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Cardiovascular

New algorithm to quantify cardiopulmonary interaction in patients with atrial fibrillation: a proof-of-concept study

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Abstract

Background: Traditional formulas to calculate pulse pressure variation (PPV) cannot be used in patients with atrial fibrillation (AF). We have developed a new algorithm that accounts for arrhythmia-induced pulse pressure changes, allowing us to isolate and quantify ventilation-induced pulse pressure variation (VPPV). The robustness of the algorithm was tested in patients subjected to altered loading conditions. We investigated whether changes in VPPV imposed by passive leg raising (PLR) were proportional to the pre-PLR values.

Methods: Consenting patients with active AF scheduled for an ablation of the pulmonary vein under general anaesthesia and mechanical ventilation were included. Loading conditions were altered by PLR. ECG and invasive pressure data were acquired during 60 s periods before and after PLR. A generalised additive model was constructed for each patient on each observation period. The impact of AF was modelled on the two preceding RR intervals of each beat (RR_0 and RR_{-1}). The impact of ventilation and the long-term pulse pressure trends were modelled as separate splines. Ventilation-induced pulse pressure variation was defined as the percentage of the maximal change in pulse pressure during the ventilation cycle.

Results: Nine patients were studied. The predictive abilities of the models had a median r^2 of 0.92 (inter-quartile range: 89.2–94.2). Pre-PLR VPPV ranged from 0.1% to 27.9%. After PLR, VPPV decreased to 0–11.3% ($P<0.014$). The relation between the Pre-PLR values and the magnitude of the changes imposed by the PLR was statistically significant ($P<0.001$).

Conclusions: Our algorithm enables quantification of VPPV in patients with AF with the ability to detect changing loading conditions.

Keywords: algorithm; atrial fibrillation; cardiopulmonary interaction; dynamic filling parameter; haemodynamic; mechanical ventilation; pulse pressure variation

Editor's key points

- Common dynamic haemodynamic indices, such as pulse pressure ventilation, cannot be used in patients with atrial fibrillation.
- This study evaluated a new algorithm that accounts for arrhythmia-induced pulse pressure changes in a small patient sample.
- The impact of mechanical ventilation on pulse pressure could be quantified in patients with atrial fibrillation using this algorithm.
- This work provides a potential tool for assessing fluid responsiveness in patients with atrial fibrillation.

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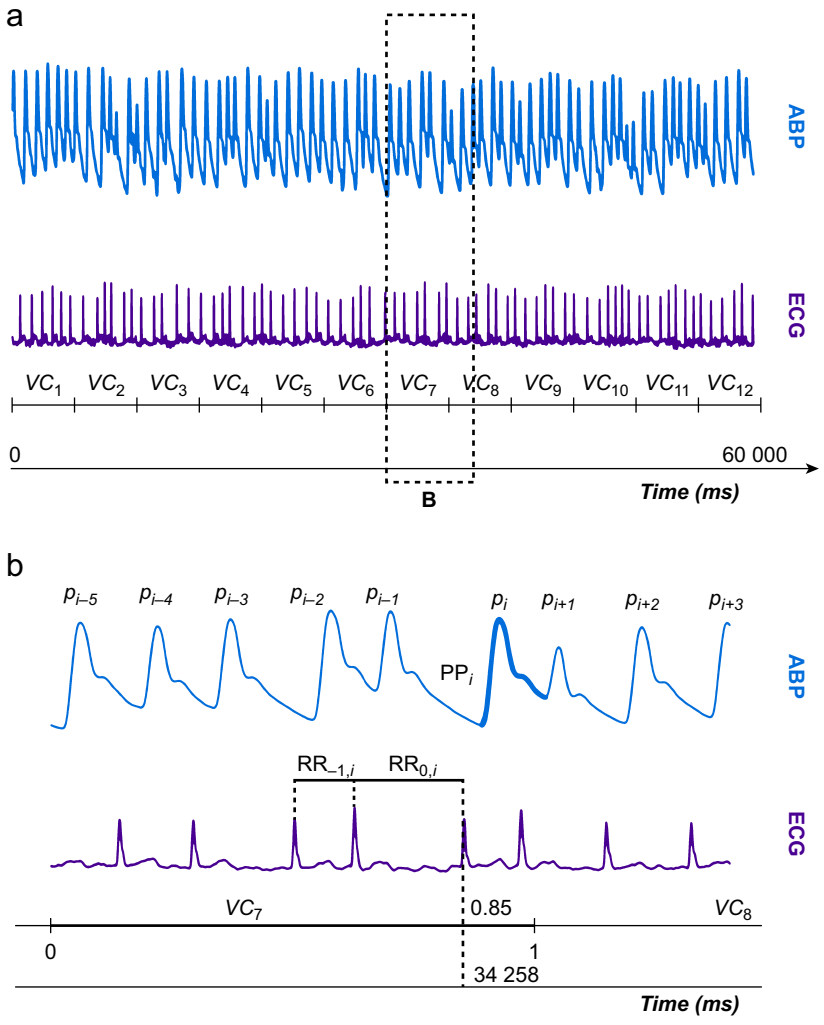

