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Comparison of baroreflex sensitivity with a fall and rise in blood pressure induced by the Valsalva manoeuvre

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Abstract

The baroreflex plays a key role in human BP (blood pressure) regulation. Its efferent limb consists of a vagal and a sympathetic component. The Valsalva manoeuvre is widely used to quantify vagal baroreflex function [BRS_vagal (vagal baroreflex sensitivity)], but most studies have focused on the R–R interval response to BP decrement, even though the subsequent response to an increment in BP is important and different. In the present study, we sought to evaluate whether BRS_vagal can be determined from $BRSvagal_{inc}$ (BRS_vagal derived from the rise in BP during phases III–IV of the Valsalva manoeuvre), to assess the association between $BRSvagal_{inc}$ and $BRSvagal_{dec}$ (BRS_vagal derived from the preceeding BP decrement) and to validate $BRSvagal_{inc}$ as an index of autonomic function. We studied patients with severe autonomic failure ($n = 49$, 25 female), mild autonomic failure ($n = 25$, 11 female) and matched normal controls ($n = 29$, 15 female). $BRSvagal_{inc}$ and $BRSvagal_{dec}$ were calculated as the regression slope of R–R interval and systolic BP during phases III–IV and the early phase II of the Valsalva manoeuvre respectively, and compared these with other autonomic indices across the groups. $BRSvagal_{inc}$ was calculated in all subjects and correlated highly with $BRSvagal_{dec}$ ($r = 0.72$, $P < 0.001$). $BRSvagal_{inc}$ also correlated significantly with BP changes during phases II and IV of the Valsalva manoeuvre and sympathetic barosensitivity. $BRSvagal_{inc}$ was significantly different between the groups, being highest in the controls and lowest in patients with severe autonomic failure. In conclusion, vagal BRS, determined by relating R–R interval with the BP increase following phase III, is a valuable autonomic index, provides additional information about vagal baroreflex function and reflects overall severity of autonomic failure.

Key words: autonomic function, baroreflex sensitivity, blood pressure, vagal, Valsalva manoeuvre

INTRODUCTION

The maintenance of postural normotension depends on a number of variables, including the status of plasma volume, venous capacitance bed and arterial baroreflexes, which regulate HR (heart rate) and vasomotor tone in response to arterial pressure [1]. A key role of the clinical autonomic laboratory is to ascertain whether OH (orthostatic hypotension) or intolerance is present and if the aetiology is neurogenic. NOH (neurogenic OH) is due to an impairment of arterial baroreflexes [2]. The Mayo Autonomic Laboratory has evaluated sympathetic and vagal components of the baroreflex by studying dynamic alterations in BP (blood pressure) and HR during the Valsalva manoeuvre. There are four main phases of the Valsalva manoeuvre. Phase I is a transient rise in BP due to increased intrathoracic pressure. Early phase II (phase II_{early}) is a fall in BP due to reduced cardiac preload (venous return) and stroke volume. The fall in BP is sensed by arterial baroreceptors in the carotid sinus and aortic arch, mediated centrally via glossopharyngeal and vagal afferents, and corrected by sympathetic activation (vasoconstriction and positive inotropic and chronotropic effects on the heart) and vagal withdrawal (cardio-acceleration). The resulting rise in BP is described as late

Abbreviations: ABP_{RT}, arterial BP recovery time; AF, autonomic failure; AUC, area under the curve; BP, blood pressure; BRS, baroreflex sensitivity; BRS_vagal, vagal component of the baroreflex; BRS_{symp}, sympathetic BRS; $BRSvagal_{dec}$, BRS_vagal derived from the preceeding BP decrement; $BRSvagal_{inc}$, BRS_vagal derived from the rise in BP during phases III–IV of the Valsalva manoeuvre; DBP, diastolic BP; HR, heart rate; $HRslope_{(dec)}$, regression slope of HR over time from phase III to the peak of phase IV; $HRslope_{(inc)}$, regression slope of HR over time during phase II_{early}; MABP, mean arterial BP; NOH, neurogenic OH; OH, orthostatic hypotension; SBP, systolic BP.

