

Accuracy of Doppler blood pressure measurement in continuous-flow left ventricular assist device patients

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Abstract

Aims Accurate blood pressure (BP) measurement in continuous-flow ventricular assist device (CF-VAD) patients is imperative to reduce stroke risk. This study assesses the accuracy of the Doppler opening pressure method compared with the gold standard arterial line method in CF-VAD patients.

Methods and results In a longitudinal cohort of HeartMate II and HVAD patients, arterial line BP and simultaneously measured Doppler opening pressure were obtained. Overall correlation, agreement between Doppler opening pressure and arterial line mean vs. systolic pressure, and the effect of arterial pulsatility on the accuracy of Doppler opening pressure were analysed. A total of 1933 pairs of Doppler opening pressure and arterial line pressure readings within 1 min of each other were identified in 154 patients (20% women, mean age 55 ± 15, 50% HeartMate II and 50% HVAD). Doppler opening pressure had good correlation with invasive mean arterial pressure ($r = 0.742$, $P < 0.0001$) and more closely approximated mean than systolic BP (mean error 2.4 vs. −8.4 mmHg). Arterial pulsatility did not have a clinically significant effect on the accuracy of the Doppler opening pressure method.

Conclusions Doppler opening pressure should be the standard non-invasive method of BP measurement in CF-VAD patients.

Keywords Heart failure; Haemodynamics; Blood pressure

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Introduction

Heart failure (HF) remains a prevalent and costly condition with an estimated 5.7 million affected patients and an annual cost of \$30.7bn in the USA.¹ Of all HF patients, an estimated 150 000–200 000 have advanced (stage D) HF refractory to medical therapy.² For this group of patients, heart transplantation has been the therapy of choice but is limited primarily by donor availability to roughly 3000 cases a year.³ As a result, durable ventricular assist device (VAD) therapy has been increasingly utilized, and nearly 18 000 continuous-flow VADs (CF-VADs) are implanted annually.⁴

Despite advances in VAD design, surgical technique, and medical management, VAD therapy is saddled by a high burden of adverse events frequently leading to death and disability. Among them, stroke, bleeding, and right ventricular failure are the most common and serious.⁴ For example, The HeartWare™ Ventricular Assist System as Destination Therapy of Advanced Heart Failure (ENDURANCE) trial showed an almost 30% risk of stroke per patient-year among HeartWare HVAD patients.⁵ Previous clinical trials and observational studies have shown that poorly controlled blood pressure (BP) is strongly associated with stroke and other adverse events.^{6–8} Thus, BP control is paramount in managing VAD

patients. The current International Society for Heart and Lung Transplantation (ISHLT) guideline for CF-VAD patients recommends BP management with a goal mean arterial pressure (MAP) of <80 mmHg, and the recently published ENDURANCE Supplemental Trial evaluating the impact of BP management on stroke rates used a MAP goal of ≤ 85 mmHg.^{9,10}

In order to improve BP control in CF-VAD patients, it is essential to have a reliable and preferably non-invasive method of measurement. Arterial line measurement remains the gold standard for BP measurement in CF-VAD patients, but it is invasive and generally requires monitoring in an intensive care unit. Non-invasive BP measurement in CF-VAD patients can be challenging as most CF-VAD patients have limited arterial pulsatility. Traditional auscultatory (Korotkoff sound) method and automated oscillometric method both presuppose pulsatility and often fail to obtain a reading in CF-VAD patients.¹¹ Even when a reading is obtained, the decreased signal-to-noise ratio jeopardizes its reliability. Using the Doppler ultrasound method to obtain an opening pressure is a non-invasive alternative that is increasingly adopted. For this method, a Doppler ultrasound probe is placed on the brachial artery, a standard cuff is inflated proximally on the ipsilateral arm, and pressure is recorded as the opening pressure when a flow signal is first detected as the cuff is deflated.

