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Improved Blood Pressure Prediction Using Systolic Flow Correction of Pulse Wave Velocity

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Abstract—Hypertension is a significant worldwide health issue. Continuous blood pressure monitoring is important for early detection of hypertension, and for improving treatment efficacy and compliance. Pulse wave velocity (*PWV*) has the potential to allow for a continuous blood pressure monitoring device; however published studies demonstrate significant variability in this correlation. In a recently presented physics-based mathematical model of *PWV*, flow velocity is additive to the classic pressure wave as estimated by arterial material properties, suggesting flow velocity correction may be important for cuff-less non-invasive blood pressure measures. The present study examined the impact of systolic flow correction of a measured *PWV* on blood pressure prediction accuracy using data from two published *in vivo* studies. Both studies examined the relationship between *PWV* and blood pressure under pharmacological manipulation, one in mongrel dogs and the other in healthy adult males. Systolic flow correction of the measured *PWV* improves the R^2 correlation to blood pressure from 0.51 to 0.75 for the mongrel dog study, and 0.05 to 0.70 for the human subjects study. The results support the hypothesis that systolic flow correction is an essential element of non-invasive, cuff-less blood pressure estimation based on *PWV* measures.

Keywords—Pulse wave velocity, Blood pressure, Wave propagation, True transit time, 1D mathematical model.

INTRODUCTION

Approximately 1 billion people suffer from hypertension, worldwide[35] increasing risk of debilitating and sometimes fatal events such as stroke and myocardial infarction. Hypertension often occurs without symptoms and is identified through physician visits and cuff-based blood pressure measurement. Continuous blood pressure (BP) monitoring is important for early detection of hypertension, for improving the treatment adherence of patients, and for identifying an excessive or insufficient antihypertensive effect of drugs.[8] Continuous BP measurement may aid in the diagnosis of resistant hypertension, where multiple classes of antihypertensive agents are ineffective in managing the blood pressure for the subject.[5] It may also be useful for the diagnosis of white coat and masked hypertension, and provides the only means of identifying abnormal BP shifts that occur during sleep (normally decreases by 10–20%) which are correlated with adverse cardiovascular events.[8] The ability to continuously monitor a person's blood pressure would lead to improved awareness and cost-effective preventive therapy.

Pulse wave velocity (*PWV*) is a non-invasive measure that offers the promise to continuously monitor blood pressure and has been studied extensively.[1,2,16,24] The *PWV* is calculated based on a measured true transit time (*TT*) and an arterial distance between measurement points as shown in Fig. 1. Measurements may be at two locations on the same artery, or often the electrocardiogram (ECG) r-wave is used as a starting reference combined with a distal measurement point with or without correction for pre-ejection period (*PEP*). While many studies consider only *TT*, it may be considered an equivalent corollary to *PWV* as these measures are linked through a distance that is constant within each study.

The Moens–Korteweg (c_{MK}) Eq. (1) was derived in 1878 from the wave equation for propagation of a pressure impulse within a thin-walled, perfectly elastic ($v = 0.5$), cylindrical tube.[19]

$$c = c_{MK} = \sqrt{\frac{\bar{E}h}{2r_0\rho}} \tag{1}$$

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Intra-Arterial *PWV*	
Gold Standard Invasive Method	Simultaneous pressure recorded invasively with pressure sensors just before the aortic root [a] and above the aortic bifurcation [b]
Alternative Method	Sequential ECG-gated recordings, just before the aortic root [a] and above the aortic bifurcation [b]
Distance	Length measured by radiographic images or catheter lengths
Non-invasive *PWV*	
Gold Standard Method	Simultaneous carotid [c] and femoral artery tonometry [d]
Alternative Method	ECG r-wave, impedance plethysmography for PEP, and distal pulse wave at the index finger [e].
Distance	Length measured from the sternal notch to the femoral artery at the groin or to the index finger