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phase II (phase II_{late}). At the end of the Valsalva manoeuvre, the sudden fall in intrathoracic pressure results in a transient fall in BP (phase III), lasting 1–2 s. In phase IV, venous return normalizes while cardiac output is still increased and the arterial vascular bed is still constricted, resulting in a transient BP overshoot [3]. These BP changes are accompanied by changes in HR. During phase II_{early}, HR increases in response to the fall in BP mainly as a result of vagal withdrawal. That rise in HR continues during phase II_{late} as a result of sympathetic activation. During phase IV, HR decreases in response to the BP rise and overshoot (vagal activation). Phase II_{early} and phase IV therefore lend themselves to derive information about BRS (baroreflex sensitivity).

Our programme has made significant headway in developing non-invasive methodology to quantify vagal and sympathetic components of the baroreflex [4,5]. BRS_vagal (vagal component of the baroreflex) can be quantified by relating the HR response (as the R–R interval response) to a preceding change in BP. Traditionally, BRS_vagal has been measured by the modified Oxford method, where the R–R interval response to an induced fall in BP (by intravenous boluses of nitroprusside) and an induced rise in BP (by intravenous boluses of phenylephrine) is studied sequentially [6]. BRS_vagal is determined as the slope of the R–R interval and BP response and is expressed in ms/mmHg. In the clinical autonomic laboratory, we have focused on the R–R interval response to the fall in SBP during phase II_{early} of the Valsalva manoeuvre. We have previously validated the method in patients with graded AF (autonomic failure) [4] and have generated normative values [5].

Only a few studies have been devoted to the R–R interval response to the rise in BP following the Valsalva manoeuvre. The previously described methodologies relating R–R interval to BP increase during phase IV of the manoeuvre have only limited application in the clinical autonomic laboratory, since phase IV is typically absent in patients with NOH [7–9]. There is a need for an approach that relates R–R interval to the BP increase that is reliably present not only in healthy subjects, but also in patients with AF. Therefore we sought to determine BRS_vagal by relating R–R interval to the rise in BP that follows phase III of the manoeuvre.

The aims of the present study were: (i) to evaluate whether BRS_vagal can be determined from $BRSvagal_{inc}$ (BRS_vagal derived from the rise in BP during phases III–IV of the Valsalva manoeuvre), (ii) to assess the association between $BRSvagal_{inc}$ and $BRSvagal_{dec}$ (BRS_vagal derived from the preceeding BP decrement), and (iii) to validate $BRSvagal_{inc}$ as an index of autonomic function.

MATERIALS AND METHODS

Study participants

The study was approved by the Mayo Clinic Institutional Review Board and subjects gave informed constent. We included patients with different degrees of AF and age- and sex-matched healthy control subjects. Patients with AF were divided into two groups: (i) patients with severe AF, defined as an ABP_{RT} (arterial BP recovery time) following the Valsalva manoeuvre of >10 s; and (iii) patients with mild AF, defined as an ABP_{RT} of >5 s but <10 s.

A total of 101 subjects (54 men and 57 women) were included in the study. The severe AF group included 49 patients (25 female; age, 51.5 ± 15.3 years), the mild AF group included 25 patients (11 female; age, 57.5 ± 15.7 years) and the control group included 29 subjects (15 female; age, 51.5 ± 15.3 years). We excluded patients with conditions such as cardiac, pulmonary, hepatic, renal, haematological and neoplastic disorders, and patient with neurocardiogenic syncope. Patients on medication known to cause OH or otherwise affect autonomic testing were asked to discontinue use of the drug for 5 half-lives, if such a procedure was not harmful to the well-being of the patient. For patients on levodopa/carbidopa, the drug was omitted on the day of the study and resumed after the test.

Study protocol

HR was recorded using a standard three-lead ECG (Ivy Biomedical Systems). Arterial BP was measured continuously at the finger using beat-to-beat photoplethysmographic recordings (Finapres BP monitor model 2300 and Finometer; Ohmeda).

All subjects underwent standardized autonomic reflex testing to evaluate the severity and distribution of sudomotor, sympathetic and cardiovagal function [10]. The Valsalva manoeuvre was performed with the patient supine. The patient was instructed to maintain a column at 40 mmHg for 15 s via a tube with an air leak (to ensure an open glottis). After a practice run, the subject performed a series of manoeuvres until two reproducible responses were obtained.