Fig 1. Terminology and schematic representation of the analysis of the raw data. (a) Raw data of a 60 s observation period. The arterial pressure (Line 1, red) and the ECG signal (Line 2) of the consecutive beats are shown. Line 3 shows the timing of the ventilator cycles (VC). (b) Detail from (a). For each pulse (pi), the pulse pressure (PP) and four variables were extracted. The two preceding RR intervals ($RR_{0,i}$ and $RR_{-1,i}$) as previously described,[11] the relative timing within each VC (Line 3) and its timestamp (Line 4). This procedure is repeated for every pulse within the 60 s input window. ABP, atrial blood pressure.

Dynamic filling parameters, such as stroke volume variation (SVV) and pulse pressure variation (PPV), have obtained a central place in haemodynamic management and volume therapy because of their reliability in predicting fluid responsiveness.[1,2] National and international guidelines[3,4] advise on the perioperative use of these parameters for goal-directed treatment, and they form the backbone of closed-loop haemodynamic systems that are being developed.[5] Still, there are some prerequisites to correctly use SVV and PPV.[6] These include closed chest conditions,[7,8] full mechanical ventilation at sufficiently high tidal volumes (TVs),[9] the absence of spontaneous breathing,[10] and the presence of a sinus rhythm (SR).[11,12] Some alternatives have been proposed to overcome the constraints for ventilator settings.[13,14] Major arrhythmias, such as atrial fibrillation (AF), however, remain an unresolved issue in this context. The prevalence of AF in patients presenting for surgery ranges from 0.8% to 3.7%,[15] a number that is only expected to increase in the future with an ageing population.[16] The inability to isolate the haemodynamic effects of an intrinsic irregular heart rhythm from those induced by mechanical ventilation precludes the clinical use of dynamic preload assessment with traditional monitoring techniques.

We have previously developed a model to predict the effect of an irregular heart rhythm on the beat-to-beat variation in pulse pressure (PP) in patients with AF, based on the duration of the two preceding RR intervals of each individual heartbeat.[11] This model, however, did not allow for quantification of other potential influencing factors on PP changes. Beat-to-beat changes of PP are indeed influenced by various additional factors.[17] In the current study, we present the principles of an adapted algorithm based on deconvolution of the blood pressure signal into separate functions. This allows separation of such distinct factors and the isolation and the potential quantification of ventilation-induced pulse pressure variation (VPPV).