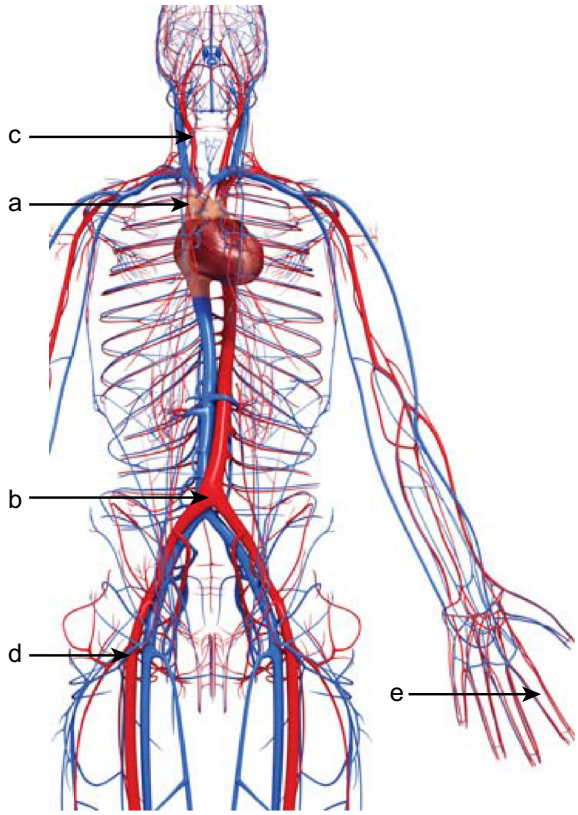

FIGURE 1. Illustration of measurement methods used for *PWV* and the associated anatomical locations.

where E is the elastic modulus for the wall, $\bar{E} = E/(1 - v^2)$, v is Poisson coefficient, h is the constant thickness of the wall, r_0 is the cross sectional radius of the unstressed cylindrical vessel at zero pressure ($p = 0$) and ρ is the density of blood. Details of the derivation may be found in a review by Hardung.[10] Young's modulus in this equation is the modulus of elasticity at zero pressure, however the modulus of elasticity changes with pressure. To match experimental data Hughes *et al.*[15] made an empirical correction to the Young's modulus as:

$$E = E_0 e^{\alpha p} \tag{2}$$

where α is a vessel coefficient, E_0 is the elastic modulus at zero pressure, and p is transmural pressure. The vessel coefficient was selected to match a specific canine's excised aorta based on a single plot of static pressure vs. Young's modulus.

Bramwell and Hill recognized that an increase in pressure increases the pulse wave velocity. They concluded that the foot to foot wave velocity increased proportional to diastolic pressure.[3,12] Varying pressure from 20 mmHg to over 200 mmHg they found an exponential relationship between *PWV* and pressure. Continuing experiments, where the velocity of different points on the pressure wave were measured optically and with a sphygmograph, suggests the systolic peak of the pressure pulse travels at higher velocity than the diastolic foot.[3] Histand-Anliker superimposed a low amplitude pulse train directly on the aorta to enable *PWV* calculations at different locations on the pulse wave (SBP, DBP).[13] They found a wave speed change of ~30% between diastole and systole. The interesting implication is that pressure pulse foot based *PWV* estimations are likely correlated with diastolic pressure; an implication supported by *in vivo* studies. Researchers have used this knowledge and empirically modified the c_{MK} equation (1) to use the dynamic Young's modulus Eq. (2) to link blood pressure into the Moens–Kortweg equation.[15,18]

Payne *et al.* conducted an *in vivo* study to determine the correlation between blood pressure and transit time on twelve healthy men.[29] Four vasoactive drugs (glycerol trinitrite, angiotensin II, norepinephrine, salbutamol) were administered intravenously to modulate physiological state. Two types of transit time were considered: ECG r-wave to the foot of the distal pulse wave (rPTT), and ECG r-wave to the foot of the distal pulse wave minus PEP to provide an estimate of TT. In both cases the distal pulse wave was measured using photoplethysmography at the dominant index

finger. They found TT was most closely correlated to diastolic blood pressure (DBP) $R^2 = 0.85$, while rPTT was most closely correlated to systolic blood pressure (SBP) $R^2 = 0.39$.

Ochiai *et al.* conducted a similar *in vivo* study with ten mongrel dogs that determined the correlation between blood pressure and *PWV*.[25] Hypertension was induced by continuous infusion of dobutamine and phenylephrine, while hypotension was induced by deepening isoflourane anesthesia, acute blood loss, and nitroglycerine infusion. Two types of transit time were considered: rPTT measured by the ECG r-wave to the foot of the pressure wave measured at the bifurcation of the abdominal aorta, and TT measured by the pressure wave at the ascending aorta to the pressure wave measured at the bifurcation of the abdominal aorta. Two intra-arterial catheter tip pressure transducers were placed distal to the aortic root and abdominal aorta bifurcation as shown in Fig. 1, locations a and b respectively. They found TT was most closely correlated to both DBP $R^2 = 0.92$, and SBP $R^2 = 0.81$ across all conditions. The correlation of TT to both DBP and SBP, and rPTT to SBP ($R^2 = 0.59$) were higher for Ochiai *et al.* than those found by Payne *et al.*, likely due to the internal aortic measurement locations. It is known that some of the drugs used in the studies affect the elastic arteries differently than the muscular arteries.[33] Nitroglycerin for example produces a peripheral vascular effect by relaxing the smooth muscle. The mid-sized peripheral arteries are muscular in nature and thus susceptible to nitroglycerin action.

