within 4 minutes after calibration) and with the 2 automated brachial cuffs (area under the receiver operating characteristic curve ≥0.91, positive and negative likelihood ratios ≥5 and ≤0.20, respectively). The performance for the detection of response to therapy or of hypertension was slightly lower.

CONCLUSIONS: In a large population of intensive care unit patients, CNAP did not fulfill the ISO criteria and exhibited a relevant between-calibration drift. However, CNAP measurements collected within 4 minutes after calibration were reliable for detecting hypotension, as were oscillometric devices, while providing beat-to-beat measurements. Interestingly, an alternative automated brachial cuff was more reliable than the native one, used for calibration. This information is important to clinicians using those devices and for further development of the CNAP technology. (Anesth Analg 2016;123:1126–35)

In approximately one-third of intensive care unit (ICU) patients, arterial blood pressure (BP) is measured via an intraarterial catheter.[1] An automated oscillometric brachial cuff is the widely used noninvasive alternative.[2,3] The risks of the intraarterial catheter (bloodstream infections,[4] thrombosis[5]) are well known. However, besides being an easy access for blood sampling, there is a lack of data regarding its benefits.[1] The intraarterial catheter allows a beat-to-beat monitoring of BP, whereas brachial cuff measurements are intermittent. Performing brachial cuff measurements at

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wide intervals may delay the detection of sudden changes of BP. On the contrary, closer intervals expose patients to cuff inflation–induced injuries.[6,7]

CNAP™ (Continuous Noninvasive Arterial Pressure), an appealing noninvasive device for beat-to-beat monitoring of BP, aims to bridge the gap between the intraarterial catheter and the automated brachial cuff.[8] It relies on the principle of volume clamp-based measurements. Transdigital infrared photoplethysmography (across 1 finger) measures small changes in light absorption, which are proportional to changes in finger blood volume. Using a feedback loop, a pressure controller keeps the blood volume constant in a finger wrapped with a cuff. Hence, the finger cuff pressure reflects the digital BP. The brachial BP is derived from the digital BP via a proprietary algorithm including a calibration (at up to 15-minute intervals) with an oscillometric brachial cuff.

In critically ill patients, finger plethysmography and oscillometry may be inaccurate. When the photoplethysmographic signal is insufficient, that is, during peripheral vasoconstriction, the device often fails to display a BP waveform. More troublesome, the reliability of automated brachial cuffs (used for calibration) is a matter of debate.[9–12] The reliability of CNAP measurements has been scarcely assessed in ICU and surgical patients,[13–17] and most studies suffer from the use of a nonconsensual definition of the reliability itself.[17–19] Of note, no study compared, in the same patients, intraarterial measurements to these 2 noninvasive alternatives: volume clamp-based and oscillometric measurements. In addition, if not absolutely accurate and precise, CNAP could still provide important clinical information such as the detection of hypotension, response to therapy, and hypertension, but data are lacking.

Between-calibration changes (spontaneous or therapy-induced) in the properties of the arterial tree may cause a significant drift of CNAP-displayed values with regard to the actual BP. Only a few studies reported data concerning CNAP's trending ability with heterogeneous results.[15,20,21]

In a large population of ICU patients, our primary aim was to assess the agreement between the CNAP finger cuff and reference intraarterial measurements. For comparison, 2 oscillometric automated brachial cuffs, widely used worldwide, were also tested: the one included in the CNAP technology for calibration and an alternative cuff. We applied the International Organization for Standardization (ISO) standard 81060-2:2013,[22] which has been adopted as the United States National Standard for the validation of BP measuring devices. It is an improvement of the previously used Association for the Advancement of Medical Instrumentation Standard.[23]

In addition, the ability to detect hypotension (intraarterial systolic BP <90 mm Hg or mean BP <65 mm Hg[24]), response to therapy (therapy-induced increase in mean BP >10%),[11] and hypertension (intraarterial systolic BP >140 mm Hg or diastolic BP >90 mm Hg)[25] was assessed. We also measured the between-calibration drift of the CNAP in specific situations: cardiovascular intervention or no intervention.

METHODS

Setting

Patients were included from the surgical ICU of University Hospital Laënnec (Nantes, France) over a 21-month period (June 2012 to February 2014) and from the medical ICU of the Regional Hospital of Orléans (France) over a 12-month period (July 2012 to July 2013).

Patients

Adult patients were included in this prospective study if an arterial line was present and if the BP was stable over 10 minutes (no change in vasoactive drugs dosage and no significant [>10%] variation of mean BP).

Patients were not included if they had contraindications for cuff placement, for supine position, or had a difference >5 mm Hg in brachial mean BP between the upper limbs (anatomically induced bias). In case of a cuff inflation–induced increase in heart rate (>5 beats/min) or in mean BP (>5 mm Hg), indicating potential measurement-induced pain, cuff inflation was interrupted and the patient was excluded from the study.

Acute circulatory failure was defined by the presence of at least one of the following criteria: hypotension (invasive systolic BP <90 mm Hg and/or mean BP <65 mm Hg), oliguria (<0.5 mL/kg/h) considered to be related to circulatory failure, arterial lactate >2.5 mmol/L, skin mottling, or vasopressor and/or inotropic drug infusion.

