Journal of Electrocardiology 52 (2019) 47–52

Contents lists available at ScienceDirect

Journal of Electrocardiology

journal homepage: www.jecgonline.com

# Poor reliability of P-wave terminal force $V_1$ in ischemic stroke

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ARTICLE INFO

*Keywords:*
Stroke
P-wave terminal force V
Embolic stroke of undetermined source
Electrocardiology

ABSTRACT

*Introduction:* Several ECG markers are postulated to represent underlying atrial remodelling and have been associated with ischemic stroke. P-wave terminal force in lead $V_1$ ($PTFV_1$) is one such marker. We examined the factors that contribute to the reliability of $PTFV_1$ and its association with ischemic stroke.

*Material and methods:* Four hundred and thirty-five patients that presented with an ischemic stroke or transient ischemic attack (TIA) were identified through a prospectively maintained multi-site institutional stroke database. Control group consisted of age matched patients without prior history of an ischemic stroke or TIA. All patients underwent a 12-lead ECG and 24-hour Holter monitoring during the study period to exclude atrial fibrillation.

*Results:* Morphology consistent with $PTFV_1$ occurred commonly in both the stroke/TIA and control groups. There was no significant difference in the median $PTFV_1$ value between the stroke 3.96 mV ms [Interquartile range (IQR) 2.78–5.58] and control 4.23 mV ms [IQR 2.91–5.57] groups. Measurements of $PTFV_1$ demonstrated excellent intra-observer reliability on assessment of the same P-wave (Intra class correlation (ICC) 0.91, $p < 0.001$) with narrow limits of agreement 2.21 to −2.95 mV ms. A change in the P wave assessed led to a significant reduction in reliability (ICC 0.79, $p < 0.001$). Inter-observer, inter P-wave assessment demonstrated further reduction in reliability (ICC 0.68, $p < 0.002$) with wide limits of agreement 6.17 to −5.78 mV ms, indicating significant under and overestimation of $PTFV_1$.

*Conclusion:* The utility of $PTFV_1$ as a clinical marker for ischemic stroke is limited by the reduction in reliability associated with inter-observer and inter P-wave measurements.



## Introduction

Ischemic strokes result in significant morbidity, loss of function and death. The incidence of ischemic strokes is projected to rise in view of the ageing population [1]. Atrial fibrillation (AF) is widely believed to be the cause for a significant proportion of ischemic strokes [2]. The presence of an atrial myopathy has been postulated in patients with ischemic stroke independent of atrial fibrillation. Electrophysiological and biochemical abnormalities, including elevated fibrotic and inflammatory markers, are preferentially associated with cardioembolic stroke subtype alluding to an underlying myopathic process [3–6].

Several ECG markers thought to represent underlying atrial remodelling have been associated with ischemic stroke and AF [7–9]. They are postulated to be more reliable at identifying patients at risk of stroke than the detection of subclinical AF [10–12]. P-wave terminal force in $V_1$ ($PTFV_1$) is one such marker derived from a standard 12 lead ECG. $PTFV_1$ has been associated with both elevated left atrial volume and pressure and may represent atrial adverse remodelling [13,14]. However, there is clinical equipoise regarding the utility of this marker in predicting ischemic stroke [13,14].

The inconsistencies in data could be indicative of poor reliability of the measure, as $PTFV_1$ is inherently difficult to measure [15]. Furthermore, previous studies have not provided sufficiently detailed methodology to allow for reproducible measurement of $PTFV_1$, particularly in the presence of subtle baseline and beat to beat P-wave variability that could impact on the accuracy of measurements.

We performed a study to assess the reliability of $PTFV_1$ as a clinical measure and its association with cerebrovascular events. We assessed the reliability of inter-observer and inter P-wave $PTFV_1$ measurements using a standardised technique in an attempt to reduce variability of measurements.

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https://doi.org/10.1016/j.jelectrocard.2018.11.007
0022-0736/

## Material and methods

### Study design

A case-control study was conducted among patients that presented to three metropolitan hospitals with an ischemic cerebrovascular event, stroke or transient ischemic attack (TIA), between May 2011 and December 2015.