Other studies have considered the effect of left ventricular ejection time (LVET) and its relationship to pressure and *PWV*.[23,24,32] Nurnberger *et al.* conducted a study of young, healthy males to determine if LVET was a determinant of *PWV*.[24] He studied 102 subjects under resting conditions and then six subjects under stimulation of β- or α- adrenoreceptors. They found that LVET may be an important determinant of *PWV* under resting conditions and andrenergic conditions in young, healthy males. A similar study over a large population of 3020 untreated subjects was conducted by Salvi *et al.*[32] They found an inverse linear association between *PWV* and LVET across all five age groups (<25, 25–44, 45–64, 65–84, and >85 years; $p < 0.0001$, $R^2 = 0.35$).

Building on this work we previously developed a non-linear traveling wave based mathematical approach to predict the dependence of *PWV* on transmural pressure and *LVET*. This first principles model reduces to the Moens–Korteweg speed of propagation under conditions of linear elasticity and zero pressure. An *in vitro* cardiovascular hemodynamic simulator was used to validate the theoretical predictions confirming an inverse quadratic relationship between *LVET* and PWV.[23] However the fundamental equations suggest that it is a flow velocity and the properties of the aortic wall, and not *LVET* explicitly, that influences *PWV* in arterial segments. In this study we found analytically and empirically that flow velocity is additive to the *PWV* predicted based on pressure and material properties alone.

While published results establish correlation between SBP or DBP and measures of pulse wave velocity (*PWV*, TT, rPTT), no measure has emerged as a robust predictor of blood pressure across the full physiologic range. The aim of this study is to test the theory that accounting for the flow contribution to *PWV* based on fundamental physics of wave propagation in nonlinear elastic arteries, will improve overall blood pressure prediction. The approach used is based on a novel mathematical model predicting *PWV*, accounting for nonlinear aspects of a convective fluid phenomena, hyperelastic constitutive relations, and finite deformation of the arterial wall.[22] In this work we propose the use of peak flow to correct *PWV* for determination of systolic blood pressure. To test our theory we use the mean data presented in Payne *et al.* and Ochiai *et al.*[25,29] Using linear regression and the coefficient of determination, we compare the correlation between pressure and measured *PWV*, flow corrected *PWV* (PWV_f), and rPTT.

Fluid–Structure Interaction Model

The potential of estimating arterial blood pressure based on *PWV* has been investigated based on statistical regression models, or empirical representation of an incremental isotropic elastic modulus as a function of a transmural pressure.[6,7] Models treating arteries as fluid-filled compliant thin walled cylindrical membrane shells have been validated using data from *in vitro* and *in vivo* studies.[20,22] Recent work accounting for nonlinear aspects of a convective fluid phenomena, hyperelastic constitutive relations, and finite deformation of the arterial wall affecting *PWV* is associated with the forward running wave velocity[22] as shown in Eq. (3). A derivation using the method of Riemann invariants is presented in Appendix A. PWV_f is a function of axial flow velocity (u), wall normal displacement nondimensionalized by vessel radius (η), blood density (ρ), and transmural pressure (p).

$$PWV_f = u + \sqrt{\frac{1+\eta}{2\rho} p_\eta} = u + PWV_p \qquad (3)$$

The partial derivative indicates sensitivity of pressure with respect to the wall normal deflection, and has a clear interpretation as tangent (incremental) moduli

in finite strain inelasticity. The right term of Eq. (3) presents PWV_f as a superposition of a peak flow velocity (u) and a pressure dependent PWV_p.

Flow Corrected PWV

PWV is classically measured at the foot of the forward moving distal pressure wave, since estimation from the peaks, or peak-to-peak velocity, can give considerable errors due to contamination with reflected waves.[21,26] During the diastolic cardiac phase the axial flow velocity is close to zero, allowing Eq. (3) to simplify to $PWV_f = PWV_p$. In both Payne and Ochiai, the diastolic PWV is used; there was no determination of a systolic PWV associated with peak flow and the peak of the distal wave.