Variables

The baseline values of SBP (systolic BP), DBP (diastolic BP, and MABP (mean arterial BP) were determined with the subject rested and supine for at least 20 min preceding the Valsalva manoeuvre, and were derived as a 30 s average before the Valsalva manoeuvre. ABP_{RT} was defined as time in seconds from the valley of phase III until BP returned to baseline. The magnitude of BP changes was determined for phase II_{early}, phase II_{late} and phase IV. BRS_{symp} (sympathetic BRS) was calculated as the SBP decrement associated with phase III divided by ABP_{RT} [4]. R–R interval responses to a BP rise ($BRSvagal_{inc}$) was defined as the regression slope of the R–R interval over SBP from the start of phase III to the peak of phase IV (or SBP return to baseline). The R–R interval response to a BP fall ($BRSvagal_{dec}$) was expressed as the regression slope of the R–R interval over SBP during phase II_{early}.

Previous experience with the use of $BRSvagal_{dec}$ has led to the observation that subjects with excessively rapid BP changes during phase II_{early} can have spuriously low regression slopes, presumably due to a supramaximal stimulus and limitations in the speed of the vagally mediated HR response. Although not strictly assessing BRS, we have used an alternative parameter, HRslope, that seems to provide helpful information in those situations. HRslope is derived as the regression slope of HR over time (in seconds) during phase II_{early} [$HRslope_{(inc)}$] and from phase III

Table 1 **Baseline BP and HR indices for the controls and patients with graded AF**
Values are means ± S.D. *$P < 0.05$ compared with severe AF, †$P < 0.05$ compared with mild AF, and ǂ$P < 0.05$ compared with control.

Parameter	Severe AF ($n = 49$)	Mild AF ($n = 25$)	Control ($n = 29$)
SBP (mmHg)	152.0 ± 26.4†ǂ	135.5 ± 22.9*	132.7 ± 14.6*
MABP (mmHg)	101.6 ± 18.4†ǂ	90.7 ± 13.9*	91.8 ± 9.9*
DBP (mmHg)	76.7 ± 17.4	68.7 ± 12.9	71.8 ± 9.0
HR (beats/min)	78.5 ± 15.5ǂ	72.7 ± 10.9*	62.5 ± 8.2*†

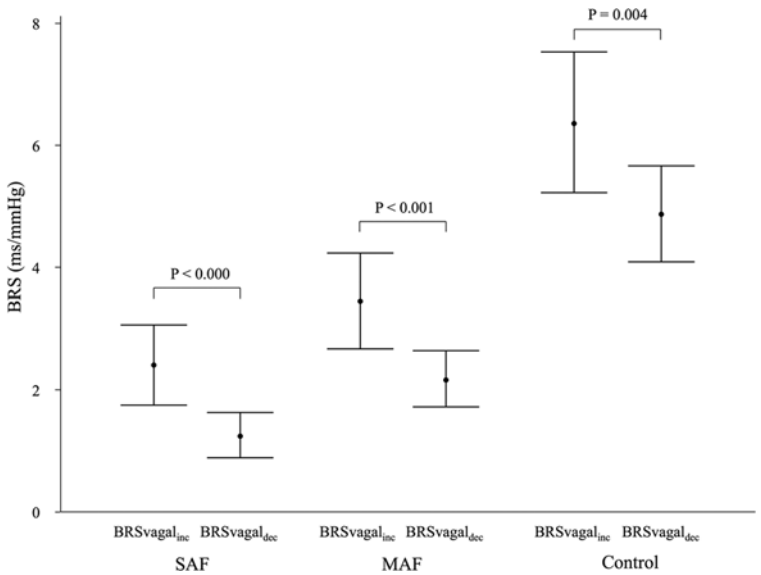

Figure 1 **Vagal BRS for BRSvagal$_{dec}$ and BRSvagal$_{inc}$ in controls, and patients with mild (MAF) and severe (SAF) AF**
Error bar represents the 95% confidence interval.

to the peak of phase IV [HRslope$_{(dec)}$]. We have included this parameter in the present study as well to explore its validity.