Despite more frequent use of the Doppler opening pressure method in clinical trials and routine practice, its accuracy and clinical usefulness have not been adequately studied. A few previous small studies had inconsistent results, and none were conclusive owing to small sample sizes.^{11–13} As a result, clinical trialists and front line clinicians have little evidence on which to build their BP measurement protocol. The recent ENDURANCE Supplemental Trial used a mixture of automated cuff and Doppler opening pressure method and arbitrarily subtracted 5 mmHg from the Doppler opening pressure to impute MAP. As far as we know, there are no published data to support the validity of this protocol. In this study, we aimed to comprehensively address the following unanswered issues: (i) the correlation and accuracy of the Doppler opening pressure compared with gold standard arterial line BP, (ii) whether Doppler opening pressure more accurately approximates MAP or systolic BP (SBP), and (iii) the effect arterial pulsatility has on the accuracy of Doppler opening pressure.

Methods

Sample

A prospective, longitudinal cohort of 154 patients who received either a HeartMate II™ left VAD (LVAD) or HeartWare HVAD at the University of Washington Medical Center was included. Non-invasive BP measurement in CF-VAD patients was prospectively obtained by Doppler opening pressure

per institutional protocol. When patients had an arterial line for invasive BP monitoring for any clinical indication, both arterial line MAP and Doppler opening pressure were recorded. All 154 patients had an arterial line at some point after VAD implantation. We obtained all pairs of Doppler opening pressures and arterial line BPs that were measured on the same patient within 1 min of each other from January 2015 to April 2018. Only BP measurements obtained during VAD support were included. All data were queried from the medical centre's electronic clinical data warehouse that stores data from our electronic health record system. Extreme outliers of Doppler opening pressure and arterial line BP (MAP < 30, MAP > 150, or arterial line pulse pressure < 0) were adjudicated as charting errors (<1% of sample). The study conformed to the principles outlined in the Declaration of Helsinki and was approved by the University of Washington institutional review board.

Statistical analysis

To assess the overall correlation of Doppler opening pressure and arterial line MAP, we fitted a linear regression model to paired observations using generalized estimating equations with independent working covariance and robust standard errors (SEs). To account for the hierarchical nature of the observations grouped by patient, we also fitted a model with compound symmetric working covariance. Correlation coefficients (r) were derived from the two models.

To determine whether Doppler opening pressure more closely approximates arterial line MAP or SBP, we compared the mean difference between Doppler opening pressure and arterial line MAP and between Doppler opening pressure and arterial line SBP. In addition, to determine the effect of arterial pulsatility on the accuracy of Doppler opening pressure, we calculated the mean error of Doppler opening pressure stratified by arterial line pulse pressure.

Results

Sample size

Our sample included 154 patients who underwent a total of 81 HeartMate II and 80 HeartWare LVAD implantations. Seven patients required VAD exchange resulting in two VAD implantations per patient during our study period. A total of 1933 paired Doppler and arterial line BP measurements were included for analysis (HeartMate II 994 pairs and HVAD 939 pairs). There was a median of seven paired measurements (inter-quartile range, 3–13) per patient-VAD. Patient baseline characteristics are summarized in *Table 1*.

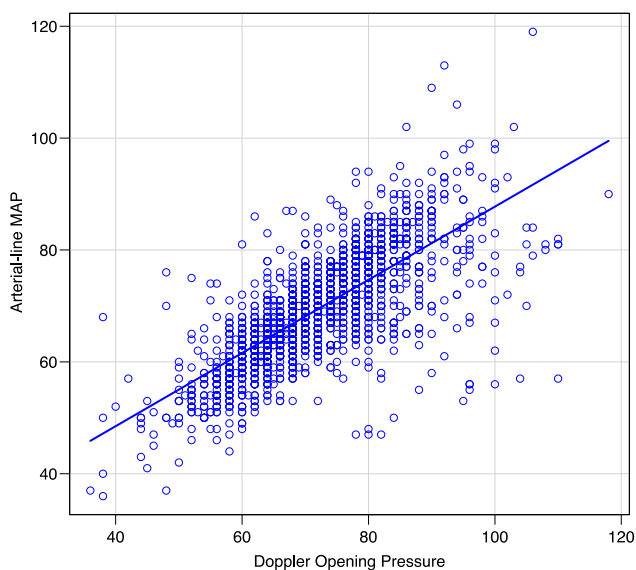
Table 1 Baseline characteristics

Characteristics	Patients (n = 154)
Age at VAD implantation (years)	54.6 ± 14.8
Female	19.5
Race (% White)	76.6
Device (n = 161)	
HeartMate II	50.3
HVAD	49.7
Mean arterial blood pressure (mmHg)	69.1 ± 9.7 (n = 1933)
Arterial pulse pressure (mmHg)	13 [7, 23] (n = 1933)

Values are mean ± SD, median [inter-quartile range], or %.