A systolic PWV can be estimated from a foot based PWV measure with account of flow velocity as in Eq. (3) and a calibration based on arterial pressure and radius. Equation (3) reformulated to explicitly indicate a classical PWV measurement location for systolic and diastolic are shown in Eqs. (4), (5) respectively.

$$PWV_f = u + \sqrt{\frac{[(1+\eta)p_\eta]_{pk}}{2\rho}} \tag{4}$$

$$PWV = \sqrt{\frac{[(1+\eta)p_\eta]_{ft}}{2\rho}} \tag{5}$$

This leads to a systolic PWV based on a diastolic PWV measure in Eq. (6).

$$PWV_f = u + PWV\sqrt{\frac{[(1+\eta)p_\eta]_{pk}}{[(1+\eta)p_\eta]_{ft}}} \tag{6}$$

The subscripts pk and ft relate to the properties measured at the peak and foot respectively, and PWV is measured at the foot of the forward moving distal pressure wave. For linear elasticity $p_\eta = constant$, $\eta = \frac{pR}{Eh}$, in which E—linear elastic modulus, R—internal radius of the vessel, h- wall thickness, Eq. (6) can be written in a simplified form

$$PWV_f = u + PWV\sqrt{\frac{1+\frac{p_{pk}R_{pk}}{Eh}}{1+\frac{p_{ft}R_{ft}}{Eh}}} \tag{7}$$

The numerical result under the square root is a correction coefficient that accounts for shifts in PWV due to transmural pressure. In this work the correction coefficient was set to unity since the required measurements were not recorded in the referenced papers.[25,29] PWV is calculated by dividing the constant arterial distance by the foot to foot transit time of the pressure wave with referenced lengths provided in the supplemental section for Ochiai *et al.* and Payne *et al.*

METHODS

While flow was not directly measured in the referenced papers, the peak flow velocity can be estimated using measured values of ejection volume, LVET and aortic radius. Peak flow velocity (m/s) was calculated using the systolic aorta cross-sectional area (CSA) assuming a circular cross-section, LVET, cardiac output (CO) and heart rate (HR).[26]

$$u = \frac{CO/HR}{CSA}/LVET \tag{8}$$

Left ventricular ejection time (LVET) was calculated from PEP using a conservative fixed ratio of $PEP/LVET = 1/3$,[17,26] and an average aortic radius was used for each species, human and dog.[17,27] Systolic PWV was corrected for flow, using Eq. (7). A simple modification of Eq. (8) accounting for a typical profile of a time dependent aortic flow, is presented in supplemental section titled aortic flow and systolic flow velocity. The SBP and mean blood pressure was presented by Ochiai *et al.* and the DBP was calculated by equation (S1). Statistical analysis was completed to calculate the coefficient of determination (R^2) and analysis of variance (ANOVA).

Payne *et al.* modulated cardiac output in healthy male subjects (mean age 22 years) using four drugs. Angiotensin II is a peptide hormone that causes vasoconstriction and a decrease in CO.[14] Glycerol trinitrate, commonly used to treat angina, is known to decrease both CO and ejection volume. Norepinephrine released by the sympathetic nervous system increases the force that ventricular muscle fibers contract and effects both cardiac output and ejection volume.[9] Salbutamol is a vasodilator that causes a significant increase in heart rate and associated CO.[4,31] Blood pressure and PWV averages across all subjects for baseline and each pharmaceutical manipulation were used in this analysis. While the Payne *et al.* data lacks a direct cardiac output measure, literature provides averages for baseline and each of the pharmaceuticals as shown in Table SIII.

While the PWV vs. pressure curve is nonlinear,[15,20,22,26] both Payne *et al.* and Ochiai *et al.* fit a linear model using regression analysis. We have used the same R-squared statistics to compare with their published results.

RESULTS

To test our theory that a PWV_f based estimate of SBP is more accurate than PWV uncorrected for flow and rPTT, we used data from both Ochiai *et al.* and Payne *et al.*[25,29] This data allowed us to compare the coefficient of determination across the different physiological changes induced in the two studies and assess the statistical significance.