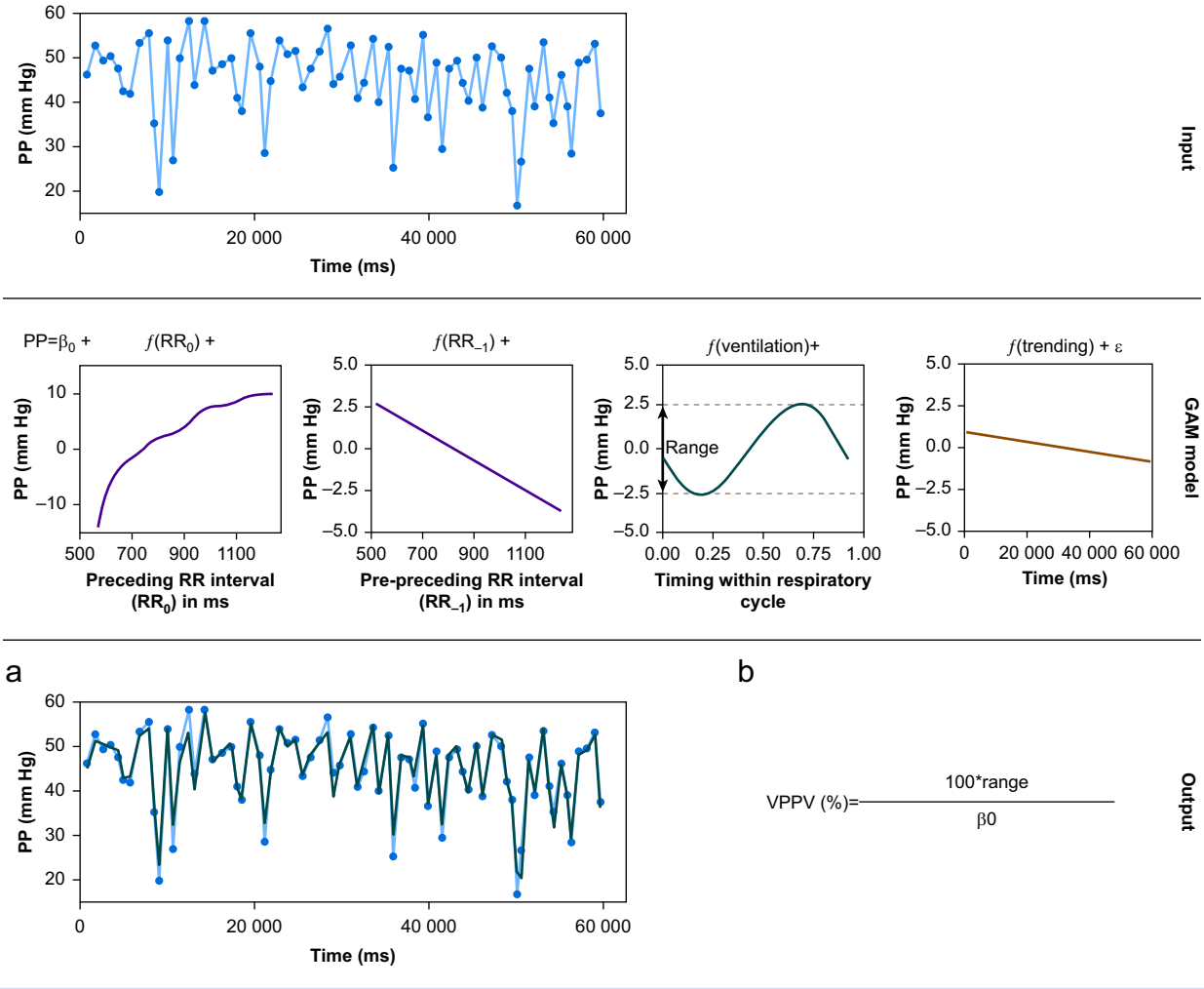

Fig 2. Schematic presentation of the analysis procedure. Input (upper panel): example of a full 60 s window. All consecutive, timestamped beats are plotted against the individual pulse pressure (PP; mm Hg). All individual beats are coded according to the procedure described in Fig 1. GAM model (middle panel): a general additive Model is calculated. PP is predicted as the sum of intercept (β_0) and the four functions: RR_0, RR_{-1}, the timing within the ventilation cycle, and the timestamp of each beat. Output (lower panel): (a) Example of the reconstructed signal. The fitted values for PP, based on the unique values of predictors of every beat, are projected in red over the raw signal for comparison. (b) Formula for quantification of the effect of ventilation (red function; middle panel) as a percentage of the range of the function over the intercept of the model.

To prove this, we tested the response of this new parameter to altered loading conditions induced by a passive leg raising (PLR) manoeuvre. Extrapolating from the knowledge of PPV in patients with a regular heartbeat,[18,19] we investigated the relationship between changes in VPPV imposed by PLR and the pre-PLR value. We hypothesised a proportional decrease of VPPV.

Methods

Compliance with ethical standards

After approval of the institutional trial board and ethics committee of Ghent University Hospital, Ghent, Belgium, this study was registered with the local code EC/2011/145 and with number B670201110842 for Belgium. Informed consent was obtained from all participants according to the Declaration of Helsinki and International Conference on Harmonisation/ Good Clinical Practice. The study took place between December 2011 and March 2014. This report concerns the second part of the study. The first part of the study consists of the same cohort of patients and is previously published.[11] Because of practical reasons (the presence of the researcher, availability of study monitors, etc.), a convenience sample was taken of consecutive patients who were planned for a pulmonary vein isolation under general anaesthesia. Patients were included if they fulfilled the following criteria: (i) age >18 yr; (ii) AF during the study period; and (iii) ASA 1, 2, or 3. Exclusion criteria were (i) participation in a clinical trial within the past 30 days, (ii) chronic obstructive pulmonary disease, (iii) right ventricular failure, (iv) aortic valve insufficiency or stenosis, and (v) an average heart rate of >140 beats min^{-1}.

