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Tracking blood pressure changes by means of non-invasive intermittent blood pressure measurements in clinical application

Tracking capabilities of non-invasive intermittent blood pressure measurement devices fulfilling DIN EN ISO 81060-2 – A simulation study

Abstract: Considering accuracy/precision cut-offs of 5 ± 8 mmHg and cut-off values for inter-class correlation coefficients ($ICC=0.37\dots 1$, from DIN EN ISO 81060-2), absolute and relative errors in time independent measurement of blood pressure changes with non-invasive intermittent devices (NiBP) are derived mathematically for mean arterial blood pressure range of 40-180 mmHg. As a clinically relevant value for change of arterial blood pressure 20% of the baseline blood pressure is considered. The mean ratio between the change of BP measured by the NiBP and measured by the invasive reference device ($TE_{\%}$) were proposed as quality measure for the evaluation of NiBP device tracking capability. The proposed measure $TE_{\%}$ is theoretically independent of absolute accuracy but depends on precision and ICC of a device. NiBP devices show considerable maximum $TE_{\%}$ of 41% in tracking mean blood pressure changes respectively. In 10% of the measurements in the low blood pressure range $TE_{\%}$ exceeding 100%. The mean 50th/90th $TE_{\%}$ percentile over the whole blood pressure range were 25/61%, respectively. Furthermore, $TE_{\%}$ was relatively insensitive to assumed blood pressure range but sensitive to ICC.

NiBP devices have high relative error in tracking blood pressure changes that make those devices not well-suited for tracking blood pressure changes. The proposed tracking error allows the definition of reasonable accuracy/precision requirements of NBP devices.

Keywords: blood pressure measurement, inter-class correlation, standard, accuracy, precision, tracking blood pressure changes

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1 Introduction

Non-invasive continuous blood pressure devices (cNiBP) are being developed and increasingly used in clinical environment with measurement principles ranging from optical, optoelectrical to compensatory pressure measurements. To standardize and evaluate the quality in tracking blood pressure ΔP_{ref} changes in clinical application with a cNiBP (ΔP_{NiBP}), a relative tracking error $TE_{\%}$:

$$TE_{\%} = \frac{\Delta P_{NiBP} - \Delta P_{ref}}{\Delta P_{ref}} \quad (1)$$

has been proposed [1] and reasonable clinically relevant cut-offs are discussed in the development of an international standard for cNiBP devices. This is particularly important since cNiBP might potentially replace invasive monitoring or allow continuous BP monitoring in clinical applications where continuous monitoring is not available today, e.g. management of hypertensive crisis.

In clinical application invasive continuous BP monitoring is used regularly to prevent peri-operative hypotension. The physicians' goal in perioperative anaesthesia is to keep mean arterial pressure (MAP) above 60 mmHg or MAP change lower than 20 % of the pre-operative baseline MAP [2]. In the quest of defining relevant clinical cut-offs, tracking abilities of intermittent non-invasive blood pressure devices (NiBP) are typically referenced.

However, the tracking capabilities of such devices are not extensively investigated to the authors' knowledge. In this contribution, the theoretical range of tracking capabilities in terms of $TE_{\%}$ for clinically used NiBP devices is derived mathematically based on accuracy and precision criteria defined in DIN EN ISO 81060-2. Finally cut-off values for cNiBP devices are proposed and implications for NiBP devices are discussed.

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2 Methods

The minimum requirements for accuracy and precision of NiBP devices is defined as $\mu \pm s_n = 5 \pm 8$ mmHg (mean $\pm$ standard deviation over all paired measurements) in DIN EN ISO 81060-2. One additional requirement limits the with-in subject standard deviation S_m in the range of 4.79 to 6.95 mmHg depending on mean difference μ . Theoretically, overall variation between device differences may be separated into with-in subject δ_j and a random effects term ϵ_{ij} in the realm of variance analysis according to:

$$Y_{ij} = \mu + \delta_j + \epsilon_{ij} \quad (2)$$

with δ_j and ϵ_{ij} having zero mean value and are not correlated. Intra-class correlation coefficient may then be derived from:

$$ICC = \frac{s_m^2}{s_n^2} = \frac{s_m^2}{s_m^2 + s_e^2} \quad (3)$$

relating with-in subject precision S_m to grand total precision S_n , that in turn is the sum of S_m and a random Gaussian distributed error term S_e . ICC is theoretically bound in the range of 0 to 1.

During a blood pressure change $\Delta P_{ref} = P_2 - P_1$ within one subject a change in blood pressure is measured with an NiBP (ΔP_{NiBP}) and the respective error is defined as:

$$\Delta P = (P_2 + \mu \pm S_m) - (P_1 + \mu \pm S_m) - (P_2 - P_1) \quad (4)$$

This error would have the following theoretical mean and standard deviation being Gaussian distributed.

$$\mu_\Delta = 0 \text{ and } S_\Delta = \sqrt{2} S_m \quad (5)$$

However, experimentally determined μ_Δ might take positive values in the range up to 2.4 mmHg (10^6 simulations, 85 paired

Figure 1: Violin plots of blood pressure measured with NiBP device ($\mu = 5$ mmHg, $S_m = 4$ mmHg) at time points T_1 and T_2 in the same individual and the respective difference (right) during a fall of reference blood pressure by 20 mmHg.

measurements, 95% confidence interval: -2.41 to 2.41 mmHg). Therefore a maximal $^{exp}\mu_\Delta = 2$ mmHg is considered here.