Flow Correction Improves Aortic PWV Correlation to Blood Pressure

Measured and flow corrected PWV and associated blood pressures for the mongrel dog aorta study of Ochiai *et al.* are provided in Table SII. A linear regression was performed and the associated coefficient of determination was calculated and compared as shown in Figs. 2a and 2b for PWV and PWV_f respectively for SBP. The same comparison was made for SBP and DBP (Figs. 2c and 2d). For both comparisons, PWV_f [Eq. (7)], significantly improves the linear fit of the data. ANOVA showed there is a significant positive relationship between pressure and PWV_f, $R^2 = 0.75$ and $p < 0.0001$. Multivariable ANOVA also shows there is a significant positive relationship for both systolic pressure and flow to PWV, $p < 0.0001$. Analysis of diastolic pressure vs. PWV resulted in a significant positive relationship with $R^2 = 0.92$ and $p < 0.01$ consistent with prior studies.[16,18,25,26,29]

Flow Correction Improves Peripheral PWV Correlation to Blood Pressure

Measured and flow corrected PWV and associated blood pressures for the human subject study of Payne *et al.*, with the distal PWV measurement point at the index finger, are provided in Table SIII. A linear regression was performed and the associated coeffi-

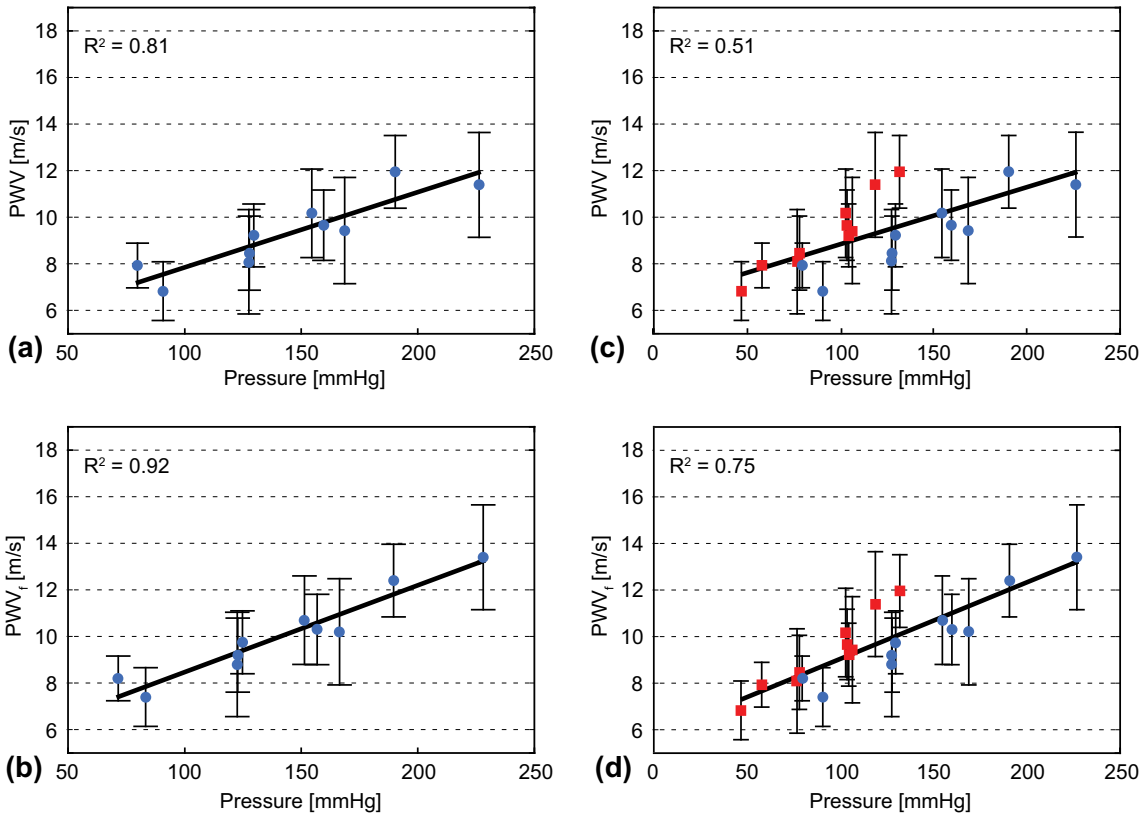

FIGURE 2. ***PWV_f* measured in the aorta improves blood pressure prediction. Error bars represent the standard deviation of *PWV* calculated from the referenced TT measurements from Ref. 25 and uncertainty in measures required for calculation of flow velocity. For all figures, the systolic pressure is represented by a circle and diastolic pressure is represented by a *square*. The left side includes SBP only while the right side includes all pressures (SBP and DBP). (a) *PWV* uncorrected for flow across measured SBP. (b) *PWV_f* corrected for flow velocity improves the correlation to SBP alone. (c) The lowest correlation was observed with *PWV* uncorrected for flow across measured pressures. (d) *PWV_f* corrected for flow velocity improves the overall correlation across all pressures. Analysis of diastolic pressure vs. *PWV* (data not shown) produced an $R^2 = 0.92$.**