Patients within the stroke and TIA group were identified through a prospectively maintained stroke unit database. Inclusion criteria were: 1) age ≥ 18 years; 2) adjudicated to have had an ischemic stroke or TIA by a stroke physician; 3) underwent 24-hour Holter monitoring following their index stroke or TIA; and 4) had a 12 lead ECG available for analysis. Exclusion criteria were: 1) haemorrhagic stroke; 2) history of atrial fibrillation or atrial flutter; 3) AF diagnosed on post stroke Holter monitoring or during follow up; 4) underlying severe cardiomyopathy; 5) previous coronary artery bypass grafting or 6) severe chronic obstructive airways disease.

Eligible patients were compared to a group of age-matched controls, without prior history of stroke, TIA or AF, and underwent Holter monitoring to exclude subclinical AF. The stroke/TIA and control groups were matched in a 2:1 ratio with the same exclusion criteria applied to both groups.

The research protocol was approved by the institutional Human Research Ethics Committee.

### Clinical assessment and outcome measures

All patients adjudicated as having a stroke or TIA underwent investigation and treatment as per the national stroke guidelines recommendation for standard of care [16]. This included physical examination, blood measurements, 12 lead ECG, pulse oximetry, cerebrovascular imaging and vascular assessment.

Baseline demographic and clinical data were collected from electronic health records along with vascular risk factors to allow for calculation of a $CHA_2DS_2VASc$ score, medication use, and details of repeat presentations with recurrent stroke or TIA.

All patients underwent Holter monitoring with 24 h of continuous rhythm capture utilising the SEER Light Holter Monitor (GE Healthcare, Milwaukee, USA). Data were analyzed offline upon completion of the monitoring period by cardiac technicians and subsequently reviewed by a cardiac electrophysiologist. Rhythm analysis was conducted using MARS Ambulatory ECG Analysis System (GE Healthcare, Milwaukee, USA). The ECGs were obtained on a MAC 5500 HD resting ECG system (GE Healthcare, Milwaukee, USA).

### P wave measurements

A 12 lead ECG was recorded at 10 mm/mV with a paper speed of 25 mm/s after standard lead placement. The ECGs were analyzed in a digital format and all measurements obtained at a minimum five times digital zoom. The digital callipers were calibrated against the reference pulse, with measurements obtained in millimetres and converted to a unit of mV ms.

$PTFV_1$ was defined as the amplitude of the downward deflection of the terminal portion of the P-wave in lead V1 multiplied by its duration [17,18]. The baseline was defined by a straight line that extends from the middle of the TP segment immediately prior to the P-wave of interest, to the following TP segment. The amplitude was measured from the nadir of the P-wave till the point of intersection with the baseline (Fig. 1).

As described in previous studies, $PTFV_1$ was only measured if the P-wave morphology in lead $V_1$ had a negative or biphasic component [15]. An elevated $PTFV_1$ was defined as a value >4 mV ms as described in previous studies [17,19–22].

$PTFV_1$ was measured by a single observer blinded to the patient group. A subset of 30 ECGs were analyzed by the same observer on a different P-wave and by second observer on the same P-wave to assess inter P-wave and inter-observer variability.

Interatrial conduction block was identified based on a P-wave duration ≥120 ms. P wave morphology as previously defined with a biphasic morphology in leads II, III, and aVF or biphasic morphology in leads III and aVF in association with a notched P in lead II [12].

### Statistics

Demographic data, disease status and outcome measures are presented as proportions and summarised by descriptive statistics. Data were tested for normality and parametric or non-parametric tests applied as appropriate, with mean ± standard deviation for parametric data and median with interquartile ranges for non-parametric data. Differences between groups with a parametric distribution were tested by an unpaired *t*-test for continuous variables and Chi-square test for categorical variables. Non-parametric data were analyzed using the Mann Whitney *U* test and Kruskal-Wallis test. Correlation trends were analyzed using Spearman's rho for non-parametric data or Cochran-Armitage test for ordinal data. A $p$-value $< 0.05$ was deemed statistically significant. $PTFV_1$ values that lay outside 99.9 percentile were categorised as clinical implausible outliers and excluded from analysis. Markers associated with stroke and an elevated $PTFV_1$ were identified by univariate and multivariate logistical regression.