In order to derive cut-off values irrespective of sign, the absolute of the numerator of Equation 1 has to be considered and thus $|TE_\%|$ is distributed according to folded Gaussian distribution and percentiles P of $|TE_\%|$ were derived numerically from

$$\frac{1}{2} \left[\text{erf} \left(\frac{x+\mu}{\sqrt{2}\sigma} \right) + \text{erf} \left(\frac{x-\mu}{\sqrt{2}\sigma} \right) \right] - P = 0 \quad (6)$$

using Newton-Raphson minimization.

A clinically relevant change of true blood pressure ΔMAP_{rel} not to be missed by the attending physician is assumed to be 20 % of baseline MAP. Therefore $TE_\%$ and its percentiles depend on the considered range of baseline MAP. MAP independent cut-offs for $TE_\%$ are proposed as mean of 50th and 90th percentiles taken over the considered MAP range. While physiological MAP ranges approx. from 60 to 140 mmHg, the effect of chosen MAP range on mean percentiles is investigated exceeding the range of implicit definition of hypotension and severe hypertension MAP equals to 70 and 133 mmHg, respectively according to international standard [3-4]. All modelling and analysis was done using R statistical programming language [5].

3 Results & Implications

3.1 Inter-class correlation of NiBP

ICC for NiBP devices fulfilling DIN EN ISO 81060-2 ranged between 0.34 and 1 with worst acceptable S_m and S_n (Figure 2). For the analysis of tracking blood pressure capabilities and $TE_\%$, ICC values of 0.4, 0.75 and 1 are considered.

3.2 Baseline MAP, $TE_\%$ and $^{exp}\mu_\Delta$

ΔMAP_{rel} range from 8 mmHg (for 40 mmHg) to 36 mmHg (for 180 mmHg) depending on the baseline MAP according to the 20% criterion. It might be argued if values as low as 40 mmHg are clinically relevant. Since ΔMAP_{rel} is 12 mmHg for 60 mmHg we conclude that at least 10 mmHg may be considered as lowest value to be captured for devices tracing continuous blood pressure changes.

Figure 3: ICC of NiBP devices according to DIN EN ISO 81060-2 with $S_n = 8$ mmHg.

Table 1: Percentiles of absolute TE (in mmHg) over the full range of MAP values for selected hypothetical NiBP with specific ICCs.

Perc.	ICC = 0.4		ICC = 0.75		ICC = 1	
	$\mu=2$	$\mu=0$	$\mu=2$	$\mu=0$	$\mu=2$	$\mu=0$
10 th	0.4	0.2	0.8	0.8	1.4	1.4
50 th	2.1	1.2	4.5	4.3	7.8	7.6
90 th	4.3	3.0	11.0	10.5	18.9	18.6

Absolute tracing error took values from 0 .. 2 .. 4 mmHg (10th .. 50th .. 90th percentile), 1 .. 5 .. 11 mmHg and 1 .. 8 .. 19 mmHg (Table 1).

This translated into a relative tracking error $TE_{\%}$ ranging from 1 .. 6 .. 12 % (10th .. 50th .. 90th percentile) at higher end of the considered MAP range and 5 .. 26 .. 54 % at MAP = 40 mmHg for a theoretical device having low ICC = 0.4 (e.g. $S_m = 5.1$ mmHg, $S_n = 8.0$ mmHg, Figure 2) and 4 .. 21 .. 52 % at higher end of MAP range and 18 .. 95 .. 233 % at MAP = 40 mmHg for a hypothetical device having ICC = 1 (e.g. $S_m = 5.0$ mmHg, $S_n = 5.0$ mmHg).

Modelling experimental $^{exp}\mu_{\Delta}$ into the simulation, showed only minor influences on 10th percentile in the range of 0 to 6 %.

3.3 Influence of considered MAP range

The range of baseline values had an effect on the mean 50th and 90th percentile over the MAP range depending on device ICC from 1 to 7 % and 2 to 16 %, respectively (Table 2).

Table 2: Dependence of mean of 50th and 90th percentile of $TE_{\%}$ in % on considered MAP range for hypothetical NiBP with spec. ICCs.

MAP	40-180 mmHg		60-160 mmHg		80-140 mmHg	
	50 th	90 th	50 th	90 th	50 th	90 th
ICC						
0.4	11	24	10	22	10	20
0.75	25	61	22	55	21	52
1	43	105	39	94	36	89

Figure 2: 50th and 90th percentile of absolute tracing error $TE_{\%}$ in % for typical values of inter-class correlation (ICC) and theoretical folded Gaussian distribution of differences between two Gaussian distributed measurements with $^{exp}\mu_{\Delta} = 0$ mmHg. Practically, $^{exp}\mu_{\Delta}$ may only be reached for infinite measurements. Therefore an $^{exp}\mu_{\Delta} = 2$ mmHg was derived from simulations with 85 single measurements acc. to DIN EN ISO 81060-2.

3 Conclusions

The presented theoretical analysis based on existing accuracy and precision criteria of international standards has the following implications for the blood pressure tracking capability of non-invasive intermittent blood pressure devices:

- Tracking blood pressure changes with NiBP may have an error of up to 19 mmHg.
- During hypotension this may result in an error of 54 to >200 %.
- During hypertension this may result in a relative error of 12 to 52 %.

Mean relative tracking error 50th and 90th percentiles of NiBP devices with low precision, but still meeting ISO EN 81060-2 criteria, may be as high as 25 and 60 %, respectively. This error may be considered to high to use NiBP devices for tracking blood pressure changes in cardiovascular unstable hypotonic patients in ICUs and operation theatres, aside from the generally low temporal resolution. These mean values should be considered when determining accuracy and precision requirements for up-coming non-invasive continuous blood pressure devices for clinical application. Additionally inter-class correlation may be discussed as an additional requirement for intermittent as well as continuous NBP devices.

TE_% cut-off values for continuous NiBP devices shall be well below mean values determined here for NiBP devices.

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