Ethics

The ethics board of Orléans Hospital (ref 2013-1) approved the study design and waived the need for written consent because the study procedures fulfilled the criteria of a noninterventional study as defined by French law.[26] Patients' next of kin and the patients themselves (if they regained capacity) were informed of their participation and of their right to refuse the use of the data. This article is in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement for the reporting of observational studies.[33]

Material

CNAP Technology

A finger cuff of appropriate size was placed according to the manufacturer's guidelines and was connected to a Dräger Infinity™ Delta monitor (Dräger Medical Systems, Lübeck, Germany) via the Infinity CNAP Smartpod (Dräger Medical Systems, software version 2.238). On the opposite upper limb, a brachial cuff, also chosen according to manufacturer's guidelines (after measurement of brachial circumference), was placed 2 cm above the antecubital fossa. The brachial cuff was connected to the Dräger Infinity *Delta* monitor for oscillometric calibration of CNAP finger cuff measurements (Supplemental Digital Content 1, http://links.lww.com/AA/B418).

Alternative Oscillometric Brachial Cuff

Measurements were also taken with the automated brachial cuff readily available in the participating ICUs: Philips Intellivue™ MP70 monitor (Philips Medical Systems, Best, The Netherlands). Because this monitor could not be connected to the CNAP, these "alternative brachial cuff" measurements did not contribute to CNAP calibration and, hence, did not impact CNAP readings.

Intraarterial Measurements

An intraarterial radial (ipsilateral to the CNAP finger cuff) or femoral catheter was connected to a pressure transducer (T100209A; Edwards Lifesciences, Irvine, CA), zeroed at the level of the midaxillary line. To avoid any investigator-related

reading bias because of the possible variability of the instantaneous displayed value of invasive BP, pairs of intraarterial and noninvasive measurements were collected, in real time, from the trend database of the monitor rather than from the main screen.

Study Protocol

First Set of Measurements: ISO Standard Testing

In strict supine position and after flushing the arterial line,[27] 3 pairs of intraarterial and noninvasive BP measurements were prospectively collected (at 60-second intervals) with each device in predefined order (Figure 1).

Second Set of Measurements: Evaluation of CNAP Trending Ability and Drift

After brachial cuff calibration, pairs of CNAP finger cuff and intraarterial measurements were collected at 2-minute intervals for a 15-minute observation period, that is, until the next calibration (Figure 1). Meanwhile, at the discretion of the attending physician, patients with circulatory failure could undergo a cardiovascular intervention (started within the first minutes of the observation period): intravascular volume expansion, passive leg raising, initiation/change in dosage of vasopressor or inotropic medications, or combination of interventions.

Third Set of Measurements: Assessment of Response to Therapy

In patients having undergone a cardiovascular intervention, 3 additionnal pairs of BP measurements were collected (Figure 1).

Statistical Analysis

Study Size

To test new BP measuring devices against invasive BP measurements, the ISO standard[22] requires that at least 15 patients must be studied. No more than 10 valid measurements shall be taken per patient. There shall be a minimum of 150 valid BP measurements.

As planned per protocol, several patients (n = 200) were shared with a study addressing the impact of arrhythmia on brachial cuff measurements.[28] Therefore, a significant proportion of our included patients was expected to have arrhythmia. To exclude a potential influence on our findings, a subgroup analysis assessing the impact of arrhythmia on CNAP measurements appeared relevant and then required 150 valid BP measurements during arrhythmia. Furthermore, noninvasive measurements were expected to fail in some patients. Therefore, we planned to triple the ISO minimal requirement to include at least 450 valid measurements per device in our "first set of measurements" phase in at least 150 patients (3 measurements per device and per patient).

Statistical Tests

Main Analysis: ISO Standard Testing of the First Set of Measurements

The error (bias) of noninvasive measurements was calculated (bias = noninvasive − intraarterial measurement). Owing to pathophysiological variations of our reference intraarterial readings during the noninvasive determination of BP, the ISO standard proposes the "zero-zone" approach[19]: the zero-zone is defined as the range of ±1 SD around the mean value of 3 intraarterial measurements in each patient.[22] Thus, a noninvasive measurement within the zero-zone was associated with a 0 mm Hg error when compared with intraarterial readings. If the value obtained from each noninvasive measurement was outside the zero-zone, the value of the noninvasive measurement was subtracted from the adjacent limit of the zero-zone to calculate the bias. To meet the ISO standard, the mean bias between the 2 techniques must be ≤5 mm Hg and the SD of the errors ≤8 mm Hg.[22]

Secondary Analyses

The agreement between intraarterial and noninvasive readings of BP was also assessed by Bland-Altman analysis for repeated measurements.[29]