Statistical analysis

Continuous variables are expressed as means ± S.D. We used one-way ANOVA with post-hoc Bonferroni analysis to examine group differences, and a paired Student's *t* test was used to analyse normally distributed data. The relationship between SBP and R–R interval was assessed using regression analysis. Regression and correlation analysis, using Pearson's or Spearman's test, was performed as appropriate. All statistical tests were two-tailed and $P < 0.05$ was considered significant for all comparisons. Receiver operator characteristic curve analysis was used to assess predictive values and cut-off values for BRSvagal$_{inc}$ and BRSvagal$_{dec}$, as well as HRslope$_{(inc)}$ and HRslope$_{(dec)}$.

Receiver operator characteristic curve

A receiver operator characteristic curve was used to calculate the relationship between sensitivity and specificity for the control group compared with the mild and severe AF groups, and for evaluating the diagnostic performance of BRSvagal$_{dec}$ and BRSvagal$_{inc}$. The curve cut-off value was determined by tying the sensitivity to a value of greater than 90%, with a few exceptions where the sum of sensitivity and specificity is maximal even though the sensitivity is below 90%.

RESULTS

Baseline haemodynamic indices

Baseline BP and HR indices are summarized in Table 1. There were differences in SBP, MABP and HR between the groups ($P = 0.001$ for SBP, $P = 0.004$ for MABP and $P < 0.001$ for HR). Post-hoc comparisons revealed significant differences in SBP and MABP between severe AF and controls, and severe AF and mild AF. Baseline HR was different between severe AF and controls, and mild AF and controls. Baseline DBP did not differ among the groups.

BRS indices and parameters of the Valsalva manoeuvre

BRSvagal$_{inc}$ was calculated in all subjects across all of the patient groups (Figure 1 and Table 2). Group values for BRSvagal$_{inc}$, BRSvagal$_{dec}$ and BRS$_{symp}$ were all highest in the controls and were lowest in severe AF (Figure 1 and Table 2). There were significant overall differences between the groups (*P* values all <0.001). BRSvagal$_{inc}$ was significantly higher than BRSvagal$_{dec}$ in all of the groups (Figure 1). Post-hoc analysis showed that the difference in BRSvagal$_{inc}$ and BRSvagal$_{dec}$ was significant between severe AF and the controls, and mild AF and the controls (Figure 1 and Table 2). BRS$_{symp}$ was significantly different

Table 2 Valsalva manoeuvre and BRS parameters in controls and patients with AF

Values are means ± S.D. *$P < 0.05$ compared with severe AF, †$P < 0.05$ compared with mild AF, and ǂ$P < 0.05$ compared with control.

Parameter	Severe AF	Mild AF	Control
$BRSvagal_{inc}$ (ms/mmHg)	2.46 ± 2.30ǂ	3.51 ± 1.98ǂ	6.50 ± 3.10*†
$BRSvagal_{dec}$ (ms/mmHg)	1.27 ± 1.31ǂ	2.24 ± 1.19ǂ	4.99 ± 2.11*†
BRS_{symp} (mmHg/s)	3.28 ± 1.81†ǂ	10.07 ± 3.29*ǂ	32.21 ± 14.31*†
Phase II_{early} (mmHg)	31.25 ± 16.6†ǂ	22.79 ± 11.17*ǂ	6.94 ± 9.05*†
Phase II_{late} (mmHg)	1.53 ± 2.51ǂ	1.40 ± 2.12ǂ	12.38 ± 6.83*†
Phase IV (mmHg)	4.48 ± 5.11†ǂ	9.77 ± 6.38*ǂ	22.51 ± 11.98*†
ABP_{RT} (s)	28.78 ± 14.30†ǂ	7.08 ± 1.40*ǂ	1.72 ± 0.82*†
$HRslope_{(inc)}$ (beat/s)	0.75 ± 0.84†ǂ	1.15 ± 0.99*ǂ	3.02 ± 1.53*†
$HRslope_{(dec)}$ (beat/s)	− 0.86 ± 1.03ǂ	− 1.92 ± 2.27ǂ	− 7.06 ± 3.88*†

Table 3 Correlations between BRS with components of Valsalva manoeuvre, pressure recovery time and HR slope