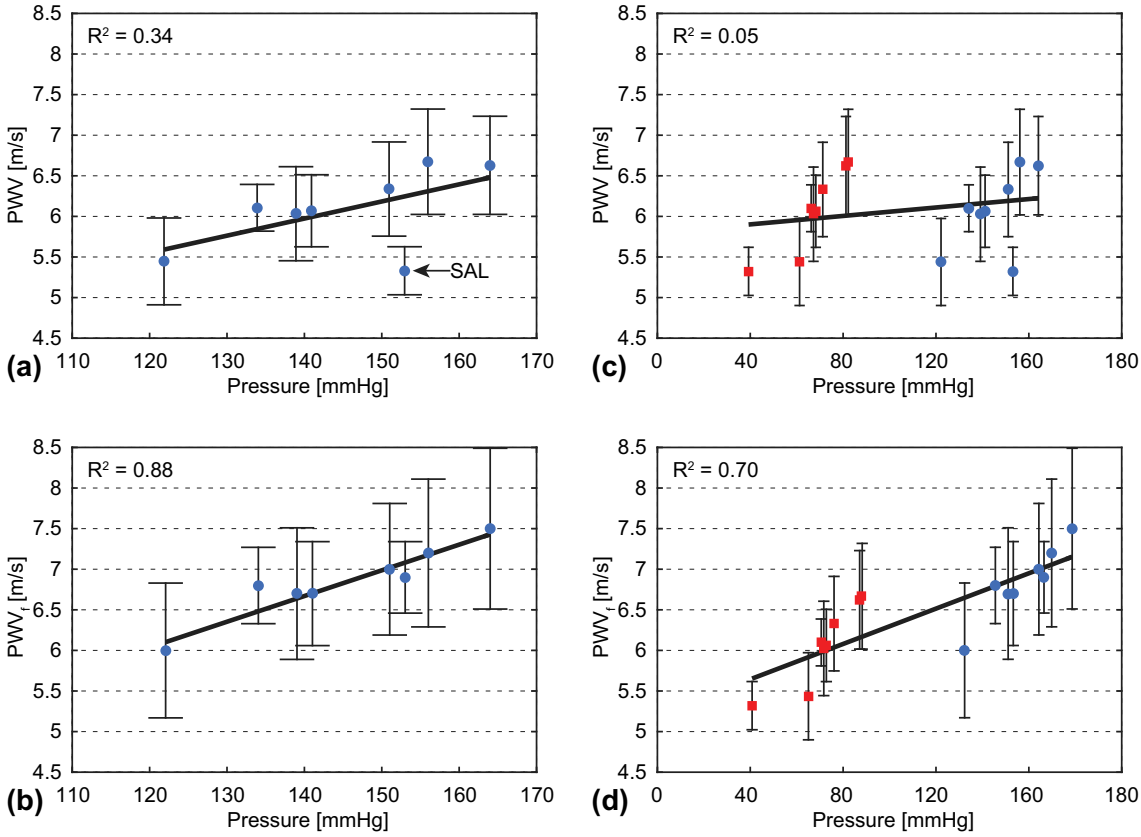

FIGURE 3. ***PWV$_f$*** **measured at the finger improves blood pressure prediction. Error bars represent the standard deviation for *PWV* calculated from the referenced *TT* measurement[29] and uncertainty in measures required for calculation of flow velocity. For all figures, the systolic pressure is represented by a circle and diastolic pressure is represented by a square. The *left side* includes SBP only while the right side includes all pressures (SBP and DBP). (a) *PWV* uncorrected for flow across measured SBP. Salbutomol (SAL) was furthest of any other measure from the trend line. (b) *PWV* corrected for flow velocity improves the correlation to SBP alone. (c) The lowest correlation was observed with *PWV* uncorrected for flow across measured pressures. (d) *PWV$_f$* corrected for flow velocity improves the overall correlation across all pressures. Analysis of diastolic pressure vs. *PWV* (data not shown) produced $R^2 = 0.85$.**

TABLE 1. Linear correlation for rPTT, *PWV*, *PWV$_f$* with pressure (SBP, DBP)

