Title Page

A trial of 3 non-invasive BP monitors compared with invasive BP assessment in AF and sinus rhythm

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Abstract

Objective: To investigate accuracy of 3 non-invasive BP devices in AF compared with invasive arterial BP.

Methods: One hundred patients aged 45 to 90 years, 63% male (50 in AF and 50 age matched controls in sinus rhythm (SR)) were identified with arterial lines measuring beat-to-beat BP fluctuation. Non-invasive BP measurements utilising the manual sphygmomanometer (MS), PulseCor R6.5 (PC) and automated sphygmomanometer (AS) were taken simultaneously with invasive BP in a randomised sequence. This was repeated three times in each patient.

Results: In SR differences in systolic BP (SBP) for MS, AS and PC were -0.34 mmHg (95% CI -2.31 to 1.63; p=0.733), -3.80 mmHg (95% CI -5.73 to -1.87; p=0.0001) and -3.90 mmHg (95% CI -5.90 to -1.90; p=0.0001) and for diastolic BP (DBP) were 6.02mmHg (95% CI 4.39 to 7.64), 8.95 mmHg (95% CI 7.36 to 10.55; p<0.0001) and 7.54 mmHg (95% CI 5.89 to 9.18; p<0.0001), respectively. In AF mean differences in SBP for MS, AS and PC were -7.33 mmHg (95% CI -9.11 to -5.55; p<0.0001), -5.29 mmHg (95% CI -7.08 to -3.50; p<0.0001) and -5.75 mmHg (95% CI -7.54 to -3.96; p<0.0001) respectively and for DBP were 5.28 mmHg (95% CI 4.03 to 6.54; p<0.0001), 6.26 mmHg (95% CI 5.00 to 7.52; p<0.0001) and 6.89 mmHg (95% CI 5.64 to 8.15; p<0.0001) respectively.

Conclusions: The MS is accurate in SR due to direct assessment of Korotkoff sounds. Noninvasive BP assessment in AF is significantly less accurate. These findings have important prognostic and therapeutic implications.

Key Messages

What is already known about this subject? Accurate non-invasive BP measurement is essential to manage and prognosticate patients but is impossible in AF due to beat-to-beat variability of stroke volume and significant BP fluctuation preventing consistent assessment of Korotkoff sounds. Intra-arterial BP is the most accurate method of ascertaining true BP.

What does this study add? The traditional manual sphygmomanometer is highly accurate in sinus rhythm. All non-invasive device perform less well in AF.

How might this impact on clinical practice? The results of this study support increasing the use of ambulatory BP monitors in AF patients. This method is currently regarded as the most accurate non-invasive assessment of BP and, in taking multiple readings, the extreme variables in BP associated with AF would tend to regress to the true mean.

Introduction

Hypertension is the leading cause of cardiovascular comorbidity and mortality and is the most significant risk factor for atrial fibrillation (AF) [1]. Accurate recording of blood pressure (BP) is crucial to both prognosticate and allow correct evidence-based management of patients [2] but is challenging in AF due to beat-to-beat variability of stroke volume and significant BP fluctuation preventing consistent assessment of Korotkoff sounds [3]. The American Heart Association in their Recommendations for Blood Pressure Measurements state that intra-arterial BP is the most accurate method of ascertaining true BP [4, 5]. However, it is impractical to insert invasive arterial cannulae to routinely measure BP. Therefore, medical professionals rely upon non-invasive BP (NIBP) assessment to make clinical decisions.

The aim of the study was to evaluate the accuracy of 3 non-invasive BP assessment modalities compared to intra-arterial assessment of BP in AF. The automated sphygmomanometer (AS) is the most commonly used device worldwide and is relied upon to inform management decisions for millions of patients annually. The traditional manual sphygmomanometer (MS) is now almost obsolete in clinical practice due to the extensive training requirement for health professionals and the time-consuming nature of this approach. The PulseCor R6.5 (PC) is a novel device which measure peripheral BP from an oscillometric pressure cuff and also estimates central pressures in the ascending aorta using a physics-based model applied to low-frequency suprasystolic brachial artery pressure waveforms to reconstruct the central pressure. In addition, the device records pulse pressure fluctuation and arterial stiffness but it has never been tested in AF.