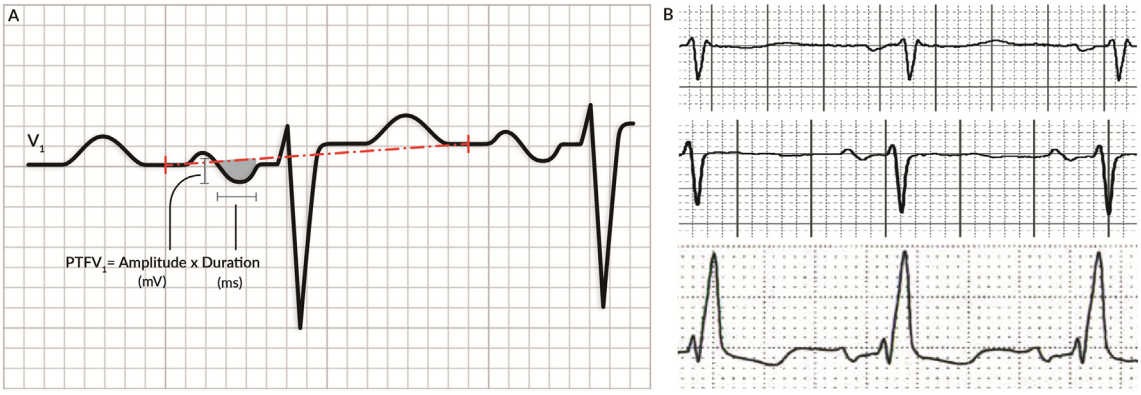


**Fig. 1.** (A) $PTFV_1$ was calculated by identifying the baseline represented by the straight line across the TP segments. The amplitude was measured from the nadir of the P-wave till the point of intersection with the baseline. (B) Variations in P-wave morphology and baseline wander can affect measurements and calculation of $PTFV_1$.

Intra and inter-observer reliability was assessed using Bland-Altman plots and Intraclass correlation with two-way random effects model. All statistical analyzes were performed with SPSS Statistics 24.0 (IBM, Chicago, IL, USA).

## Results

In total, 3235 patients presented with a stroke or TIA during the study inclusion period; 431 were excluded for intracranial haemorrhage identified on computed tomography. Only patients that underwent Holter monitoring and a 12 lead ECG at the study site were included. In the final analysis, 435 patients with a stroke or TIA were compared against 226 age-matched patients that underwent Holter monitoring and ECG recording during the same time period (Fig. 2). The control group was composed of patients that underwent Holter monitoring for investigation of chest pain, syncope, pre-syncope and palpitations.

Baseline characteristics stratified according to study groups are shown in Table 1. In both groups, the mean age was 70 years and the majority of patients were male. Patients with a stroke or TIA were significantly more likely to have comorbidities of diabetes mellitus, dyslipidaemia, and peripheral vascular disease. Seventy-six (17.5%) patients with a stroke or TIA had a prior ischemic cerebrovascular event. Despite a higher prevalence of hypertension and dyslipidaemia within the stroke or TIA cohort there were no difference in the use of statins or antihypertensive therapy.

The prevalence of interatrial conduction block was not significantly different between the stroke and control group (3.9% vs 2.7%, p 0.40). There was no difference in the occurrence of a negative or biphasic P-wave in lead V1 between the stroke/TIA and control group (90.7% vs 89.2%, *p* 0.54). Four patients from the stroke and 2 from the control group, had a calculated $PTFV_1$ value above the 99.9 percentile and were excluded from analysis involving $PTFV_1$. There were no significant differences in the median $PTFV_1$ values between the control 4.23 mV ms (IQR 2.91–5.57) and stroke/TIA 3.96 mV ms (2.78–5.58) groups. Similarly, there were no significant differences in the median $PTFV_1$ values between the 240 patients with cryptogenic stroke subtype and control group, 4.01 mV ms (IQR 2.86–5.69) and 4.23 mV ms (IQR 2.91–5.57) respectively.