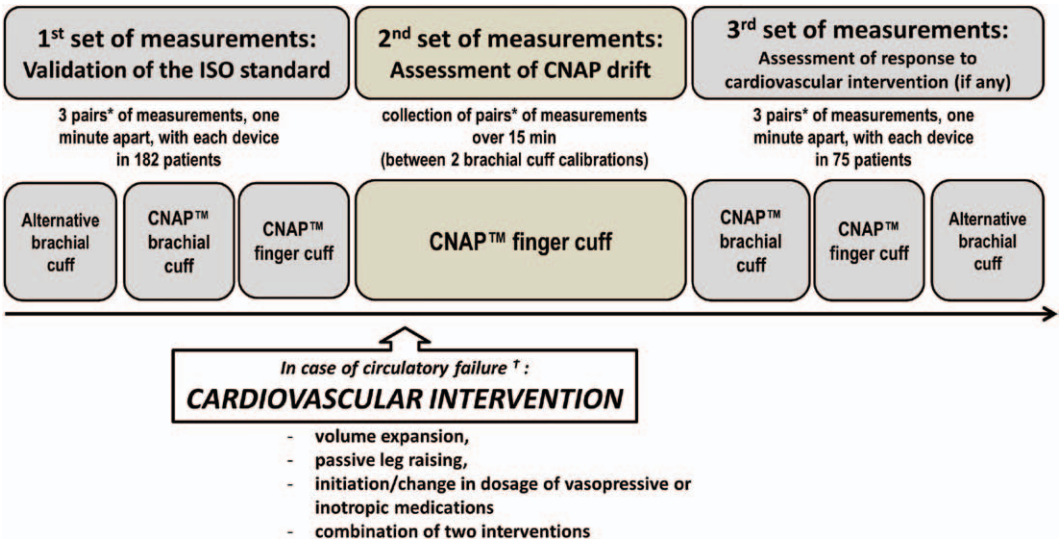

Figure 1. Study protocol. Measurements were performed in the illustrated order in all the patients.*One pair of measurements of blood pressure (BP) comprises 1 intraarterial and 1 contemporaneous noninvasive reading. †Circulatory failure was defined by the presence of at least 1 criterion among hypotension (invasive systolic BP <90 mm Hg and/or mean BP <65 mm Hg), oliguria (<0.5 mL/kg/h) considered to be related to circulatory failure, arterial lactate >2.5 mmol/L, skin mottling, vasopressor, and/or inotropic drug infusion. CNAP indicates Continuous Noninvasive Arterial Pressure.

The ability of the CNAP device for detecting hypotension (intraarterial mean BP <65 mm Hg or systolic BP <90 mm Hg[24]), response to cardiovascular intervention (intraarterial mean BP increase ≥10%),[11] and hypertension (intraarterial systolic BP >140 mm Hg or diastolic BP >90 mm Hg)[25] was assessed through area under the receiver operating characteristic curve (AUC_{ROC}) analysis[30] and likelihood ratio (LR) calculation. An exact binomial confidence interval (CI) for the AUC_{ROC} was calculated. We considered that a minimal value of 5 for the positive LR (or a maximal value of 0.2 for the negative LR) was associated with "good" positive (or negative, respectively) diagnostic performance.[31]

To analyze the trending ability of CNAP readings over 15 minutes, the concordance rate of changes in mean BP was calculated (via a 4-quadrant plot analysis) as the percentage of data points with the same direction of change after excluding central data of the plot (which tend to be randomly distributed among the 4 quadrants).[32] Exclusion zones of 5% and 10% were applied.[21] A concordance rate >90% indicates reliable trending ability.[32]

Categorical data were expressed as percentages. Continuous variables with Gaussian/non-Gaussian distribution (as assessed graphically) were expressed as mean ± SD and median (interquartile range [IQR]), respectively.

Between-group comparisons relied on χ^2, Student *t*, and Mann-Whitney tests. The time course of the bias between CNAP and intraarterial measurements was compared with Student *t* test at 7 time points after calibration (from minute 1 to minute 14) in patients undergoing a cardiovascular intervention or no intervention. In each group (cardiovascular intervention or not), we performed a 1-way analysis of variance for repeated measurements to determine whether, and at which time points, the bias significantly deviated from initial bias. To adjust for these multiple comparisons, we fixed the *P* value at 0.007 (by Bonferroni correction). Otherwise a $P < 0.05$ was considered significant. Analysis was performed on anonymous data with MedCalc™ 12.7.7 (MedCalc Software bvba, Ostend, Belgium). No data imputation was performed.

RESULTS

No CNAP finger cuff measurement was displayed in 32 of 218 included patients (15%). Patients with CNAP failure were included earlier in their ICU stay and had more frequent signs of tissular hypoperfusion (more frequently mottling skin, longer capillary refill time) than patients with CNAP detection of BP signal (Table 1). Four patients were excluded (Figure 2). Therefore, 182 patients were analyzed for comparison of 3 noninvasive devices with intraarterial measurements (Figure 2; Table 1) and 178 underwent a trending ability analysis.

Agreement Between Noninvasive and Intraarterial Measurements of BP (First Set of Measurements)

Mean BP

The CNAP finger cuff mean BP was more accurate than measurements taken with the brachial cuff used for its calibration (comparison of biases: $P < 0.0001$; Table 2) but did not meet the ISO standard: mean bias ± SD of 6.2 ± 6.2 mm Hg (maximal tolerated: 5 ± 8 mm Hg) (Table 2; Figure 3; Supplemental Digital Content 2, http://links.lww.com/AA/B418). Of note, the alternative automated brachial cuff (Philips Intellivue *MP70*) fulfilled the ISO criteria: mean bias of −1.8 ± 6.1 mm Hg (Table 2).

Similar agreement was found when splitting the population according to cardiac rhythm (arrhythmia [$n = 68$ {37%}] versus regular rhythm [$n = 114$ {63%}]) or other clinical factors (eg, site of the arterial catheter, respiratory or circulatory status, sex) (Supplemental Digital Content 3, http://links.lww.com/AA/B418). In the vast majority of these subgroups, CNAP measurements did not reach the ISO standard requirements.

Systolic and Diastolic BP

The alternative automated brachial cuff passed the ISO testing for diastolic but not for systolic BP measurements, whereas the CNAP finger cuff and CNAP brachial cuff failed for both (Table 2).