Methods

This prospective randomised study was performed at Eastbourne General Hospital, East Sussex Healthcare NHS Trust and was approved by the national ethics committee. Written informed consent was obtained from all patients. Inclusion criteria were patients aged over 18 years who could consent to the study with an indwelling arterial catheter in situ either on the intensive care unit (ICU) or undergoing an invasive cardiac procedure mandating insertion of an arterial line in the cardiac catheterization laboratory at Eastbourne General Hospital. The exclusion criteria were age <18 years or haemodynamic instability.

Invasive pressure measurements

For the 50 patients in AF and the 50 patients in SR, either femoral or radial arterial access was used to introduce a 4 F sheath under local anaesthesia employing the Seldinger technique which has been described previously [6]. Invasive measurements were collected at the start of the diagnostic coronary investigation for cardiac catherisation laboratory patients.

First, the arterial pressure transducer was leveled and zeroed to the intersection of the anterior axillary line and the 5^{th} intercostal space. Invasive systolic BP (SBP) and diastolic BP (DBP) were recorded whilst simultaneously recording NIBP according to manufacturers' instructions. NIBP measurements were repeated three times for each device in a randomised sequence.

Manual Sphygmomanometer (MS)

MS measurements were performed by three independent and experienced operators (WE, AA and VK) for all 100 patients (50 in AF and 50 in SR). A properly sized cuff at least equal to 80% of the circumference of the upper arm was used. The cuff was wrapped around the upper right arm with the cuff's lower edge one inch above the antecubital fossa. The stethoscope's

diaphragm was lightly pressed over the brachial artery just below the cuff's edge. The cuff was inflated rapidly to 180 mmHg. Air was then released from the cuff at a moderate rate (3mm/sec). Korotkoff sound 1 was identified as the onset of a clear "tapping' sound as the cuff was deflated and this defined the SBP. Korotkoff sound 5 was identified as the complete disappearance of any sound. The last audible sound defined the DBP (Korotkoff 4).

Automated Sphygmomanometer

The Philips IntelliVue MP30 (Guildford, Surrey, UK) was used in all patients. An appropriately sized cuff was chosen based on the circumference of the patients' arm. Four options were available: M1573A (20.5-28.0 cm), M1574A (27.0-35.0 cm), M1575A (34.0-43.0 cm) and M1576A (42.0-54.0 cm). The NIBP from the upper right arm was measured.

PulseCor R6.5

For all patients, the appropriately sized cuff was placed around the participant's upper right arm. The Pulsecor R6.5 (PC) (Auckland, New Zealand) device first inflated and deflated to identify oscillometric brachial SBP and DBP and then inflated again to 30 mmHg above oscillometric brachial systolic pressure for 10s during which the suprasystolic signals were recorded with the cuff, and central BP was estimated via a time-domain approach that assessed the relationship between the total oscillatory pressure in the aorta and the total oscillatory pressure under the occluded brachial artery [7].

Statistical analysis

Statistical analyses were performed using SPSS statistical software (version 22, IBM Corp, New York, USA) and SAS 9.4 (SAS Institute, Cary NC). Data are expressed as percentages for discrete variables and as mean ± standard deviation for continuous variables. Continuous

variables were compared by ANOVA. Categorical comparisons were compared using Chi-square analysis and non-parametric inferential statistical analyses were performed using Mann-Whitney U and Wilcoxon signed-rank test.

The agreement between invasive and noninvasive pressures was estimated using generalized linear mixed models, grouping repeated observations within subjects with random intercepts for patients. A p-value of less than 0.05 was considered significant.