An elevated $PTFV_1$ was defined by the presence of a P-wave morphology consistent with $PTFV_1$ and a $PTFV_1$ value above 4.0 mV ms as described previously. The prevalence of an elevated $PTFV_1$ in the

**Table 1**
Characteristics of study participants.

| | Control n = 226 n (%) | Stroke/TIA n = 435 n (%) | *p* value |
|---|---|---|---|
| Age, y (SD) | 70.7 (11.5) | 70.0 (12.4) | 0.47 |
| Sex, female | 79 (35.0) | 187 (43.0) | <**0.05** |
| Vascular risk factors | | | |
| Hypertension | 121 (53.5) | 276 (63.4) | 0.14 |
| Dyslipidaemia | 79 (35.0) | 197 (45.3) | <**0.05** |
| Diabetes mellitus | 36 (15.9) | 109 (25.1) | <**0.01** |
| Any smoking | 40 (17.7) | 113 (26.0) | 0.17 |
| Previous stroke/TIA | 0 | 76 (17.5) | – |
| Myocardial infarction | 40 (17.7) | 79 (18.2) | 0.83 |
| Peripheral vascular disease | 5 (2.2) | 25 (5.7) | <**0.05 (f)** |
| Heart failure | 9 (4.0) | 24 (5.5) | 0.39 |
| $CHA_2DS_2VASc$ score (median) | 3.0 | 5.0 | <**0.01** |

SD indicates standard deviation; f, Fishers exact test; TIA, transient ischemic attack.
Bold highlights statistically significant values.

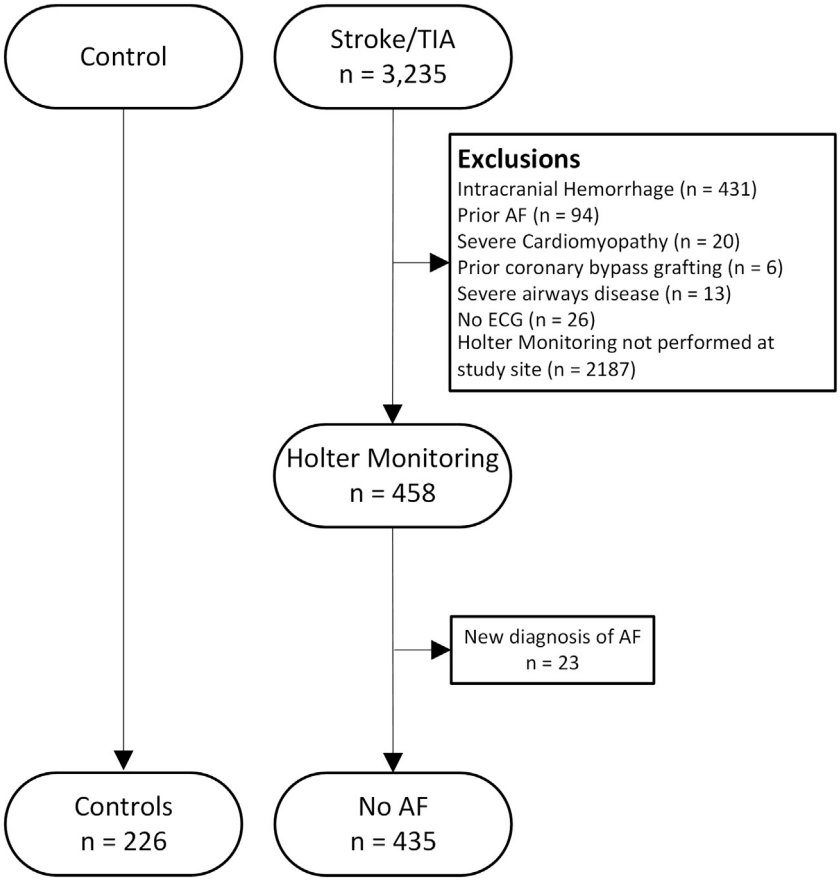


**Fig. 2.** Patient selection: inclusions and exclusions.

**Table 2**
Baseline characteristics and $PTFV_1$.

| | Normal $PTFV_1$ n = 291 n (%) | Elevated $PTFV_1$ n = 296 n (%) | *p* value |
|---|---|---|---|
| Age, y (SD) | 69.8 (11.4) | 71.1 (12.3) | 0.11 |
| Sex, female | 117 (40.2) | 123 (41.6) | 0.74 |
| Stroke/TIA | 196 (67.4) | 188 (63.5) | 0.33 |
| Vascular risk factors | | | |
| Hypertension | 171 (58.8) | 182 (61.5) | 0.50 |
| Dyslipidaemia | 128 (44.0) | 115 (38.9) | 0.21 |
| Diabetes mellitus | 98 (24.7) | 35 (20.3) | 0.19 |
| Smoking | 70 (24.1) | 68 (23.0) | 0.76 |
| Peripheral vascular disease | 12 (4.1) | 12 (4.1) | 0.97 |
| History of heart failure | 11 (3.8) | 18 (6.1) | 0.20 |
| $CHA_2DS_2VASc$ score-median (IQR) | 4 (2–6) | 4 (2–6) | 0.45 |

SD indicates standard deviation; TIA, transient ischemic attack.

stroke/TIA and control group was, 49.0% and 53.2% (*p* 0.33), respectively. Conventional vascular risk factors were not associated with an elevated $PTFV_1$ on univariate analysis (Table 2).