CNAP Finger Cuff Trending Ability and Drift

During the 15-minute observation period (ie, between 2 calibrations), the direction of changes in CNAP finger cuff measurements poorly reflected the direction of changes in intraarterial mean BP (concordance rate <70% and upper boundary of its 95% CI <80%; Figure 4A). Indeed, the bias between intraarterial and CNAP finger cuff readings of mean BP decreased over the 15 minutes after calibration. From the 6th minute ($P < 0.0001$) in the 75 patients undergoing a cardiovascular intervention and the 8th minute ($P < 0.0001$) otherwise ($n = 103$), the bias between intraarterial and CNAP finger cuff measurements was statistically different from the bias associated with the first displayed CNAP finger cuff measurement (Figure 4B). In other words, the drift since the last calibration, that is, the change of this bias over time, was of higher magnitude in patients undergoing a cardiovascular intervention than in patients with no cardiovascular intervention: the drift reached a statistically significant difference ($P < 0.007$) between these 2 groups at the 12th minute (−6.7 ± 9.6 and −2.6 ± 7.4 mm Hg, respectively; $P = 0.002$) and 14th minute (−7.5 ± 10.2 and −2.9 ± 7.9 mm Hg, respectively; $P = 0.0006$).

Detection of Hypotension and Hypertension

A similar and reliable performance was observed for the detection of an intraarterial mean BP <65 mm Hg with the 3 noninvasive devices (Figure 5; Supplemental Digital Content 4, http://links.lww.com/AA/B418): AUC_{ROC} ≥0.94 (95% CI upper boundary ≥0.90), positive and negative LRs >5 (95% CI lower boundary ≥4.8) and <0.20 (95% CI upper boundary ≤0.3), respectively (first set of measurements).

To evaluate the impact of time course since calibration on the CNAP finger cuff's discriminative ability, pairs of CNAP and intraarterial readings collected from minutes 1 to 14 were sequentially analyzed. The ability to detect an intraarterial mean BP <65 mm Hg worsened with time: AUC_{ROC} = 0.95 (0.91–0.98) 1 minute after calibration and AUC_{ROC} = 0.83 (0.77–0.88) 14 minutes after calibration ($P = 0.009$). Hence, the CNAP finger cuff allowed a reliable detection of hypotension within 4 minutes after calibration: at minute 4, AUC_{ROC} = 0.94 (0.89–0.97), positive LR 5.9 (4.0–8.9), negative LR 0.12 (0.04–0.3) for a 75-mm Hg cutoff. For

Table 1. Patients' Characteristics

	CNAP success in displaying BP	CNAP failure in displaying BP	*P*
Whole population	*n* = 182 patients	*n* = 32 patients	
Age (y)	64 ± 13	64 ± 14	0.99
Females	42 (23%)	11 (34%)	0.25
Simplified acute physiology score II	41 ± 18	49 ± 24	0.03
Body mass index (weight [kg]/height^2 [m^2])	27 ± 5	27 ± 6	0.96
Brachial circumference (cm)	30 ± 4	29 ± 4	0.42
Vascular disease: established diagnosis[a] of			
Coronary artery disease	60 (33%)	9 (28%)	0.88
Atherosclerosis of the lower limbs	30 (16%)	7 (22%)	0.32
Carotid stenosis	30 (16%)	5 (16%)	0.94
Aortic calcifications	16 (9%)	1 (3%)	0.27
Main diagnosis at admission			0.0004
Shock	59 (33%)	16 (50%)	
Coma	36 (20%)	3 (9%)	
Postoperative care	48 (27%)	5 (16%)	
Respiratory failure	25 (14%)	2 (6%)	
Trauma	4 (2%)	0 (0%)	
Multiple organ failure	5 (3%)	0 (0%)	
Renal failure	1 (<1%)	2 (6%)	
Other	2 (1%)	4 (13%)	
Heart rate (beats per minute)	92 ± 21	99 ± 26	0.09
Systolic BP (mm Hg)	121 ± 22	111 ± 27	0.041
Diastolic BP (mm Hg)	58 ± 10	56 ± 13	0.60
Mean BP (mm Hg)	77 ± 13	74 ± 17	0.24
Mechanical ventilation	144 (79%)	30 (94%)	0.09
Ramsay sedation scale[b]			0.13
>4	101 (56%)	24 (75%)	
4	33 (18%)	3 (9%)	
≤3	46 (26%)	5 (16%)	
Cardiac arrhythmia[c]	68 (37%)	14 (44%)	0.24
Capillary refill time			<0.0001
<2 s	105 (58%)	7 (22%)	
2–4 s	62 (34%)	8 (25%)	
>4 s	12 (7%)	17 (53%)	
Not measured	3 (1.6%)	0 (0%)	
Tissue edema			0.16
None	86 (47%)	21 (66%)	
Moderate (only ankles, hands, elbows, sides)	59 (32%)	7 (22%)	
Important	37 (20%)	4 (12%)	
Body core temperature ≤36.5°C	23 (13%)	9 (28%)	0.08
Delay between ICU admission and measurements (days, median [IQR])	4.4 [1.5–8]	1.6 [0.5–6.2]	0.018
Patients with circulatory failure	111 (61%)	26 (81%)	0.045
Type of circulatory failure (main cause)			0.51
Septic shock and severe sepsis	59/111 (43%)	13/26 (50%)	
Cardiogenic shock	34/111 (31%)	4/26 (15%)	
Effects of mechanical ventilation and sedation[d]	12/111 (11%)	2/26 (8%)	
Hemorrhagic shock	5/111 (4%)	1/26 (4%)	
Others (trauma, hypovolemia, combinations, etc)	14/111 (11%)	6/26 (33%)	
Mean BP <65 mm Hg	31/111 (28%)	8/111 (31%)	0.99
Skin mottling	26/111 (23%)	18/26 (69%)	<0.0001
Catecholamines (μg/kg/min)	*n* = 88 (79%)	*n* = 20 (77%)	1.0
	0.3 (0.1–0.4)	0.6 (0.04–1.0)	0.60
Norepinephrine	*n* = 66 (61%)	*n* = 17 (65%)	0.82
	5.1 (3.0–8.1)	6.2 (5.8–11.2)	0.21
Dobutamine	*n* = 33 (30%)	*n* = 5 (19%)	0.40
	NA	NA	
Others	*n* = 6 (6%)	*n* = 4 (15%)	0.19
Delay between onset of circulatory failure and measurements			
<6 h	22 (20%)	7 (26%)	0.66
<24 h	40 (36%)	15 (56%)	0.10