Parameter	$BRSvagal_{inc}$	$BRSvagal_{dec}$	BRS_{symp}	Phase II_{early}	Phase II_{late}	Phase IV	ABP_{RT}	$HRslope_{(inc)}$	$HRslope_{(dec)}$
$BRSvagal_{inc}$	–	0.721	0.413	− 0.460	0.422	0.282	− 0.466	0.531	− 0.636
$BRSvagal_{dec}$		–	0.571	− 0.515	0.551	0.443	− 0.571	0.722	− 0.661
BRS_{symp}			–	− 0.418	0.816	0.792	− 0.612	0.646	− 0.705
Phase II_{early}				–	− 0.485	− 0.401	0.550	− 0.611	0.418
Phase II_{late}					–	0.605	− 0.458	0.489	− 0.586
Phase IV						–	− 0.550	0.642	− 0.702
ABP_{RT}							–	− 0.522	0.517
$HRslope_{(inc)}$								–	− 0.817
$HRslope_{(dec)}$									–

between all of the groups. Similarly, $HRslope_{(inc)}$ and $HRslope_{(dec)}$ were highest (absolute values) in the controls and lowest in severe AF, with similar overall and post-hoc group differences as the BRS parameters (Table 2).

The amplitude of phase II_{late} and phase IV was highest in the controls and was markedly blunted in both of the patient groups. The amplitude of phase II_{early} was highest in severe AF. There was again an overall significant difference between groups ($P < 0.001$). Group-by-group comparisons are summarized in Table 2.

Correlation between BRS and other parameters derived from the Valsalva manoeuvre

We correlated the parameters of BRS to the magnitude of BP changes during Valsalva manoeuvre, ABP_{RT} and HRslope. The correlations were all significant ($P < 0.001$). The coefficients are listed in Table 3. Notably, $BRSvagal_{inc}$ significantly correlated with previously utilized phases of the Valsalva manoeuvre and sympathetic barosensitivity, with the highest correlations with $BRSvagal_{dec}$. The relationship between $BRSvagal_{inc}$ and $BRSvagal_{dec}$ for all patient groups is shown in Figure 2. $HRslope_{(inc)}$ was significantly lower than $HRslope_{(dec)}$ in controls, but not in the patient groups (Table 2).

Receiver operator characteristic curve analysis

Receiver operator characteristic curve analysis was used to determine optimal cut-off values from normal for the severe AF and mild AF groups for $BRSvagal_{inc}$ and $BRSvagal_{dec}$. AUCs (areas under the curve) for $BRSvagal_{inc}$ and $BRSvagal_{dec}$ are shown in Figure 3.

The AUC for $BRSvagal_{inc}$ was 0.86 and the AUC for $BRSvagal_{dec}$ was 0.94 in the model of comparing severe AF with controls (Figure 3A). The cut-off value of $BRSvagal_{inc}$ was 5.99 for differentiating severe AF from controls with a sensitivity of 0.94 and specificity of 0.62. The cut-off value of $BRSvagal_{dec}$ was 2.34 for differentiating severe AF from controls with a sensitivity of 0.82 and specificity of 0.93.

The AUC for $BRSvagal_{inc}$ was 0.78 and the AUC for $BRSvagal_{dec}$ was 0.88 in the model of comparing mild AF with controls (Figure 3B). The cut-off value of $BRSvagal_{inc}$ was 5.66 for differentiating mild AF from controls, with a sensitivity and specificity of 0.88 and 0.62 respectively. The cut-off value of $BRSvagal_{dec}$ was 3.03 for differentiating mild AF from controls, with a sensitivity and specificity of 0.88 and 0.83 respectively.

Receiver operator characteristic curves were also created for $HRslope_{(inc)}$ and $HRslope_{(dec)}$. A cut-off value for $HRslope_{(inc)}$ of 1.58 separated controls from severe AF with 90% sensitivity and 83% specificity, whereas a cut-off value of 2.44 separated controls from mild AF with 88% sensitivity and 69% specificity. A cut-off value for $HRslope_{(dec)}$ of − 1.66 separated controls from severe AF with 84% sensitivity and 97% specificity, whereas a cut-off value of − 2.30 separated controls from mild AF with 88% sensitivity and 90% specificity.