$PTFV_1$ had excellent reliability for intra-observer, intra P-wave measurements (ICC 0.91, $p < 0.001$) with narrow 95% limits of agreement (LoA), −2.95 to 2.21 mV ms, on Bland-Altman analysis. There was a sequential reduction in reliability for inter-observer, intra P-wave measurements (ICC 0.85, $p < 0.001$) and intra-observer, inter P-wave measurements (ICC 0.79, $p < 0.001$). Inter-observer, inter P-wave measurements were the least reproducible with only moderate reliability (ICC 0.68, $p < 0.01$) and the widest 95% LoA, −5.78 to 6.17 mV ms, on Bland-Altman analysis (Fig. 3).

## Discussion

In this cohort of patients, an increased $PTFV_1$ was not associated with ischemic stroke and this remained consistent for the cryptogenic stroke subtype. Further analysis exploring predictors for an elevated $PTFV_1$ defined as a value >4.0 mV ms failed to demonstrate an association with stroke or traditional vascular risk factors. Most importantly, while $PTFV_1$ could be measured reliably by the same assessor using the same P-wave utilising this rigorous methodology, reliability reduced significantly with both inter P-wave and inter-observer measurements.

Research into the pathophysiological basis of $PTFV_1$ dates back to the 1970s when an association between an elevated $PTFV_1$ and left atrial pressure during cardiac catheterisation was demonstrated. Investigators have subsequently reported excellent specificity for an elevated $PTFV_1$ in predicting left atrial enlargement on echocardiography, conversely others have shown that increased left atrial abnormalities correlated with electrocardiographic markers only in the context of a cardiomyopathy [14,21,23,24].

More recently, several studies have explored the relationship between $PTFV_1$ and clinical outcomes such as atrial fibrillation, silent vascular brain injuries and ischemic stroke [25]. Similar to the pathophysiological studies, the data remains inconsistent. A subanalysis of the Northern Manhattan Study and the Multi-Ethnic Study of Atherosclerosis study, that longitudinally followed patients for subsequent cerebrovascular or cardiovascular events demonstrated a significantly higher mean $PTFV_1$ value in the stroke group compared with the control group [18,26]. However, Social Insurance Institution's Coronary Heart Disease Study did not demonstrate a significant association between elevated $PTFV_1$ and ischemic stroke [27].