Abbreviations: CNAP, Continuous Noninvasive Arterial Pressure; ICU, intensive care unit; IQR, interquartile range.

[a]Data collected in the medical file.

[b]Ramsay sedation scale, ranging from 1 (anxious and/or agitated and/or restless) to 6 (unresponsive).[35]

[c]Atrial fibrillation, atrial flutter, or frequent extrasystoles (≥1 of 6 heart beats).

[d]Including patients with brain injury and inadequate brain perfusion because of deep sedation.

the detection of intraarterial systolic BP <90 mm Hg, CNAP finger cuff readings were also reliable within 4 minutes after calibration (AUC_{ROC} at minute 4 = 0.94 [0.90–0.97]).

The ability to detect an intraarterial systolic BP >140 mm Hg was also similar among the 3 devices (AUC_{ROC} ≥0.88) with negative LRs <0.20 but positive LRs <5 (Figure 5; Supplemental Digital Content 4, http://links.lww.com/AA/B418).

Detection of Response to Therapy

CNAP finger cuff measurements after recalibration and the 2 automated brachial cuffs similarly detected a >10% increase in intraarterial mean BP with AUC_{ROC}s ≥0.89, positive LRs >5 but negative LRs slightly >0.2 (Figure 5; Supplemental Digital Content 4, http://links.lww.com/AA/B418).

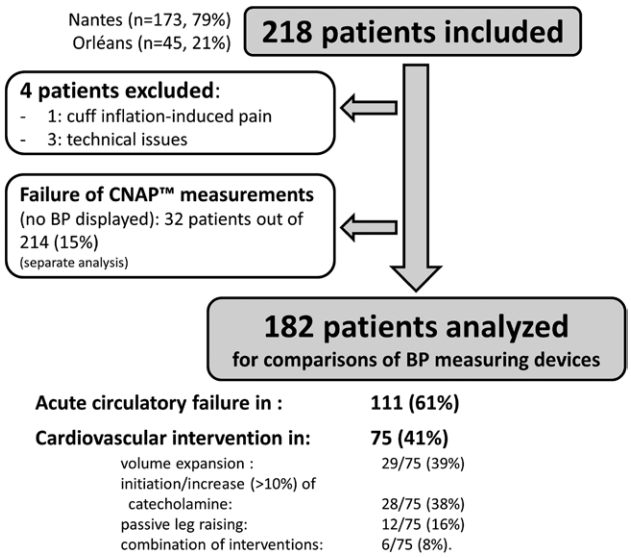

Figure 2. Study flowchart. CNAP indicates Continuous Noninvasive Arterial Pressure.

CNAP finger cuff readings at the 14th minute, that is, just before recalibration, misclassified many responders (75%) into nonresponders (Supplemental Digital Content 5, http://links.lww.com/AA/B418).

DISCUSSION

In ICU patients, CNAP beat-to-beat estimates of BP did not meet the criteria of acceptability of the United States national standard for the validation of BP measuring devices, the ISO standard.[22] The inaccuracy of CNAP's finger cuff calibration with its native automated brachial cuff may have contributed to this finding. There is a more reliable automated brachial cuff than the one tested. In addition, the drift of beat-to-beat CNAP finger cuff readings was relevant, especially if a short-term cardiovascular intervention was performed, stressing the need for frequent recalibrations. However, within 4 minutes after calibration, the CNAP finger cuff reliably detected hypotension.

Strengths of the Study

This is the largest study (182 patients) addressing the reliability of a noninvasive device for continuous BP monitoring (CNAP or even other devices).[17] In addition, few studies included ICU patients.[13–16] This is the first study testing, in the same population, noninvasive continuous and intermittent measurements of BP (Table 2).

CNAP Reliability

Beyond their limited size, most studies addressing CNAP's reliability lacked the use of the ISO standard or inadequately applied the standard, that is, did not consider the abovementioned zero-zone.[15,17,21] Hence, the use of nonconsensual definitions of the reliability itself may explain the heterogeneous conclusions of previous studies.[18] Applying the ISO criteria, our study highlights that the poor accuracy of CNAP calibration with the native automated brachial cuff is a major weakness of the currently commercialized CNAP device.