Study procedure

All patients had a standard induction and maintenance of anaesthesia. A combination of bolus sufentanil 0.1–0.2 mcg kg^{-1}, propofol 2 mg kg^{-1}, and cisatracurium 0.15 mg kg^{-1} was used for induction. After intubation, sevoflurane (end-tidal concentration: 1.7–2.0%) was used for maintenance of anaesthesia and supplemented with aliquots of sufentanil 5 mcg to control analgesia. Besides the standard monitoring (5-lead ECG, pulse oximetry, and noninvasive blood pressure), a 3F catheter (Arterial Leadercath®; Vygon, Écouen, France) was placed in the radial artery. The transducer was levelled at the mid-axillary line and zeroed to atmospheric pressure.

During the different registration periods, ECG (Lead II and V2) and arterial pressure signals were stored at a sample rate of 1000 Hz using LabSystem™ Pro version 2.4a (BARD Electrophysiology, Lowell, MA, USA). Two registration periods of 60 s were used for further analysis: after stabilisation, a baseline measurement was taken with the anaesthetised patient in semi-recumbent position, and the same measurements were repeated immediately after careful adjustment of the bed position to perform the PLR manoeuvre, as described previously.[20]

Ventilator settings were the same for both periods: ventilatory frequency of 12 bpm with a I:E ratio of 1:2 and a TV of 8 ml kg^{-1} with PEEP set at 5 cm H_2O.

Data analysis

Data were analysed offline using a personal MATLAB® script based on the methods described by Li and colleagues.[21] For each observation period, PPV was calculated in the traditional way, as published previously.[22] These calculated values are referred to as 'PPV'. From the raw data of a 60 s observation period (Fig. 1a), four variables were determined in addition to PP for every individual beat. The first two variables, the preceding RR interval (RR_0) and the second preceding RR interval (RR_{-1}), were determined as described previously[11] (Fig. 1b). The third variable is the relative timing of the R wave of the ECG of the particular heartbeat within the 5 s respiratory cycle (Fig. 1b, line 3). The fourth variable that accounts for trending is the absolute time of the particular heartbeat within the 60 s observation period (Fig. 1b, line 4).

Modelling

Starting from the raw PP data of each observation period of 60 s (Fig. 2, upper panel), the individual impact of each of the variables was identified. A generalised additive model (GAM) was determined to predict PP based on RR_0 and RR_{-1} (the effect of an irregular heartbeat), 'ventilation' (the effect of ventilation), and trending of the pulse over time (the effect of low-frequency changes in PP).[17] Generalised additive model is an expansion of the traditional multiple linear regression model, allowing a non-linear function for each of the variables as follows[23]:

GAM formula: $PP=\beta_0+f(RR_0)+f(RR_{-1})+f(\text{ventilation})+f(\text{trend})+\varepsilon$ (Fig. 2)

The functions used in the model were penalised natural cubic splines for RR_0, RR_{-1}, and trend, and cyclic splines for ventilation, allowing for flexible non-linear modelling (for further explanation, see Supplementary material).

Table 1 Patient characteristics of included patients. Data are expressed as median (range). ACE, angiotensin-converting enzyme; CHA2DS2–VASc, congestive heart failure, hypertension, age, diabetes mellitus, and stroke–vascular disease, age, and sex category.

Sex (male/female)	6/3
Caucasian (%)	100
Age (yr)	59 (55–78)
Weight (kg)	95 (65–112)
Length (cm)	183 (160–185)
Cardiovascular comorbidity (*n*)	
Hypertension	6
Hypercholesterolaemia	1
Ischaemic heart disease	1
Corrected valvular disease	1
Corrected congenital heart disease	1
Congestive heart failure	0
Diabetes mellitus/metabolic syndrome (*n*)	3
Stroke/transient ischaemic attack (*n*)	2
Medication (*n*)	
Amiodarone	2
Digoxin	1
Flecainide	2
Beta blockers	5
Calcium channel blockers	2
ACE inhibitor/angiotensin II blockers	2
Diuretics	3
CHA2DS2–VASc score	1.5 (1–5)
ASA physical status	2 (2–3)

Ventilation-induced pulse pressure variation was calculated, in analogy of the classical model for PPV, as the range of impact of ventilation on PP, normalised for the mean of PP. The intercept of the GAM, β_0, is mathematically equal to the mean of the PP values of the data points included in the model:

$$\text{VPPV} = 100 * \frac{(f[\text{ventilation}]_{\max} - f[\text{ventilation}]_{\min})}{\beta_0}$$

The impact of variations in the length of the observation window was estimated in a *post hoc* analysis as follows. The algorithm to quantify VPPV was applied successively in progressively shorter windows, starting at the reference episode of 60 s with successive reductions of 1 s until the model indicated failure to solve the function. The resulting VPPVs were calculated for every step in the procedure, and absolute differences with the corresponding reference value ($VPPV_{60}$) were determined.