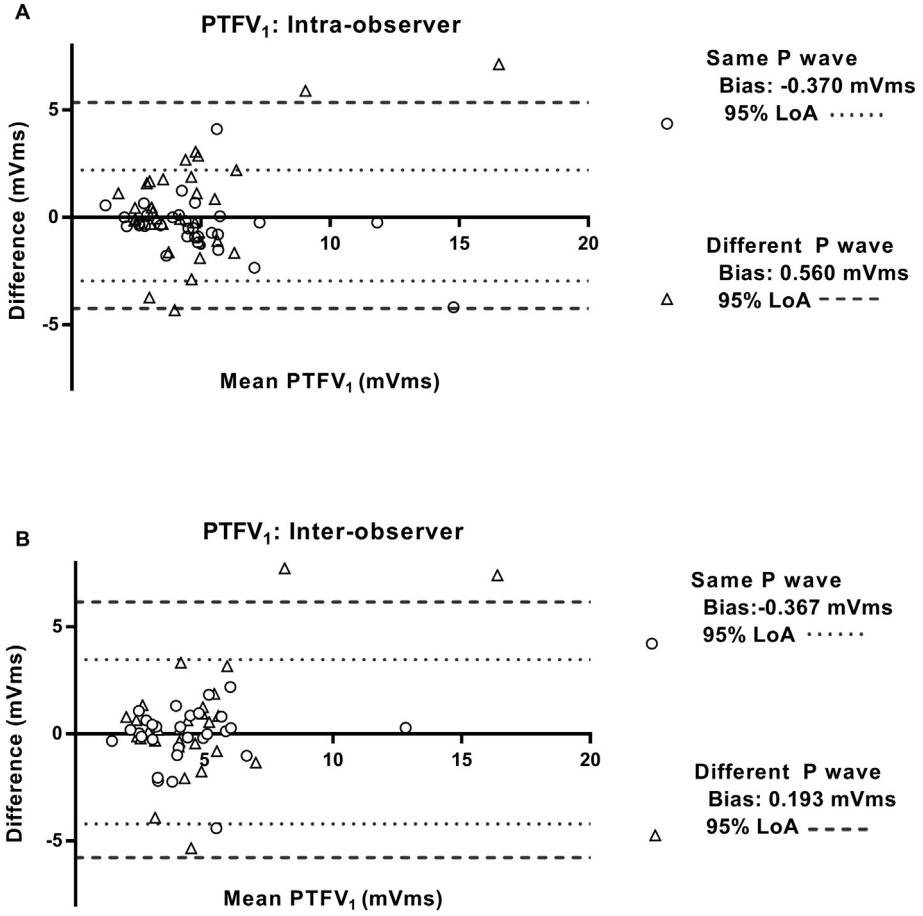


**Fig. 3.** Bland-Altman analysis with 95% limits of agreement (LoA) and bias for $PTFV_1$ measurements. The small bias highlights the lack of systematic under or over estimation of $PTFV_1$. (A) Demonstrates intra-observer, intra P-wave assessment with narrow LoA, a marked widening of LoA is observed with intra-observer, inter P-wave assessment. (B) Demonstrates inter-observer assessment of P waves, with the widest LoA noted with inter-observer, inter P-wave measurements.

The present study did not demonstrate a significant association between stroke and $PTFV_1$. Furthermore, conventional vascular risk factors were not significantly associated with an elevated $PTFV_1$. It is feasible, that the lack of a significant difference in $PTFV_1$ between the stroke and control group could be a result of selection bias, due to an elevated baseline $PTFV_1$ in patients that presented for Holter monitoring who subsequently formed the control group. AF has been associated with an elevated $PTFV_1$ and despite excluding manifest AF and subclinical AF detected on Holter monitoring, the patients who present for Holter monitoring is likely to have a higher prevalence of occult undiagnosed AF than a community-based patient cohort. However, data from two large longitudinal cohort studies observed discordant results for $PTFV_1$ as a predictor for AF, as a significant association with $PTFV_1$ was only noted in the ARIC study [19].

The conflicting pathophysiological and clinical data raise questions about the clinical reliability and validity of this marker. $PTFV_1$ is an inherently difficult marker to calculate as it relies on the accurate measurement of low amplitude deflections on an ECG, which is subsequently multiplied, resulting in the potential magnification of measurement errors. Previous studies have provided inter-observer reliability that ranged from poor to good, however a robust assessment of factors that affect its reliability has not been outlined [15,18,27]. Our study using a rigorous methodology exposes potential flaws in measuring $PTFV_1$. Even when using a standardised methodology, the specific p-wave measured can markedly affect the result, as can measurements by different observers.

The robust nature of our standardised methodology for $PTFV_1$ measurements was demonstrated by the excellent reliability, ICC of 0.91 with narrow limits of agreement, of intra-observer, intra P-wave $PTFV_1$ measurements. While a change in either the observer or the P wave measured led to a reduction in reliability, the impact of inter-P wave measurements was more pronounced. However, the largest significant reduction in reliability occurred with a change in both the observer and the P-wave measured, with an ICC of 0.68 and a very wide 95% limit of agreement. The wide limits of agreement in particular suggests both significant over and underestimation of $PTFV_1$.

Poor reproducibility of P-wave dispersion and $PTFV_1$ was demonstrated by Snyder et al. with reduction in reliability noted during a single visit and with a further reduction in reliability demonstrated between visits [15]. However, to date, the present study is the first to have analyzed the individual factors that contribute to this reduction in reliability of $PTFV_1$. Our findings raise concerns over the real-world utility of this measure, whereby different assessors will evaluate different P-waves to derive the $PTFV_1$ value.