Correlation of Doppler opening pressure and arterial line mean arterial pressure

Doppler opening pressure had a highly statistically significant linear correlation with paired arterial line MAP (P -value < 0.0001) (Figure 1). Correlation analyses assuming independent samples and hierarchical samples resulted in similar results. For linear regression assuming independent samples, the intercept was 22.32 (SE = 3.77) and the slope was 0.654 (SE = 0.056) with a correlation coefficient r of 0.741. For generalized estimating equation model using compound symmetric working covariance, the intercept was 22.97 (SE = 1.07) and the slope was 0.658 (SE = 0.014) with a correlation coefficient r of 0.742. The correlation is better for HeartMate II than HVAD patients [HM2: r = 0.776 (95% CI 0.750, 0.799); HVAD: r = 0.709 (95% CI 0.675, 0.739)] (Table 2).

Figure 1 Overall correlation of Doppler opening pressure and arterial line mean arterial pressure (MAP) (P -value < 0.0001).**Table 2** Correlation and accuracy of Doppler opening pressure vs. arterial line mean arterial pressure

Device	r	Mean error	Median error	% within ±10
HeartMate II (n = 994)	0.776	2.0 [6.9]	2 [-2, 5]	87
HVAD (n = 939)	0.709	2.8 [8.2]	1 [-2, 5]	86
Combined (n = 1933)	0.741	2.4 [7.5]	1 [-2, 5]	87

All pressure units are in mmHg. r is correlation coefficient. Inter-quartile ranges are reported with median errors, and SDs are reported with mean errors.

Accuracy of Doppler opening pressure compared with arterial line mean arterial pressure vs. systolic blood pressure

Paired Doppler opening pressures and arterial line MAPs had a mean difference (Doppler minus arterial line MAP) of 2.4 mmHg (SD = 7.5 mmHg); 67% of the paired observations had a difference within ±5 mmHg, and 87% were within ±10 mmHg (Figure 2).

Paired Doppler opening pressures and arterial line SBPs had a mean difference (Doppler minus arterial line SBP) of -8.4 mmHg (SD = 8.5 mmHg); 37% of the paired observations had a difference within ±5 mmHg, and 64% were within ±10 mmHg (Figure 3).

Effect of pulse pressure on the accuracy of Doppler opening pressure

The accuracy of Doppler opening pressure compared with arterial MAP was assessed over different pulse pressure ranges