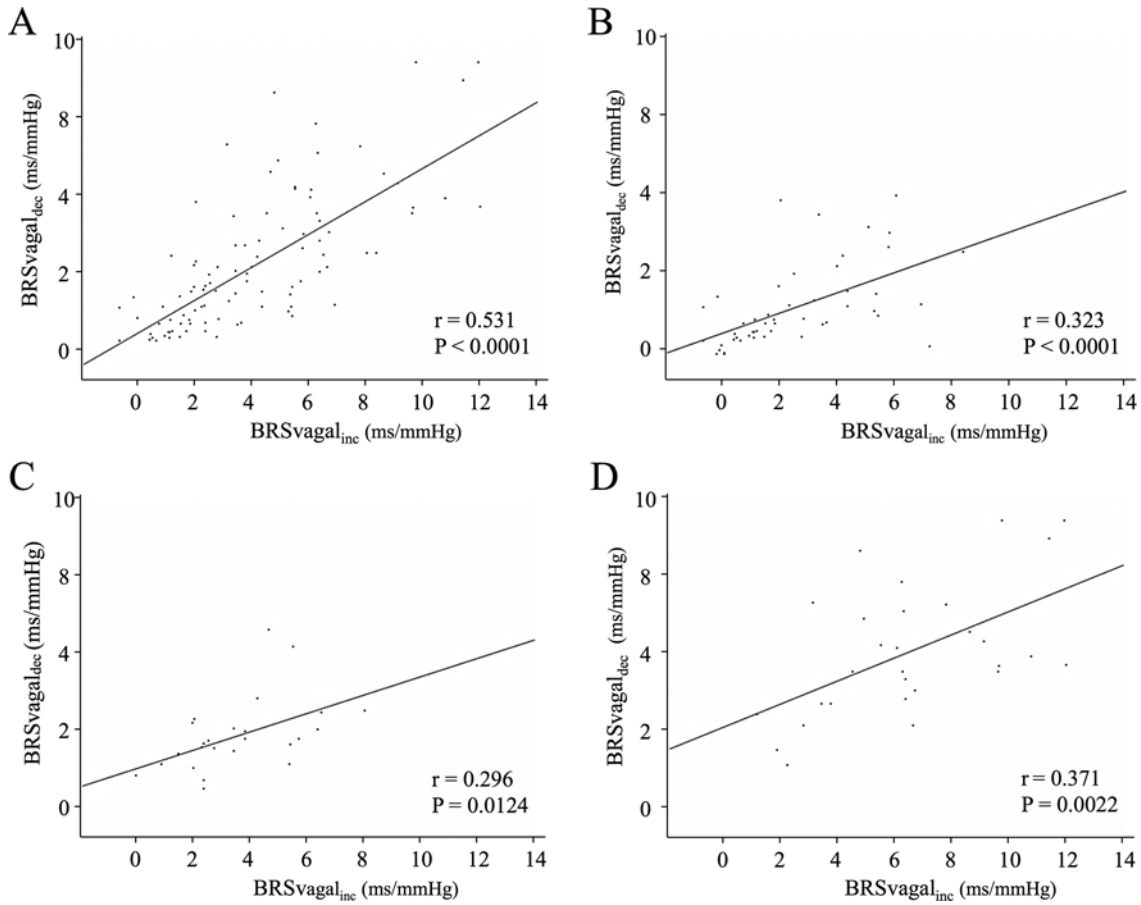

Figure 2 **Correlation between BRSvagal$_{dec}$ and BRSvagal$_{inc}$ in (A) all study subjects, (B) severe AF, (C) mild AF and (D) control**