Statistical analysis

After testing for normality with the Shapiro–Wilk test, data are reported as median (inter-quartile range [IQR]) or mean (standard deviation) as appropriate. Comparisons between the two measurement periods were performed using a paired *t*-test or a paired Wilcoxon test for PPV and VPPV values. Correlation was assessed using the Spearman rank correlation coefficient. A *P* value <0.05 was considered statistically significant. Goodness of fit of each individual GAM was assessed based on the r^2. All statistical analyses were done using R (version 3.5.0; R Foundation for Statistical Computing, Vienna, Austria) base packages and 'mgcv' package (1.8–24; Woods SN) for GAM.[24]

Results

Ten patients were included in the study. Because of a technical problem with the invasive arterial blood pressure measurement, one patient was excluded. The patient characteristics are displayed in Table 1.

For all 18 observation periods (baseline and PLR in nine patients), the goodness of fit of the model was determined. The median amount of deviation of PP explained by the model was 91.3% (IQR: 89.2–94.2). The individual GAMs can be found in Supplementary Appendix 2.

RR_0 and RR_{-1}, the two predictors used to describe the effect of AF, were statistically significant in all 18 observation periods. Trending, the predictor for overall PP changes during the observation period, was significant in seven of the 18 observation periods. The ventilation function was statistically significant in seven of the nine observation periods before PLR, suggesting the presence of significant cardiopulmonary interaction. After PLR, this distinct cyclic ventilation pattern was present in only two out of nine patients. The shape of the ventilation spline ranged from a horizontal line (no effect) to a clear sinus-like curve (see Supplementary Appendix 2). The relative timing of the predicted peak was not constant. The time, however, between the maximum and minimum values of the functions was 51 (3)% of the duration of the ventilatory cycle.

The magnitude of VPPV decreased significantly after PLR, whilst PP increased significantly with this manoeuvre (Table 2). There was a linear relationship between baseline VPPVs and the change in VPPV after PLR ($P<0.0001$). The Spearman's rank correlation coefficient was −0.92 ($P=<0.001$), indicating a strong negative correlation (Fig. 3). In comparison with VPPV values calculated with this new method in patients with AF, the corresponding PPV values obtained with the traditional algorithm were much higher, although PPV before and after the PLR differed significantly (Table 2). However, the Spearman's rank correlation coefficient between pre-PLR value and its absolute change was −0.38 ($P=0.21$), indicating a weaker correlation for PPV than for VPPV (Fig. 3). The median RR interval and its variation changed profoundly after PLR in one particular participant. Excluding the data of this potential outlier in a subsequent analysis, however, had no effect on the results (see Supplementary material).

The *post hoc* analysis on the impact of the length of observation window showed that the minimum period needed for the model to have enough data points to determine its coefficients was 23 s (20–26 s) (median; IQR). If a standard window of 46 s was used for all, 18 models would have been able to calculate a VPPV value. This corresponds to a minimal number of data points of 28 (27–30) (median; IQR), which was independent of the individual HR. The overall absolute difference between the VPPV calculated with a shorter observation window and the $VPPV_{60s}$ was 0.0% (−1.0%; 3%) (median; IQR) (see Supplementary material for individual results).

Discussion

The main finding of our study is that the impact of mechanical ventilation on PP can be quantified in patients with AF. Traditional algorithms used to assess PPV fail to discriminate between the effects of arrhythmia and cardiopulmonary interaction in patients with irregular heart rate, and they cannot be used to predict volume responsiveness in this subgroup. Our new approach is based on the separation of the blood pressure signals into the different components affecting the beat-to-beat variation in PP. It behaves like the classic dynamic filling parameters, such as PPV, in that an increase in venous return decreases the impact of mechanical ventilation on the PP, especially when the baseline value is high. Applying the classic formula in patients with AF overestimates the ventilation-induced changes in PP[25] because it cannot distinguish between the intrinsic beat-to-beat variation in PP based on the irregularity of the heart rhythm on the one hand, and the cyclic change imposed by the ventilator on the other hand (Table 2 and Fig. 3).

In a first step to separate these two effects, we previously described a method to predict individual PPs in apnoeic patients in AF (Fig. 1).[11] This method was based on the findings of Rawles,[26] who first developed a two-factor mathematical model to describe the influence of a preceding RR interval (RR_0) and pre-preceding RR interval (RR_{-1}) on the PP (and stroke volume) of each individual beat, respectively. Different physiological explanations have been proposed to explain this interaction between RR intervals and PP. A direct non-linear relationship between RR_0 and PP (Fig. 2) has been attributed to the effect of ventricular filling time during diastole.[27] The indirect relationship between RR_{-1} and PP (Fig. 2) is explained by the effects of diastolic time on calcium reuptake, translating into calcium availability during subsequent myocardial contraction,[28] or a potential alteration of left ventricular afterload[29] Regardless of the mechanism, in the current study, we combined this approach with two other possible sources of changes in PP, which are ventilation and trending over time.