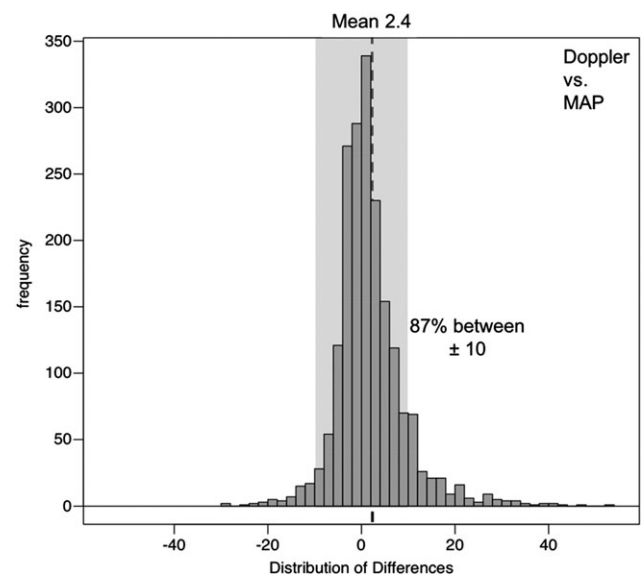
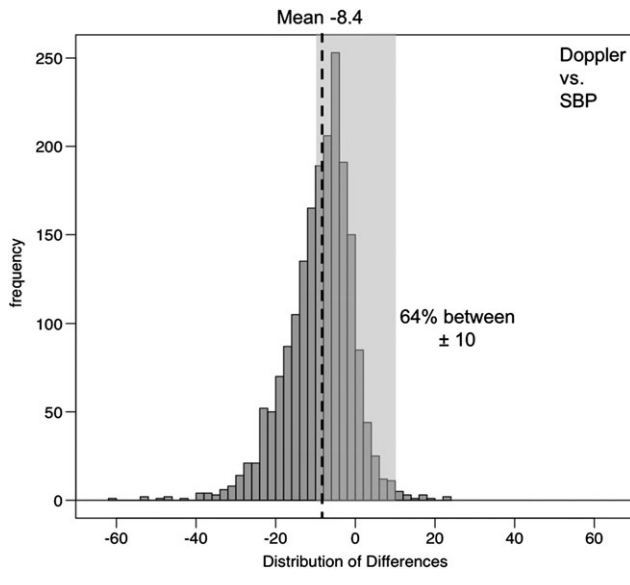
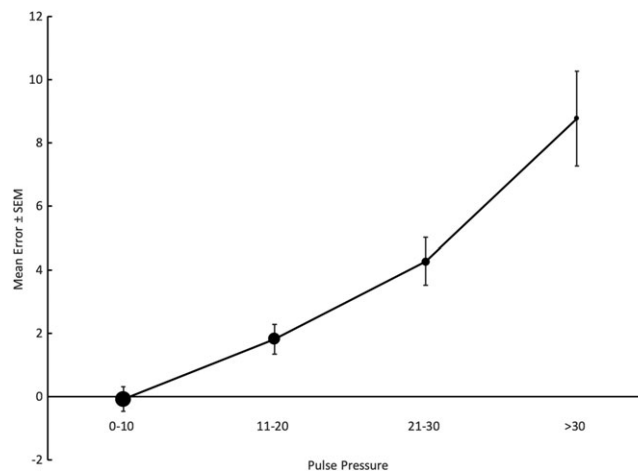
Figure 2 Distribution of differences between Doppler opening pressure and arterial line mean arterial pressure (MAP). All pressure units are in mmHg.

Figure 3 Distribution of differences between Doppler opening pressure and arterial line systolic blood pressure (SBP). All pressure units are in mmHg.



(0–10, 11–20, 21–30, and >30 mmHg). The percentages of observations in the aforementioned pulse pressure ranges are 39%, 31%, 18%, and 13%, respectively. The error of Doppler opening pressure (Doppler minus arterial line MAP) showed a statistically significant increasing trend with increasing pulse pressure (*Figure 4*). For patients with minimal pulsatility (pulse pressure, 0–10 mmHg), the mean error of Doppler opening pressure was only 0.1 mmHg. The mean error remains <5 mmHg for pulse pressure up to 30 mmHg.

Figure 4 Relationship between mean error of Doppler opening pressure and pulse pressure. All pressure units are in mmHg. The size of the round marker is proportional to the percentage of observations in each pulse pressure range.



Discussion

Significance

Our study addresses important and pressing clinical questions on the accuracy of Doppler opening pressure in measuring BP in CF-VAD patients. Previous studies on this topic were limited by small sample sizes and methodologic issues and had inconsistent results.^{11–13} Our study with 1933 paired observations is the largest sample size to date on this topic and larger than all previous studies combined, contributing to the validity of our study.

We showed that for both HeartMate II and HVAD patients, Doppler opening pressure has good correlation with arterial line MAP and more closely approximates MAP than SBP. In fact, on average, Doppler opening pressure had an error of only 2.4 mmHg, and 87% of the time Doppler opening pressure had an error <10 mmHg compared with arterial line MAP. This level of accuracy lends strong support for using Doppler opening pressure as the standard non-invasive BP measurement method in CF-VAD patients.

Our study corroborates the results of a smaller previous study that prospectively enrolled 17 HeartMate II patients and assessed the success rate and accuracy of four different non-invasive BP measurement methods.¹¹ In that study, Doppler method was the only method that reliably yielded a BP reading, and the mean difference between Doppler and arterial MAP was 0.2 mmHg compared with a mean difference between Doppler and arterial SBP of 8.6 mmHg. Another smaller previous study by Lanier *et al.* compared Doppler BP measurements vs. arterial line BP measurements in 30 HeartMate II inpatients and found that Doppler BP more closely approximated arterial line SBP (mean difference,

−4.1 mmHg) than MAP (mean difference, +9.5 mmHg).¹² This seemingly opposite result from Lanier *et al.* is likely because their study patients had much higher pulse pressure (median of 20 mmHg) than our study patients (median of 13 mmHg). In fact, when only patients with pulse pressure < 20 mmHg were analysed in the Lanier *et al.* study, Doppler BP was closer to arterial line MAP (mean difference of +3.0 mmHg) than SBP (mean difference of −5.5 mmHg).