Table 2. Agreement Between Intraarterial and Noninvasive Measurements of Blood Pressure (BP)

	Bland-Altman analysis		ISO standard	
	Mean bias ± SD (mm Hg)	Limits of agreement (mm Hg)	Mean $bias_{ISO}$ ± SD (mm Hg)	Validation of the ISO standard
Mean BP				
CNAP finger cuff[a]	7.2 ± 6.4	19.8; −5.3	6.2 ± 6.2	No
CNAP brachial cuff[b]	10.3 ± 6.9	23.7; −3.2	8.8 ± 6.8	No
Alternative brachial cuff[c]	−2.2 ± 6.4	10.3; −14.6	−1.8 ± 6.1	Yes
Systolic BP				
CNAP finger cuff[a]	−4.3 ± 13.8	22.7; −31.4	−4.1 ± 12.8	No
CNAP brachial cuff[b]	−4.1 ± 13.2	21.7; −29.9	−2.9 ± 11.5	No
Alternative brachial cuff[c]	−4.7 ± 12.6	19.9; −29.4	−4.0 ± 11.5	No
Diastolic BP				
CNAP finger cuff[a]	−9.7 ± 7.8	25.0; −5.6	−8.7 ± 7.2	No
CNAP brachial cuff[b]	−10.9 ± 6.5	23.7; −1.9	−9.6 ± 6.8	No
Alternative brachial cuff[c]	−4.99 ± 6.3	17.3; −7.3	−4.1 ± 5.8	Yes

Mean bias: mean of the differences (noninvasive − intraarterial) between the 2 techniques. Limits of agreement: mean bias ± 1.96 SD. For the calculation of the mean bias (mean $bias_{ISO}$), the ISO standard recommends taking into account the variability of intraarterial measurements via a "zero-zone" approach[19] (please see the "Statistical Analysis" section for details). Hence, the "crude" agreement calculated according to Bland and Altman slightly differs from the agreement derived from the ISO standard method. To pass the ISO testing, the mean difference (mean $bias_{ISO}$) between the 2 techniques must be ≤5 mm Hg and the SD of the errors ≤8 mm Hg.

Abbreviations: CNAP, Continuous Noninvasive Arterial Pressure; ISO, International Organization for Standardization.

[a]*Infinity CNAP Smartpod.*

[b]*Dräger Infinity Delta* monitor, used for the calibration of the CNAP technology.

[c]*Philips Intellivue MP70* monitor.

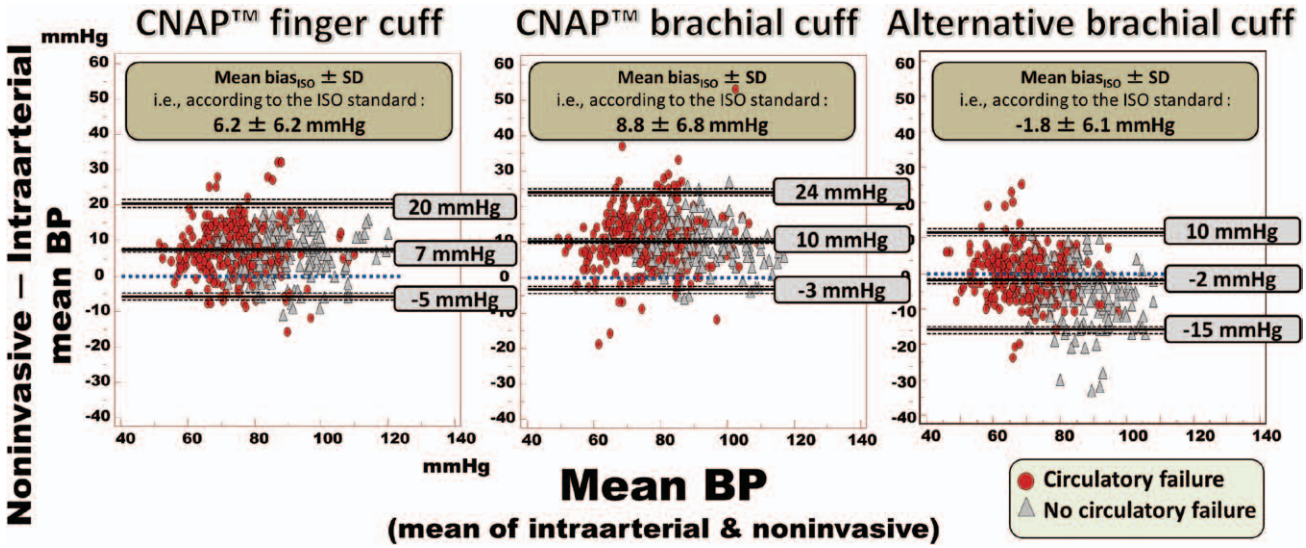

Figure 3. Agreement between intraarterial and noninvasive measurements of mean blood pressure (BP). Bland-Altman analysis, for each tested noninvasive device, of the agreement between 3 consecutive intraarterial and noninvasive measurements of mean BP in patients with (circles) and without (triangles) circulatory failure. The 3 thick horizontal lines represent the mean bias and the upper and the lower limits of agreement (mean bias ± 1.96 SD of the bias). The dotted lines represent their 95% confidence interval. The 3 Continuous Noninvasive Arterial Pressure (CNAP) finger cuff readings were collected during the 3 minutes after the brachial cuff calibration (first set of measurements, dedicated to International Organization for Standardization [ISO] standard testing, see Figure 1). For the calculation of the mean bias (mean bias$_{ISO}$), the ISO standard recommend taking into account the variability of intraarterial measurements via a "zero-zone" approach[19] (please see the Statistical Analysis section for details). Hence, the "crude" agreement calculated according to Bland and Altman slightly differs from the agreement derived from the ISO standard method (mean bias$_{ISO}$). When analyzing the CNAP finger cuff readings collected between 2 brachial cuff calibrations (ie, measurements collected from minute 1 to minute 14), the mean bias was 5.2 ± 9.5 mm Hg, with upper and lower limits of agreement of 23 and −13 mm Hg (Bland-Altman graph in Supplemental Digital Content 2, http://links.lww.com/AA/B418).