Table 2 Comparison between pre- and post-passive leg raising (PLR). IQR, inter-quartile range; PP, pulse pressure; PPV, pulse pressure variation; VPPV, ventilation-induced pulse pressure variation. HR is described using three criteria: number of heartbeats per minute, the median of the RR intervals, and the range of the RR intervals for each observation period. PP (in mm Hg) is calculated as the median of the PP of each observation period. Data are presented as median (IQR).

	Pre-PLR	Post-PLR	P-value
VPPV (%)	9.9 (0.1–27.9)	1.4 (0–11.3)	0.014
PPV (%)	134 (14.5–197.9)	36.8 (7.6–192.7)	0.019
HR			
Number of beats min^{-1}	80 (73–91)	73 (64–75)	0.09
Median RR interval (ms)	777 (660–827)	828 (804–940)	0.222
Range RR intervals (ms)	718 (506–990)	787 (628–1088)	0.667
PP (mm Hg)	33 (32–40)	48 (42–52)	0.027

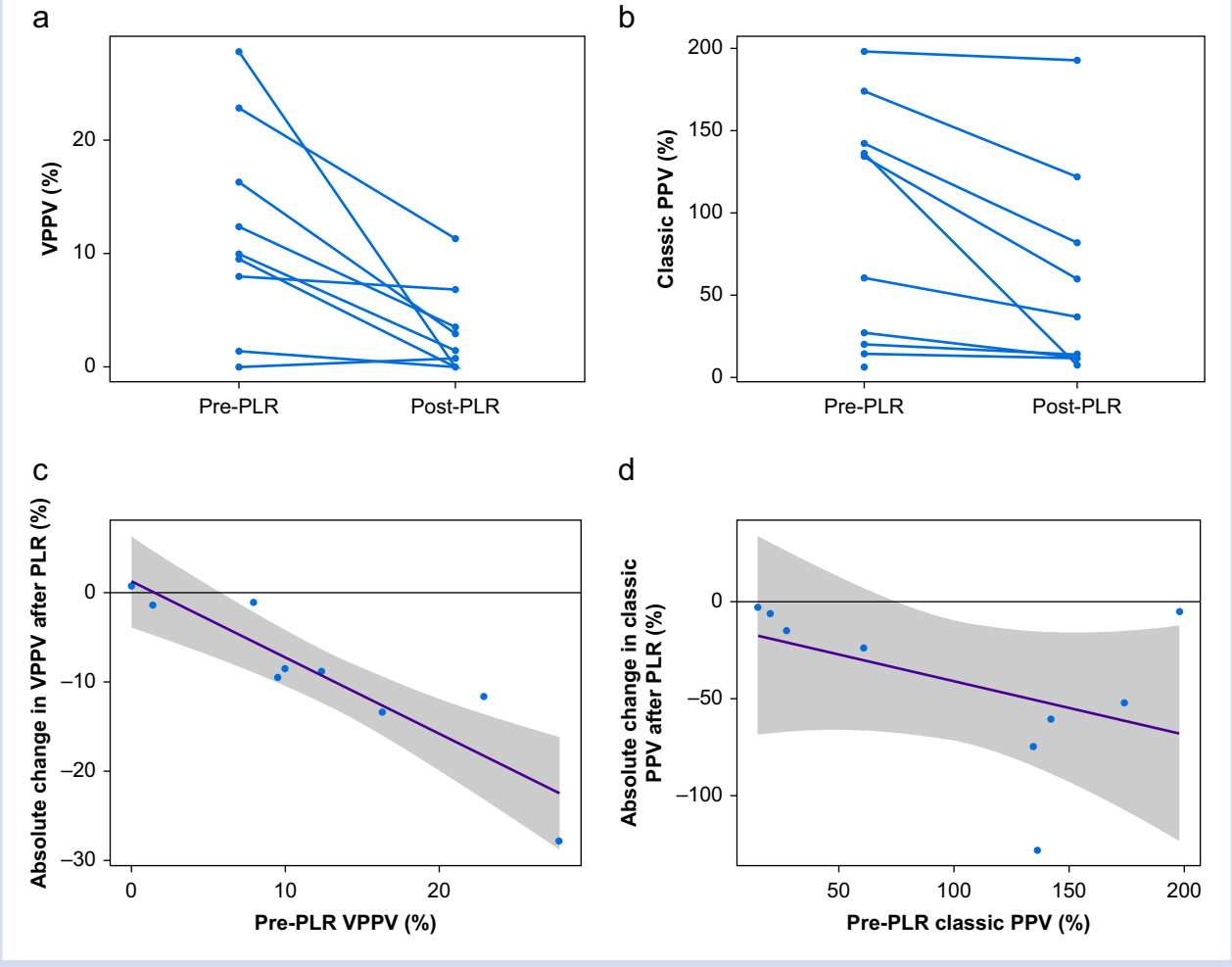

Fig 3. Pre- and post-PLR plots of (a) VPPV and (b) PPV. Individual values before PLR are plotted against their absolute change after the LR manoeuvre for (c) VPPV and (d) PPV. Spearman's rank correlation coefficients are 0.92 and 0.38 for VPPV and PPV, respectively, indicating a strong negative correlation between baseline VPPV and changes in VPPV with leg raising. PLR, passive leg raising; PPV, pulse pressure variation (%); VPPV, ventilation-induced pulse pressure variation (%). Shadow of the regression line signifies it is 95% confidence interval.

Our model is able to retrospectively decompose the successive beat-to-beat changes in PP into these three sources: intrinsic irregular heart rhythm, mechanical ventilation, and slow PP changes over time. Interestingly, our data show that amongst the four variables of the model, RR_0 is the predictor with the greatest predictive power. This explains why, in contrast to patients with regular heart rhythm, the ventilation-induced cyclic changes in PP cannot easily be recognised visually on screen, even when the ventilatory effect is substantial.

We used a GAM. This modelling technique has two advantages. First, it is very flexible. The relationship of each predictor with the dependent variable can be described by splines, a smoothing technique to describe linear or non-linear functions without knowing its exact shape or coefficients (see Supplementary Appendix).

Second, these relationships are calculated simultaneously and are additive. This means that the model consists of a simple sum of these individual functions. The function of each predictor is determined independent of each other. Because of these two properties, we used this approach to quantify the isolated impact of ventilation. To do this, we slightly changed the traditional formula to calculate PPV: the range of changes in PP imposed by the ventilator was divided by the mean value of PP (β_0 of the model; Fig. 2).