Results

One hundred and thirteen patients were screened. Thirteen patient were excluded: 7 refused consent and 6 had arterial lines displaying significant interference and artefact on the arterial trace. One hundred patients (age 45 to 90, 63% male) were recruited. Baseline demographics are displayed in Table 1.

Sinus Rhythm (see Figure 1)

In SR mean differences in SBP from invasive BP for MS, AS and PC were -0.34 mmHg (95% CI -2.31 to 1.63; p=0.733), -3.80 mmHg (95% CI -5.73 to -1.87; p=0.0001) and -3.90 mmHg (95% CI -5.90 to -1.90; p=0.0001) respectively. The mean differences in DBP from invasive BP for MS, AS and PC were 6.02 mmHg (95% CI 4.39 to 7.64; p<0.0001), 8.95 mmHg (95% CI 7.36 to 10.55; p<0.0001) and 7.54 mmHg (95% CI 5.89 to 9.18; p<0.0001) respectively.

The MS was as accurate in SBP assessment as the gold standard invasive BP assessment. The other devices were significantly less accurate.

Atrial Fibrillation (see Figure 2)

In AF mean differences in SBP for MS, AS and PC from invasive arterial pressure were -7.33mmHg (95% CI -9.11 to -5.55; p<0.0001), -5.29mmHg (95% CI -7.08 to -3.50; p<0.0001) and -5.75mmHg (95% CI -7.54 to -3.96; p<0.0001) respectively. Mean differences of DBP in AF for MS, AS and PC were 5.28mmHg (95% CI 4.03 to 6.54; p<0.0001), 6.26mmHg (95% CI 5.00 to 7.52; p<0.0001) and 6.89mmHg (95% CI 5.64 to 8.15; p<0.0001). There was significant variability between the invasive and non-invasive devices in AF.

Discussion

Hypertension and AF are 2 important public health priorities. AF, the most frequent cardiac arrhythmia, is becoming a growing burden upon healthcare systems for several reasons. AF is associated with a 5-fold increase in the risk of stroke, a 3-fold increase in the risk of heart failure, and a 2-fold increase in the risk of mortality [8]

Hypertension is more powerful predictor of mortality in high- and low-income countries [9]. Lowering BP can substantially reduce premature morbidity and mortality in selected patients [1, 10, 11]. Hypertension remains the major preventable cause of cardiovascular disease and all-cause death globally. Office BP measurement is an ESC class I recommendation for the screening and diagnosis of hypertension [12]. The most commonly used assessment of office BP in the UK and worldwide is the AS [12]. International guidelines include important treatment thresholds to both initiate and increase antihypertensive drug therapy dependent upon overall cardiovascular risk profile. Medical professionals therefore rely upon accurate assessment of BP to make critical management decisions for patients. The classification of BP is based upon a range of readings e.g. high normal BP ranges from 130-139 / 85-89 mmHg and Grade 1 hypertension is classed as 140-

159 / 90-99 mmHg [12]. The accurate classification of BP is vital for both prognostic and therapeutic reasons and inaccuracies could result in patients being mismanaged.

No device performed well in AF compared with the gold-standard invasive BP monitoring. The results of this study confirm difficulties and complexities with non-invasive assessment of BP in AF. None of the non-invasive devices tested were accurate due to continuous pulse pressure fluctuation associated with this condition. The randomness of fluctuations of the stroke volumes due to R-R variability lead to large fluctuations of the levels of both SBP and DBP. The World Health Organization (WHO) do not suggest the precise recommendations how to estimate all the range of fluctuations associated with AF. This is the first study to assess the difficulties of non-invasive BP assessment in AF utilsisng the gold-standard of BP assessment, invasive arterial assessment, as the comparator.

The current study is in keeping with previously published work demonstrating that there are limited data and significant heterogeneity in studies assessing automated BP in AF [13]. The PC has the ability to measure pulse pressure fluctuation in AF but the device measures peripheral BP in a similar way to the AS and similar inaccuracies were found.