Automated computerised algorithms for calculating $PTFV_1$ could reduce inter-observer variability and have been shown to correlate well with manual measurements [28]. However, automated algorithms will not overcome differences in measurements that arise from inter P-wave variability. It is likely that the moderate reliability observed in this study will reduce further in a real-world setting when analysing ECGs obtained at differing time points.

The limitations of the present study include: 1) the utilisation of manual measurements to calculate $PTFV_1$, but we improved reliability by adopting a rigorous methodology and by routinely using digital zoom to improve measurement accuracy; 2) a proportion of patients undertook Holter monitoring externally and therefore did not meet inclusion criteria, we cannot exclude a significant difference in $PTFV_1$ within this group of patients; 3) we did not analyze the utility of multiple P-wave measurements to derive an average $PTFV_1$ value, this may reduce the impact of P-wave dispersion on $PTFV_1$. 4) A higher threshold for characterizing $PTFV_1$ may have demonstrated a significant difference between the two groups.

In conclusion, there was no association between $PTFV_1$ and ischemic stroke in this cohort of patients. Despite using a rigorous methodology for measurements, we demonstrated only moderate reliability for inter-observer, inter P-wave measurements of $PTFV_1$. Further refinement of the methodology is required to improve the clinical utility of $PTFV_1$ as a marker of atrial myopathy and ischemic stroke.

## Declaration of interests

None.

## Sources of funding

This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Andrew W. Teh is the recipient of an Early Career Fellowship from the National Health and Medical Research Council of Australia (NHMRC). Jithin K. Sajeev is the recipient of an Australian Government Research Training Program Scholarship. Anoop N. Koshy is the recipient of a combined Postgraduate Research Scholarship from the NHMRC and National Heart Foundation of Australia. Jonathan M. Kalman is supported by a Practitioner Fellowship from the NHMRC.

## References

[1] National Stroke Foundation. Clinical guidelines for stroke management 2010 Melbourne Australia ; 2010.
[2] Wolf PA, Abbott RD, Kannel WB. Atrial fibrillation as an independent risk factor for stroke: the Framingham study. Stroke 1991;22(8):983–8.
[3] Panwar B, Jenny NS, Howard VJ, Wadley VG, Muntner P, Kissela BM, et al. Fibroblast growth factor 23 and risk of incident stroke in community-living adults. Stroke 2015;46(2):322–8.
[4] Piccardi B, Giralt D, Bustamante A, Llombart V, Garcia-Berrocoso T, Inzitari D, et al. Blood markers of inflammation and endothelial dysfunction in cardioembolic stroke: systematic review and meta-analysis. Biomarkers 2017;22(3–4):200–9.
[5] Medi C, Kalman JM, Ling LH, Teh AW, Lee G, Lee G, et al. Atrial electrical and structural remodeling associated with longstanding pulmonary hypertension and right ventricular hypertrophy in humans. J Cardiovasc Electrophysiol 2012;23(6):614–20.
[6] Kistler PM, Sanders P, Fynn SP, Stevenson IH, Spence SJ, Vohra JK, et al. Electrophysiologic and electroanatomic changes in the human atrium associated with age. J Am Coll Cardiol 2004;44(1):109–16.
[7] Kaypakli O, Koca H, Sahin DY, Okar S, Karatas F, Koc M. Association of P wave duration index with atrial fibrillation recurrence after cryoballoon catheter ablation. J Electrocardiol 2018;51(2):182–7.
[8] Lehtonen AO, Langen VL, Puukka PJ, Kahonen M, Nieminen MS, Jula AM, et al. Incidence rates, correlates, and prognosis of electrocardiographic P-wave abnormalities — a nationwide population-based study. J Electrocardiol 2017;50(6):925–32.
[9] Prasitlumkum N, Rattanawong P, Limpruttidham N, Kanitsoraphan C, Sirinvaravong N, Suppakitjanusant P, et al. Frequent premature atrial complexes as a predictor of atrial fibrillation: systematic review and meta-analysis. J Electrocardiol 2018;51(5):760–7.
[10] Larsen BS, Kumarathurai P, Falkenberg J, Nielsen OW, Sajadieh A. Excessive atrial ectopy and short atrial runs increase the risk of stroke beyond incident atrial fibrillation. J Am Coll Cardiol 2015;66(3):232–41.
[11] Kochhauser S, Dechering DG, Dittrich R, Reinke F, Ritter MA, Ramtin S, et al. Supraventricular premature beats and short atrial runs predict atrial fibrillation in continuously monitored patients with cryptogenic stroke. Stroke 2014;45(3):884–6.
[12] O'Neal WT, Kamel H, Zhang ZM, Chen LY, Alonso A, Soliman EZ. Advanced interatrial block and ischemic stroke: the Atherosclerosis Risk in Communities Study. Neurology 2016;87(4):352–6.
[13] Kasser I, Kennedy JW. The relationship of increased left atrial volume and pressure to abnormal P waves on the electrocardiogram. Circulation 1969;39(3):339–43.
[14] Hazen MS, Marwick TH, Underwood DA. Diagnostic accuracy of the resting electrocardiogram in detection and estimation of left atrial enlargement: an echocardiographic correlation in 551 patients. Am Heart J 1991;122(3 Pt 1):823–8.
[15] Snyder ML, Soliman EZ, Whitsel EA, Gellert KS, Heiss G. Short-term repeatability of electrocardiographic P wave indices and PR interval. J Electrocardiol 2014;47(2):257–63.
[16] National Stroke Foundation. Clinical guidelines for stroke management 2010. Melbourne Australia: National Stroke Foundation; 2010.
[17] Kamel H, Bartz TM, Longstreth Jr WT, Okin PM, Thacker EL, Patton KK, et al. Association between left atrial abnormality on ECG and vascular brain injury on MRI in the cardiovascular health study. Stroke 2015;46(3):711–6.
[18] Kamel H, Hunter M, Moon YP, Yaghi S, Cheung K, Di Tullio MR, et al. Electrocardiographic left atrial abnormality and risk of stroke: Northern Manhattan Study. Stroke 2015;46(11):3208–12.
[19] Magnani JW, Zhu L, Lopez F, Pencina MJ, Agarwal SK, Soliman EZ, et al. P-wave indices and atrial fibrillation: cross-cohort assessments from the Framingham Heart Study (FHS) and Atherosclerosis Risk in Communities (ARIC) study. Am Heart J 2015;169(1):53–61 e1.
[20] Liu G, Tamura A, Torigoe K, Kawano Y, Shinozaki K, Kotoku M, et al. Abnormal P-wave terminal force in lead V1 is associated with cardiac death or hospitalization for heart failure in prior myocardial infarction. Heart Vessels 2013;28(6):690–5.