In patients with AF, there is lack of good evidence to reliably predict fluid responsiveness. However, some alternatives have been proposed previously in the literature. Passive leg raising has the theoretical advantage that it is a ventilator-independent technique with minor impact of the heart rhythm. A recent meta-analysis that pooled the data of 23 clinical trials failed to conclude on the ability of PLR to predict fluid responsiveness in AF, because the majority of the included patients had SR.[30] Kim and colleagues[31] studied the capability of two techniques to predict fluid responsiveness in a group of 43 patients with AF. The first technique, PEEP-induced changes in CVP, failed to discriminate between responders and non-responders after a fluid bolus of 300 ml of colloids. Passive leg raising, on the contrary, had some predictive abilities. An increase of 7.3% in stroke volume index after PLR had a sensitivity of 71% and a specificity of 79% to

predict a cardiac output increase of 10%. However, their reported discriminatory power (AUROC of 0.771) is lower than that reported for patients in SR.[30] One explanation for this result could be that the cardiac output measurements, especially the smaller ones after PLR, are less reliably measured because of AF.[32,33] On top of this, PLR is very unpractical to perform with ongoing surgery, which undermines its widespread use in the operating theatre. Bortolotti and colleagues[34] reported on the use of respiratory changes of the inferior caval vein diameter in a group of spontaneously breathing patients with AF (53%) or frequent extrasystoles (47%) presenting with septic shock in the ICU. Surprisingly, their results were more optimistic than the results of a recent meta-analysis comparing the ability of inferior caval vein collapsibility to predict fluid responsiveness with different ventilator settings (high TV, low PEEP *vs* low TV, high PEEP).[35] So, these findings need to be reconfirmed.

Beside AF, extrasystoles may also be a reason for irregular heartbeat. Cannesson and colleagues[12] showed in a dog model that it is possible to correct classic SVV for extrasystoles. After excluding extra systoles along with the following beat and after extrapolation based on the remaining beats, their corrected SVV performed markedly better in predicting fluid responsiveness than the uncorrected SVV (ROC: 0.892 *vs* 0.596).[12] In contrast to Cannesson and colleagues,[12] Vistisen[36] did not leave out the extrasystolic beats but used them. The concept is based on the idea to use the prolonged extrasystolic filling time as a preload changing technique. Although this principle has been confirmed,[36] recent clinical data were disappointing.[37] Interestingly, the concept is partially related to our model, as the method can be seen as an attempt to provide a two-point plot of our RR_0—PP relation of the beat that follows an extrasystolic beat. However, it does not take the effect of RR_{-1} into account, which Rawles[26] demonstrated to be significant.