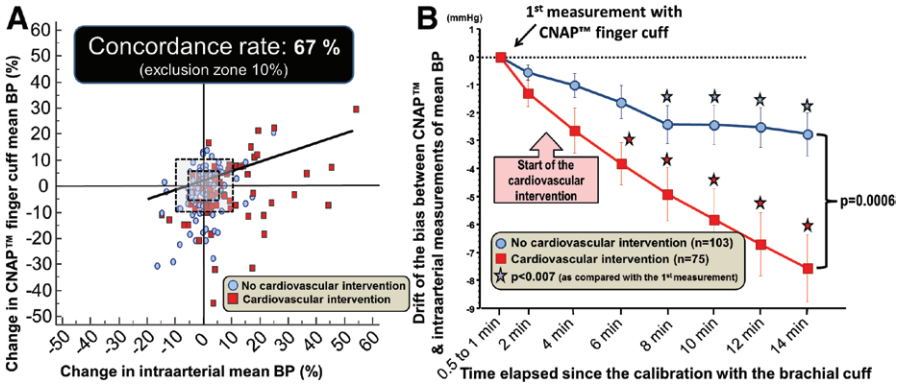

Figure 4. Trending ability and drift of Continuous Noninvasive Arterial Pressure (CNAP) finger cuff readings of mean blood pressure (BP) between 2 calibrations (15 minutes). A, Four-quadrant plots of changes in CNAP finger cuff against intraarterial measurements of mean BP. Exclusion zones of 5% and 10% are delineated by the smaller and the larger central square, respectively. Directions of changes had a concordance rate of 62% (95% CI, 53–71) (exclusion zone 5%) or 67% (95% CI, 55–79) (exclusion zone 10%). B, The drift of CNAP finger cuff measurements of mean BP over time. To account for changes in the actual patient BP, the *drift of the error* of CNAP readings (ie, the drift of the bias between CNAP readings and the reference intraarterial measurements) was analyzed rather than the simple drift of CNAP readings of BP. Dots represent mean changes in the bias. Bars represent 1 standard error. The bias between intraarterial and CNAP finger cuff readings of mean BP decreased over the 14 minutes after the calibration and stars indicate statistical difference ($P < 0.007$) with the bias of the first displayed CNAP finger cuff measurement. The drift since calibration, that is, the change of this bias over time, was of higher magnitude in patients undergoing a cardiovascular intervention than in patients with no cardiovascular intervention (at 14th min: −7.5 ± 10.2 and −2.9 ± 7.9 mm Hg, respectively, $P = 0.0008$).

The alternative automated brachial cuff we tested (Philips Intellivue MP70), in the same patients, exhibited higher accuracy even meeting the ISO standard for diastolic and mean BP, the 2 major components of BP for organ perfusion. This encouraging finding could possibly make the manufacturer markedly improve CNAP's reliability through simple replacement/upgrading of its oscillometric algorithm.

Trending Ability and Drift of CNAP Finger Cuff Beat-to-Beat Readings

Few studies with conflicting results assessed CNAP's trending ability: one study, in 25 patients in the operating room, considered the drift to be clinically irrelevant.[20] Another one, using only a comparison of early/late (up to 30 minutes after calibration) CNAP readings, found that late CNAP readings