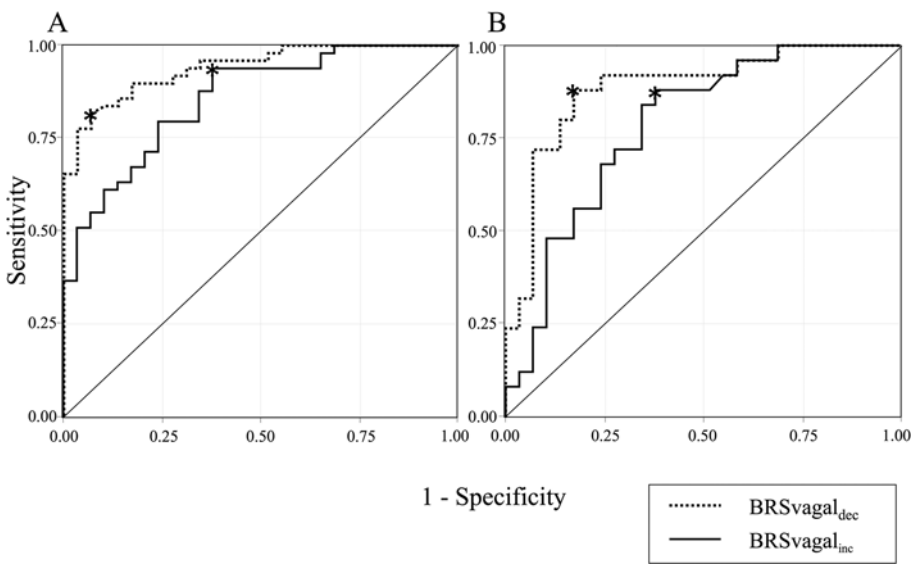

Figure 3 **Receiver operator characteristic curves showing sensitivity and 1 – specificity for BRSvagal$_{inc}$ and BRSvagal$_{dec}$ in the model comparing severe AF with control (A), and mild AF with control (B)**
*Represents the cut-off points for each value.

DISCUSSION

The pertinent findings of the present study can be summarized as follows: (i) BRS_vagal can be readily determined from the R–R interval response to the BP increase during phases III–IV of the Valsalva manoeuvre in normal controls, as well as in patients with different degrees of AF; (ii) $BRSvagal_{inc}$ shows a graded decrease with increasing degrees of AF; (iii) $BRSvagal_{inc}$ shows a high association with other indices of AF, and particularly with other indices of baroreflex function; (iv) HRslope shows a similar pattern of differences across the patient groups as BRS_vagal, and has a potential application as a surrogate marker of BRS in subjects with spuriously low BRS_vagal due to excessively rapid BP changes during the Valsalva manoeuvre; and (v) cut-off values between 5.6 and 6.0 ms/mmHg for $BRSvagal_{inc}$ and between 2.3 and 3.0 ms/mmHg for $BRSvagal_{dec}$ reasonably differentiate normal from abnormal vagal baroreflex function in middle-aged adults.

Assessing vagal baroreflex function provides important information about autonomic nervous system function and its impairment. The modified Oxford technique is considered the gold standard in assessing BRS_vagal, but requires pharmacological manipulations of BP and is therefore not suited for routine application in the clinical autonomic laboratory [6]. The Valsalva manoeuvre is part of a routine battery of tests to non-invasively assess autonomic nervous system function and has been shown to provide quantifiable information about vagal baroreflex function by assessing the vagal response to alterations in BP [9]. Although the HR or R–R interval response to the BP decrease during phase II_{early} is widely used for this purpose, previously reported indices derived from the HR or R–R interval response to the BP increase during phase IV have not found broader application, owing to the fact that patients with AF lack a BP overshoot during phase IV [9,11]. In contrast, phase III is mostly mechanical and is universally present. In the present study, we propose a parameter for vagal baroreflex function derived from the BP increase during phases III and IV, which can be derived regardless of the development of a phase IV overshoot. We were able to demonstrate that this parameter could indeed be calculated from routine BP and HR recordings of all subjects enrolled in the present study.

The next step in establishing this new parameter was to prove its validity by assessing its values across different degrees of AF and by assessing its association with other indices of baroreflex function. We could demonstrate that $BRSvagal_{inc}$ shows a graded and highly significant decrease with increasing degrees of AF. We could also show that $BRSvagal_{inc}$ has strong associations with other indices of AF and particularly with other indices of baroreflex function. The association with another index of *v*agal baroreflex function ($BRSvagal_{dec}$) was stronger than associations with indices of sympathetic baroreflex function (BRS_{symp} and ABP_{RT}). That is expected since the vagal baroreflex arc shares only the afferent but not the efferent pathways with the sympathetic baroreflex arc and is consistent with clinical and laboratory observations that each component may be selectively or differentially involved in certain autonomic disorders. This observation is also consistent with previous reports that there is no correlation between sympathetic activity and vagal baroreflex gain [5,6].