[21] Josephson ME, Kastor JA, Morganroth J. Electrocardiographic left atrial enlargement. Electrophysiologic, echocardiographic and hemodynamic correlates. Am J Cardiol 1977;39(7):967–71.
[22] Tereshchenko LG, Shah AJ, Li Y, Soliman EZ. Electrocardiographic deep terminal negativity of the P wave in V1 and risk of mortality: the National Health and Nutrition Examination Survey III. J Cardiovasc Electrophysiol 2014;25(11):1242–8.
[23] Heikkila J, Hugenholtz PG, Tabakin BS. Prediction of left heart filling pressure and its sequential change in acute myocardial infarction from the terminal force of the P wave. Br Heart J 1973;35(2):142–51.
[24] Mazzoleni A, Wolff R, Wolff L, Reiner L. Correlation between component cardiac weights and electrocardiographic patterns in 185 cases. Circulation 1964;30: 808–29.
[25] Hunter MD, Park Moon Y, Decarli C, Gutierrez J, Wright CB, Di Tullio MR, et al. Electrocardiographic left atrial abnormality and silent vascular brain injury: the Northern Manhattan Study. PLoS ONE 2018;13(10):e0203774.
[26] Kamel H, Soliman EZ, Heckbert SR, Kronmal RA, Longstreth Jr WT, Nazarian S, et al. P-wave morphology and the risk of incident ischemic stroke in the Multi-Ethnic Study of Atherosclerosis. Stroke 2014;45(9):2786–8.
[27] Eranti A, Aro AL, Kerola T, Anttonen O, Rissanen HA, Tikkanen JT, et al. Prevalence and prognostic significance of abnormal P terminal force in lead V1 of the ECG in the general population. Circ Arrhythm Electrophysiol 2014;7(6):1116–21.
[28] Kamel H, O'Neal WT, Okin PM, Loehr LR, Alonso A, Soliman EZ. Electrocardiographic left atrial abnormality and stroke subtype in the atherosclerosis risk in communities study. Ann Neurol 2015;78(5):670–8.