The majority of AF patients are hypertensive, as both conditions are common in the elderly and hypertension is a significant risk factor for AF [14]. Ambulatory BP monitoring is currently regarded as the most accurate method of hypertension diagnosis [2, 15, 16]. Given the difficulties associated with accurate NIBP assessment in AF the results from the current study would advocate lowering the threshold for performing ambulatory BP monitoring in AF patients because, in taking multiple BP readings, the extreme variables in BP associated with AF will hypothetically tend toward regression to the true mean.

The MS performs very well in the assessment of SBP in SR. SBP is the principal measurement for the classification of office BP and definitions of hypertension grade [12]. The study shows that this device can be relied upon to give accurate readings in SR. The MS

measures BP based on the onset of the first and fifth Korotkoff sounds audible over the antecubital fossa for SBP and DBP, respectively. The accuracy of the MS relies upon having a competent operator who needs to be able to select an appropriate-sized cuff (80% of the upper arm circumference), as well as being able to deflate the cuff at a relatively slow but continuous rate (2-3 mmHg/s) and accurately auscultate and discriminate between the Korotkoff sounds to provide a reproducible reading [17, 18]. The three operators in the current study were senior cardiology fellows with extensive training in MS use. Office BP is routinely performed by nursing staff and therefore the current study may not be representative of routine clinical practice. However, with adequate training nursing staff are highly proficient at utilizing the MS [19].

The widely used AS is not accurate in SR with readings almost 4mmHg lower and 9mmHg higher on average than invasive SBP and DBP respectively. The current study suggests that some patients with significantly elevated SBP might not be identified with this standard tool for BP assessment. In addition, patients with established hypertension could incorrectly be assessed to have reached their BP target putting them at risk. The importance of accurate BP assessment is highlighted in the recent ESC published SCORE (Systematic Coronary Risk Evaluation) charts which are assessments of 10-year cardiovascular disease mortality risk [2]. Accurate assessment of BP is an essential component of a SCORE assessment. The SBP inaccuracy demonstrated in the current study could have major implications. For example, a 55 year old male smoker with elevated cholesterol has an 8% 10 year risk of death if their SBP is 160 – 180mmHg but a 12% 10 year risk if their SBP > 180mmHg. The study demonstrates that the most commonly utilized assessment tool for BP assessment could potentially incorrectly prognosticate such patients leading to improper management.

The PC was not accurate in SR. However, this device has previously been shown to have high accuracy in estimating central SBP which is a better predictor of adverse cardiovascular outcomes [20]. Central pressure more directly determine cardiac loading and myocardial perfusion and knowledge of central arterial characteristics may, therefore, provide an advance in monitoring and titration of interventions in various cardiovascular diseases. Central BP was not assessed in the current study but given its importance the PC appears to have an important role in BP assessment and has been shown to have highly acceptable accuracy in central BP assessment compared with invasive arterial pressure [20]. However, patients with AF were excluded from this study and it is unknown if the accuracy of central BP in SR extrapolates to patients with AF.

Conclusion

None of the non-invasive devices were accurate in AF. The results of this study support increasing the use of ambulatory BP monitors in AF patients. This method is currently regarded as the most accurate non-invasive assessment of BP and, in taking multiple readings, the extreme variables in BP associated with AF would tend to regress to the true mean.

The MS is the most accurate assessment of SBP in SR and the results of this study advocate its use for routine office BP assessment, against trends to automated BP assessment.

Study limitations

Simultaneous assessment of BP by invasive and non-invasive means at exactly the same time and site would have improved the statistical power of the study. However, this is impossible as NIBP assessment mandates a systolic occlusion pressure which would prevent an accurate invasive reading.

Whilst all patients with AF experience heart rate variability, the degree of this will vary. Shorter RR intervals and greater heart rate variability are likely to result in even greater inaccuracy [21]. Incorporating heart rate variability into the current methodology could provide more insight into the cause of the inaccuracies found. This hypothesis requires further study.

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