	Payne R^2	Ochiai R^2	Note
rPTT to SBP	0.39	0.59	NA
PWV to DBP	0.85	0.92	NA
PWV to SBP	0.34	0.81	No flow correction
PWV$_f$ to SBP	0.88	0.92	Flow correction
PWV to Pressure	0.05	0.51	No flow correction
PWV$_f$ to Pressure	0.70	0.75	Flow correction

cient of determination was calculated and compared as shown in Figs. 3a and 3b, respectively for SBP. The same comparison was made for SBP and DBP (Figs. 3c and 3d). For both comparisons, PWV_f [Eq. (7)], significantly improves the linear fit of the data. ANOVA showed there is a significant positive relationship between pressure and PWV_f, $R^2 = 0.70$ and $p < 0.0001$. Analysis of diastolic pressure vs. *PWV* resulted in a significant positive relationship with $R^2 = 0.85$ and $p < 0.01$ consistent with prior studies.[16,18,25,26,29] Multivariable ANOVA also shows there is a significant positive relationship for both systolic pressure and flow to *PWV*, $p < 0.01$.

Flow Corrected PWV Provides the Most Robust Correlation to Blood Pressure

It has been previously reported that the rPTT provides a stronger correlation to SBP,[29] while *PWV* provides a stronger correlation to DBP.[25,29]

As shown in Table 1, there was a good correlation between *PWV* and DBP for both Payne *et al.* and Ochiai *et al.* $R^2 = 0.85$, 0.92 respectively. However, using our PWV_f produced the highest coefficient of determination when compared to both *PWV* uncorrected for flow and rPTT. It is interesting to note that Payne's peripherally measured *PWV* to SBP data had the lowest R^2, which may be due to the influence of peripheral muscular arteries vs. the elastic nature of the aorta.

DISCUSSION

The main novel contribution of the present study is the introduction of PWV_f that improves correlation to blood pressure over both uncorrected *PWV* and *rPTT*. For diastolic pressure prediction, *PWV* measured at the foot, near the diastolic point should be used. PWV_f calculated using Eq. (7) allows correlation of *PWV* to SBP, with time point measurement at the diastolic foot of the waveform; a robust measurement point.

It has been observed in some papers that *rPTT* has a stronger correlation with systolic pressure than *PWV*.[25,29] We believe this correlation occurs because of the *PEP* component of rPTT. *PEP* accounts for a substantial and variable portion of *rPTT*, ranging from 12 to 35%[29] and has been shown to inversely correlate with contractility.[26] It is likely the observed relationship between SBP and *rPTT* is due to this embedded measure of contractility. For example, exercise results in increased SBP, increased contractility and decrease in *PEP*, driving an associated increase in flow velocity that in turn increases *PWV*. The result is a two-fold influence on *rPTT*; a reduction due to reduced PEP and shorter transit time. It was found that *rPTT* had an inverse linear correlation with SBP (combined average across all subjects and drugs) for Payne *et al.* and Ochiai *et al.* as $R^2 = 0.39$, and $R^2 = 0.59$, respectively. We found that based on Eq. (7), using flow corrected *PWV* produces an $R^2 = 0.88$ and $R^2 = 0.92$, respectively.[25,29] This approach offers the strongest fit of all the permutations considered, as seen in Table 1.

In this work Eq. (8) is used as an estimate of peak flow velocity. In other work, reviewed in the supplemental section, aortic peak flow has been found to be ~ 2 times average aortic flow.[28] Using this alternate estimate of peak flow our R^2 results improved from 0.7 to 0.87 and 0.75 to 0.85 for[29] and[25] respectively. These results are consistent with historic literature where peak volumetric flow in relation to the aortic pressure is most closely associated with the forward moving systolic peak pressure wave.[26–28] For a continuous estimation of SBP a flow based measure is required. An estimate is possible using a head balistocardiogram[11] or by using a percentage of PWV.[30]

Prior studies have recognized that compensating measured *PWV* with LVET may be important.[24,32] Salvi *et al.* and Nurnberger *et al.* found that a change in ejection time of ~40 ms (~12%) caused a change of *PWV* of ~1 m/s (~17%).[24,32] Salvi *et al.*[32] performed a large population study to explore the link between *PWV* and LVET. An inverse linear association was found between *PWV* and LVET at all ages ($R^2 = 0.35$, $p < 0.0001$).[32] Nurenberger considered all hemodynamic parameters (except flow velocity) and found at rest only DBP and LVET correlated to PWV. In our previous work,[23] we showed that increased flow velocity was responsible for the increase in *PWV* under conditions of decreasing LVET and fixed ejection volume. *PWV* was substantially affected by flow velocity (~10%) and peak pressure (~2%) changes controlled by ejection time. As represented in Eq. (7) PWV_f is effected by both flow and the physical properties of the aorta as represented by the correction coefficient. At diastolic pressure when flow is close to zero, *PWV* is dominated by the physical anisotropic properties of the aorta. At systolic pressure the pulse wave velocity is also affected by flow velocity. To estimate the impact of uncertainty of the input data upon PWV_f, we performed a sensitivity analysis using a variation of ±10% for each of the following data set (*C0, LVET, CSA*). We have found the R^2 varied from 0.73 to 0.76 for Ochiai *et al.* and from 0.64 to 0.73 for Payne *et al.*