Our study is also the first to date to systematically assess the effect of arterial pulsatility on the accuracy of the Doppler opening pressure method. Even though most CF-VAD patients have limited arterial pulsatility, there remains a minority of CF-VAD patients who have clinically relevant native cardiac output via the aortic valve. It has been hypothesized that in patients with significant pulsatility (wide pulse pressure), Doppler opening pressure would be closer to SBP and might overestimate MAP. We showed that, overall, Doppler opening pressure is closer to arterial MAP than SBP. In addition, even though there is a statistically significant trend for Doppler opening pressure to overestimate MAP as pulse pressure increases, it is not a significant clinical concern, as the overestimation is <5 mmHg over a wide range of pulse pressure (0–30 mmHg).

Our results should inform future BP monitoring protocol design in clinical trials. Current clinical trials have used heterogeneous BP measurement methods. For example, the recently published ENDURANCE Supplemental Trial designed to evaluate intensive BP management on stroke risk in HVAD patients permitted use of automated BP cuff if a palpable pulse is present and Doppler method if not.¹⁰ In addition, when the Doppler method was used in the trial, 5 mmHg was subtracted from opening pressure and imputed as 'MAP'. We are not aware of any evidence to support that protocol, and according to our findings described here, the Doppler opening method should be the default method, obviating subtraction by 5 mmHg.

Limitations

Our study has a large sample size of 1933 pairs of BP measurements. Nevertheless, it is a single-centre study with the associated limitations. In our study, all patients received arterial lines for clinical indications. At first, this may appear to be a limitation; however, our findings are predicated on the physical properties of continuous flow and hydrostatic pressure, so there is no reason to assume that accuracy would be less in ambulatory outpatients. In addition, the main theoretical concern for generalizing our results to outpatients is that hospitalized patients may have a higher pulse pressure than have outpatients, which we addressed by systematically analysing the accuracy of Doppler BP measurement over different pulse pressure ranges. Lastly, HeartMate 3 data have been collected and will be the topic of a future manuscript once the US embargo on the Multicenter Study of MagLev

Technology in Patients Undergoing Mechanical Circulatory Support Therapy with HeartMate 3 (MOMENTUM 3) clinical trial data is lifted. Therefore, our conclusions may not yet be generalized to HeartMate 3 or future VAD types not represented in our study.

Future research

Having demonstrated that Doppler opening pressure method is the most accurate method of non-invasive MAP measurement in CF-VAD patients, it will be imperative to assess the implications of consistently using this method in clinical practice. Using a BP management protocol where Doppler opening pressure method is used by default will lead to better BP control and reduced neurologic events. Future studies should compare clinical practices that use different MAP measurement methods and assess whether practices routinely using Doppler opening pressure have better outcomes.

Conclusions

For HeartMate II and HVAD patients, Doppler opening pressure has good correlation with arterial line MAP and more closely approximates MAP than SBP. Additionally, Doppler opening pressure has robust accuracy over a wide range of pulse pressure (0–30 mmHg). Therefore, our study lends strong support for using Doppler opening pressure as the standard non-invasive BP measurement method in CF-VAD patients. Future studies should examine whether a BP management protocol using Doppler opening pressure by default vs. other methods is associated with fewer neurologic and other adverse events.

Conflict of interest

C.M. has consulting relationships and is an investigator for Abbott, Medtronic, and Abiomed. J.A.B. has consulting relationships with Abiomed, Abbott, and Medtronic. K.K. has a consulting relationship with Abiomed, Abbott, and Medtronic and is an investigator for Abbott, Medtronic, and SynCardia. W.L. is a consultant for Abbott and Medtronic. G.W. is a consultant for Abbott. T. Dardas has received grant funding from Medtronic. The other authors report no conflicts.

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