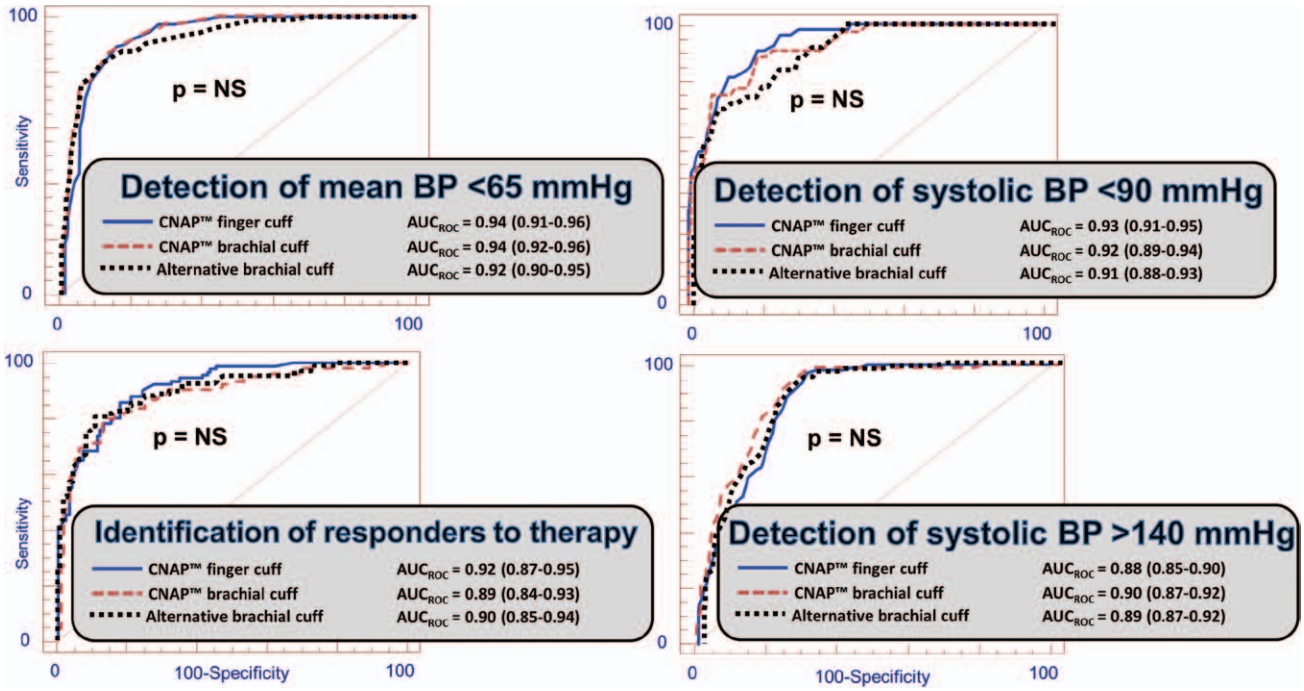

Figure 5. Noninvasive detection of hypotension, response to urgent therapy, and hypertension. Response to therapy was defined as a >10% increase in intraarterial mean blood pressure (BP) after a cardiovascular intervention. The detection of intraarterial diastolic BP >90 mm Hg was not addressed as only 4 patients exhibited intraarterial diastolic BP >90 mm Hg. Data are presented as receiver operating characteristic (ROC) curves. AUC_{ROC} were compared between devices, and *P* values indicated nonstatistically significant differences. AUC_{ROC} indicates area under the ROC curve (95% confidence interval); CNAP, Continuous Noninvasive Arterial Pressure.

were less reliable than earlier ones.[15] A third study reported, in 40 hemodynamically stable patients, better trending capabilities than that we observed but did not address the impact of cardiovascular interventions.[21] Importantly, therapy-induced changes in the properties of the arterial tree may cause a significant drift of CNAP readings with regard to the actual BP. If a cardiovascular intervention was performed over a 15-minute timespan between 2 calibrations, we found the drift of CNAP BP since the previous calibration to be markedly higher than otherwise: at the 14th minute, mean drift of −7.5 ± 10.2 vs −2.9 ± 7.9 mm Hg, $P = 0.0008$. To cope with this shortcoming, simply calibrating the CNAP at closer intervals, for example, every 5 minutes, may be sufficient to reliably detect hypotension and, to a lesser extent, therapy-induced changes in BP or hypertension.

Limitations

There are limitations to our study. The ISO standard has not been designed for critically ill patients.[22] However, it has the tremendous advantage of avoiding subjective and/or heterogeneous interpretations of what is/is not an acceptable performance.[18]

Intraarterial measurements were performed either at the radial or femoral level and the CNAP provided reconstructed brachial BP. This could be a source of physiological bias among measurements performed at brachial, radial, and femoral sites because BP varies along the arterial tree (pulse wave amplification phenomenon). Nonetheless, this phenomenon mostly alters systolic BP and, to a lesser extent, diastolic and mean BP.[34] Of note, the CNAP performed similarly when dividing the population with respect to the site of the intraarterial catheter (Supplemental Digital Content 3, http://links.lww.com/AA/B418).

Implications of Our Findings

First, the agreement of CNAP finger cuff readings with intraarterial readings improved until the next calibration. This was the result of the combination of (1) overestimation of BP by the brachial cuff calibration and (2) decrease over time (downward drift) of this CNAP overestimation of BP. In other words, mean values of CNAP measurements performed several minutes after the calibration were closer to intraarterial measurements than earlier CNAP measurements. This finding underscores that the timing of the collection of CNAP readings is of utmost importance when assessing the reliability of this device. Nevertheless, this timing has been rarely provided in previous studies addressing CNAP's reliability and may account for the heterogeneous reported performances.[17] Importantly, even for late CNAP measurements, the agreement with the intraarterial reference was imperfect (high SD) yielding insufficient detection of hypotension after the 4th minute after calibration.

Second, brachial cuff measurements and even CNAP finger cuff measurements collected within 4 minutes after the calibration enabled the identification of hypotensive patients and, to a lesser extent, hypertensive and therapy-responding patients (pending recalibration of CNAP finger cuff). This basic information may be sufficient in the resuscitation phase, before an arterial line is inserted in optimal conditions and after urgent diagnostic and therapeutic interventions are performed.

Finally, in 15% of patients, no beat-to-beat CNAP measurement could be displayed. However, brachial cuff measurements were still available in those patients and appeared as reliable as in other patients (Supplemental Digital Content 6, http://links.lww.com/AA/B418).

CONCLUSIONS

In ICU patients, CNAP did not fulfill the ISO criteria and exhibited a significant between-calibration drift. This considerably limits its usefulness. However, it reliably detected hypotension within 4 minutes after calibration. An alternative automated brachial cuff was more reliable than the native cuff used for calibration. This information is important to clinicians using those devices and for further development of the CNAP technology.

DISCLOSURES

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Contribution: This author helped in study design, conduct of the study, data collection, data analysis, and manuscript preparation.
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