We found the values for $BRSvagal_{inc}$ higher than those for $BRSvagal_{dec}$ across all of the patient groups. Rudas et al. [6] using the modified Oxford technique also reported vagal baroreflex slopes being higher when arterial pressures are rising than when they are falling, and this hysteresis was observed over pressure ranges both below and above baseline levels. The values derived for vagal baroreflex gain in this and other studies using the Oxford technique are, however, generally higher than those we found in this as well as previous studies on BRS_vagal derived from the Valsalva manoeuvre [4–6]. The reason for this difference is not known, but we speculate that it relates to temporal differences in BP changes. BP changes during the Valsalva manoeuvre occur quite rapidly, with BP changes of 50 mmHg or more over a few seconds not infrequently observed, whereas BP changes induced by pharmacological interventions are much slower. In fact, we have observed spuriously low BRS_vagal values in healthy controls with particularly rapid BP changes ('exaggerated early phase II'). This presumably relates to a supramaximal stimulus and limitations in the speed of the vagally mediated HR response.

We have therefore used an alternative parameter, HRslope, that seems to provide helpful information in those situations. This index measures the HR change during phase II_{early} and during phases III–IV as a function of time rather than as a function of BP change. Although not strictly assessing BRS, we have used this index as a surrogate marker of baroreflex function in those circumstances and have therefore included evaluations of this parameter in the present study. $HRslope_{(inc)}$ and $HRslope_{(dec)}$ showed a very similar pattern of differences across the patient groups to $BRSvagal_{inc}$ and $BRSvagal_{dec}$. Our data suggest that one can reasonably postulate normal vagal BRS if the slope of HR increment is greater than 2.44 and/or the slope of HR decrement is lower than -2.30 in cases where BRS appears spuriously low due to excessively rapid changes in BP.

Although previous studies have used the degree of OH to evaluate the severity of AF, in the present study we used the length of ABP_{RT} to distinguish the severity of AF [4,12]. We believe that the use of this parameter is superior to using the degree of OH. OH is observed only with severe degrees of sympathetic failure [10], whereas ABP_{RT} shows a graded increase with increasing degrees of AF [12]. The only direct method to measure the intactness of baroreflex-mediated sympathetic activation is through microneurographic recordings of muscle sympathetic nerve activity [13], a procedure that is too invasive, time-consuming and technically too demanding for routine clinical usage. ABP_{RT} offers the opportunity to evaluate intermediate levels of severity of sympathetic failure non-invasively.

The main limitations of the present study are that it is retrospective and depends on the accuracy of Finapres-recorded beat-to-beat BP changes. Since BRS values calculated using this method are substantially different from those derived from the modified Oxford method, BRS values should not be directly compared across the different techniques. The provided cut-off values from normal are based on relatively small numbers of subjects. A study formally establishing normative data for this new index of baroreflex function in a large group of subjects is currently in progress.

Conclusions

Vagal BRS can be readily determined from the R–R interval response to the BP increase during phases III–IV of the Valsalva manoeuvre, complimenting the assessment of baroreflex pathways in the clinical autonomic laboratory.

CLINICAL PERSPECTIVES

- In the clinical autonomic laboratory, non-invasive methodology is available to measure beat-to-beat BP and HR. The autonomic clinician can recognize patterns of AF.
- Although this qualitative approach is important, quantifying baroreflex function adds a new dimension of accuracy and sophistication. In the present study, we add the component of $BRSvagal_{inc}$, which, together with $BRSvagal_{dec}$ and BRS_{symp}, enable a complete, yet simple, analysis of baroreflex function.
- This approach has value in the diagnosis of AF and monitoring the progression of disease and the response to treatment.

AUTHOR CONTRIBUTION

Naoki Wada analysed the data, performed statistical analysis and wrote the first draft of the paper. James Schmelzer conceived the project. Tonette Gehrking, James Schmelzer, and David Sletten recruited the subjects and collected the clinical data; David Sletten provided statistical and instrumental support. Phillip Low and Wolfgang Singer designed and supervised the study, including analysis of the subjects and preparation of the paper.

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