Data for LVET was not presented in either the Ochiai *et al.* or Payne *et al.* studies. We recognize that under various physiological conditions this ratio is not always fixed. However, a conservative fixed ratio of $PEP/LVET = 0.33$ was used for all drugs and baseline.[17,26] To analyze the effect of a true measure of this ratio, salbutimol was considered, since it produced one of the largest changes in PEP (~−65 ms from the average baseline, Table SIII). Burgess *et al.* found a maximal decrease in $PEP/LVET$ of 0.070 that lasted for ~30 min for salbutamol *via* a nebulizer (2.35 mg).[4] When we decreased the $PEP/LVET$ ratio by this amount down to 0.27 (a 20% reduction) for the salbutamol data, the SBP to PWV_f R^2 value improved to 0.92 from the previously reported 0.88. It can be seen that salbutamol has the biggest impact on the uncorrected R^2 value in Fig. 3a (SAL). Since salbutamol increases cardiac output and decreases the PEP/LVET ratio, it causes the largest flow increase from the baseline.

The aortic *PWV* measure offered higher correlation than *PWV* measures at the periphery. Prior studies have found a ~20% increase in *PWV* when measured in the periphery (femoral-ankle) vs. central measures (carotid-femoral) caused by changes in arterial radius, thickness, and modulus of elasticity.[34,36] The correla-

tion difference is also likely caused by drugs that affect elastic arteries differently than the muscular arteries.[33] Nitroglycerin for example produces a peripheral vascular effect by relaxing the smooth muscle. This insight highlights that noninvasive sensors should be placed in close proximity to an elastic artery as possible for *PWV* measures to avoid the modulation of *PWV* possible in the muscular arteries.

In this work the correction coefficient was set to unity since the required measurements were not recorded in the referenced papers.[25,29] We recognize the physical properties of the aorta at SBP are different (less compliant) than those at DBP causing a faster moving pressure wave. To estimate the impact of the correction coefficient, referenced values[26] for both a canine and human were substituted into Eq. (7). The pressure to PWV_f R^2 values improved from 0.70 to 0.92 and 0.75 to 0.94 for Payne *et al.* and Ochiai *et al.* respectively. It is possible for future studies to perform per patient calibration as shown by Eq. (7) and measure the required aortic wall information using ultrasound. A PWV_f can then be calculated from a foot based *PWV* measure that is free from errors induced by reflected waves.[21,26] Additional studies are required to determine the advantage of this estimate and the associated improvement of SBP prediction.

Flow corrected PWV significantly improves PWV correlation to SBP, which is important for continuous cuffless blood pressure measures. Uncorrected data significantly overestimates a patient's systolic pressure, potentially leading to unneeded treatments. A key limitation of this study is the lack of published data that includes both flow velocity and PWV. Additional studies are required that explicitly measure aortic flow velocity along with PWV and vessel characteristics across a broad age range under varying physiological conditions.

CONCLUSION

Accounting for the flow contribution to *PWV* based on fundamental physics of wave propagation in nonlinear elastic arteries improves blood pressure prediction. It was found that flow corrected *PWV* correlates to SBP better than both uncorrected *PWV* and *rPTT* based on analysis of prior published studies with pharmaceutical induced blood pressure shifts. We found that using peak flow velocity to correct *PWV* produces robust blood pressure to PWV_f correlation for peripheral ($R^2 = 0.70$) and aortic ($R^2 = 0.75$) *PWV* measurements across the full range of physiologic pressure. Flow correction of *PWV* unifies the correlation curves, enabling both SBP and DBP to be associated with the same physical *PWV* measure.

ELECTRONIC SUPPLEMENTARY MATERIAL

The online version of this article (doi: 10.1007/s13239-016-0281-y) contains supplementary material, which is available to authorized users.

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CONFLICT OF INTEREST

Jeffrey S. Lillie, Alexander S. Liberson, and David A. Borkholder declare that they have no conflict of interest.

HUMAN AND ANIMAL RIGHTS AND INFORMED CONSENT

This article does not contain any studies with human or animal subjects performed by any of the authors.

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