The novelty of our approach is that we developed a method to filter the whole signal into its different driving processes. This enables us to quantify the isolated effect of mechanical ventilation on PP. The current study was intended to demonstrate proof of concept. It does not provide direct proof that the proposed variable is a good predictor for fluid responsiveness. We developed an algorithm that is able to quantify the impact of mechanical ventilation on PP, and we showed that this measured value changes in the same way PPV changes in patients with SR when the venous return is increased. In our protocol, we used PLR to provoke such changes. Although PLR is used in clinical practice, it is a surrogate for a real fluid challenge, and when performed suboptimal, it might lose its reliability.[20] We performed the classical PLR manoeuvre. However, we decided not to measure cardiac output, as it has previously been shown that the measurement error for both absolute values and changes in cardiac output increases in patients with AF.[32,38] This lack of accuracy is only partially corrected when longer measuring periods are used.[38] The limited power to estimate real changes in cardiac output during AF complicates its use as a gold standard to detect short-lived effects of PLR in this study. Without this reference, only indirect indicators, such as the increase in MAP and PP, could serve to assess the global haemodynamic effect of PLR. We also did not perform a control measurement after the return to the semi-recumbent post-PLR because of procedural time constraints. A return of VPPV to its baseline value would have been useful to affirm the reliability and applicability of the manoeuvre. Another limitation of our study is the low number of included patients. The primary goal of our study was to investigate the correlation between pre-PLR values for VPPV and its changes imposed by PLR. Low and mediocre correlation coefficients would undermine the usefulness of this parameter in clinical practice, as it would indicate a low signal-to-noise ratio. A *post hoc* analysis reveals that setting α=0.05 and β=0.2, a correlation coefficient of 0.8 or higher can be detected in a sample of nine patients. The determination of the exact correlation coefficient, however, would have been more reliable if more patients had been included. As calculation of VPPV is based on a regression model, some degree of measurement uncertainty has to be considered. The exact interplay between distinct functions within the algorithm and their subsequent effect on sensitivity of this new variable remains to be determined. Some of the settings of the model, such as epoch and exact timing of the ventilator, were arbitrarily chosen. We based our model on a 60 s window because this epoch seemed a reasonable period in clinical practice. Theoretically, a shorter epoch would be able to pick up more short-term changes. This advantage, however, may come with the cost of a more inaccurate determination of the parameter, limiting its use in clinical practice. In contrast, calculations based on a wider window may provide a more stable but damped model. Our *post hoc* analysis suggests that a shorter epoch is able to calculate a VPPV value. Interestingly, the minimal number of beats for the algorithm to calculate its coefficients was constant for all periods, independent of the individual HR. The accuracy of these values is still unclear. Future research, based on longitudinal data, is needed to determine the optimal epoch or the optimal number of beats.

The exact timing of the ventilation could not be measured in our protocol. As a result, shifts of the real to the arbitrarily set respiratory cycle in the current study have occurred in our analysis. This explains why the timing of the maximum of the functions is not consistent. There was, however, a minimal variance in time between maximum and minimum predicted values of about half the respiratory cycle. This might be explained by the combined direct afterload reduction effect and the delayed effect of decreased venous return of insufflation that results in a dispersion of the effect on PP from a 1:2 (I:E) ratio to a 1:1 ratio. Although we think that this lack of synchronisation does not impact the measurement of the range of these cyclic changes, incorporating the exact time-stamped data from the ventilator mechanics into the model may provide a more accurate physiological insight into these studied interactions.

All these issues need to be resolved before this model and its derived parameter, VPPV, can ultimately be tested for its ability to predict fluid responsiveness (i.e. as sole parameter or incorporated in a TV challenge).

In conclusion, our findings show the ability of a new algorithm to quantify ventilation-induced variations in PP in patients with AF in the presence of different loading conditions, thereby providing a potential tool for assessing fluid responsiveness in patients with AF.

Authors' contributions

Study design: all authors
Patient recruitment: PAHW
Data collection/analysis: PAHW
Writing of first draft: PAHW
Writing of paper: SDH, PFW, PAHW

Declarations of interest

The authors declare that a patent application has been filed, which is relevant for this work (Methods and system for haemodynamic monitoring; European patent application no. EP 19177472.8; PCT/EP2020/065034). PFW is a member of the advisory board of Vifor Pharma and Aguettant Ltd.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.bja.2020.09.039.

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