RIGHT VENTRICULAR FUNCTION IN PACED PATIENTS

- A STUDY USING PULSED DOPPLER ULTRASOUND

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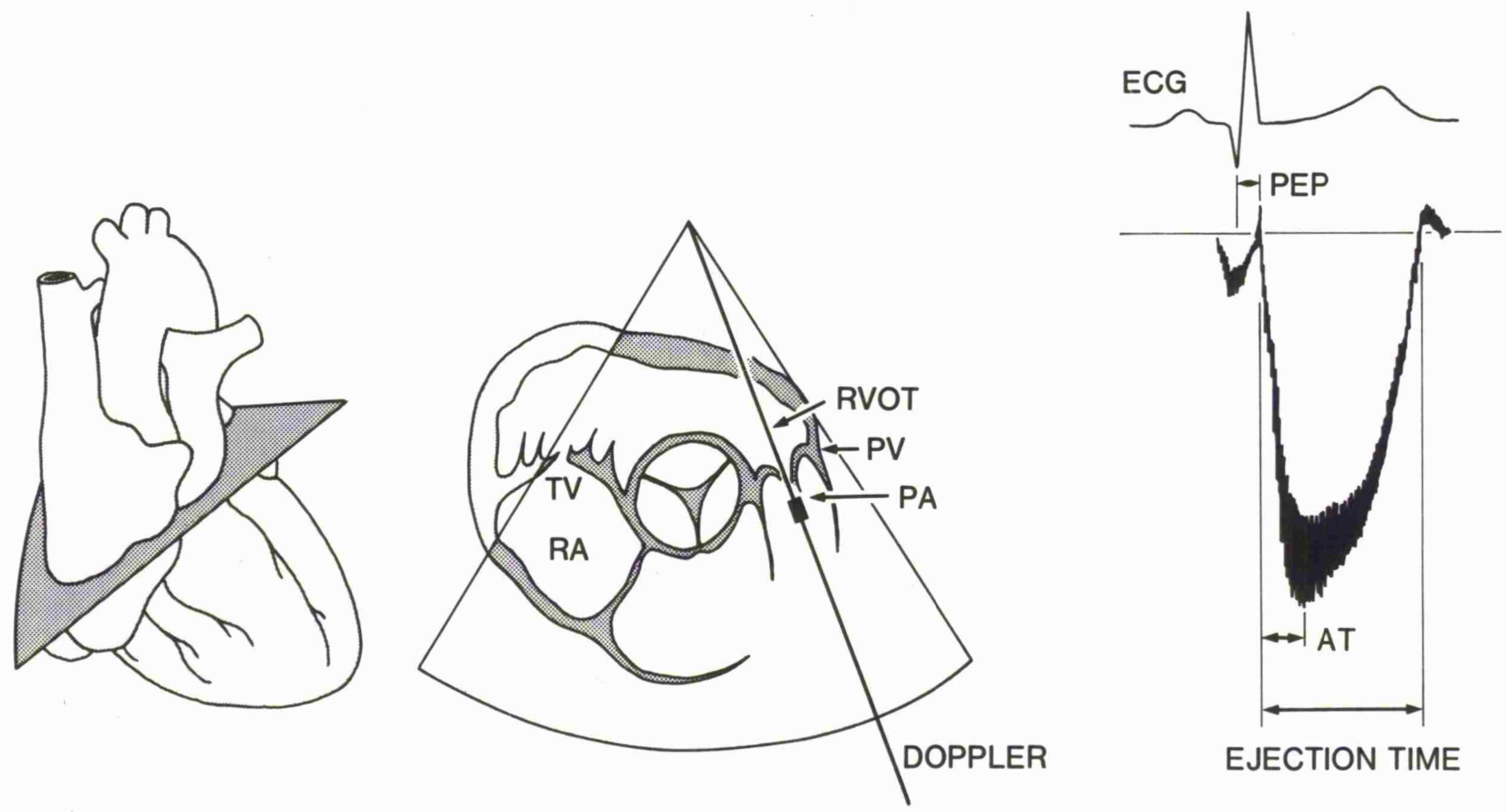
Dr MG Cheesman

Fig. 1

AREA OF INTEREST



SUMMARY

There is increasing interest in right ventricular function as an important determinant of cardiac output. However, the chamber is difficult to study, because of its shape and relationship to the left ventricle. Invasive studies, radionuclide studies and two-dimensional echocardiography are all useful approaches, but all have serious limitations.

Systolic time intervals, best measured by pulsed Doppler ultrasound in the proximal pulmonary artery, offer one method of assessing right ventricular systolic function. Previous "normal" ranges, however, could be criticised on many counts. I present data from carefully checked normal controls and compare to previous publications, and explore variability and relationships between the various systolic time intervals. Most variables have skewed frequency distributions; the ranges are somewhat wider than previously described; most heart rate corrections are found to have serious limitations; and the effect of age is explored.

Complete heart block offers a model to study the the effects of varying atrioventricular intervals whilst the ventricular rate is held unphysiologically steady by an artificial pacemaker. Given the current controversy about the merits of single- versus dual-chamber pacing, the issue is of topical interest also. The effect of varying the "P-R" interval within the physiological range is explored, and "optimal" ranges identified.

A curious "nadir" effect, previously unknown, was discovered. When P waves followed paced QRS complexes at about -50-100ms, forward flow into the pulmonary artery (as judged from systolic time intervals) fell in most patients, and in some subjects virtually ceased. As a small included invasive part of the study showed, this was accompanied by falls in RV systolic pressure and rises in right atrial pressure.

This study demonstrates that right ventricular systolic time intervals can be used to study right ventricular function in pacing situations, and is further evidence of the unsatisfactory nature of single-chamber ventricular pacing.

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List of abbreviations in text

AT	Acceleration Time
CI	Confidence Intervals
DDD	Dual-chamber pacing mode
EF	Ejection Fraction
HR	Heart Rate
LV	Left Ventricle
LVET	Left Ventricular Ejection Time
LVPEP	Left Ventricular Pre-Ejection Period
LVSTIs	Left Ventricular Systolic Time Intervals
PA	Pulmonary Artery
PAP	Pulmonary Artery Pressure
PAVmax	Maximum velocity in the proximal pulmonary artery
PV	Pulmonary Valve
PVR	Pulmonary Vascular Resistance
PR interval	Interval from onset of P wave on electrocardiogram to onset of QRS complex
QRS complex	Inscription of ventricular depolarisation on the electrocardiogram
RVET	Right Ventricular Ejection Time
RVETI	Right Ventricular Ejection Time "corrected" for heart rate
RVOT	Right Ventricular Outflow Tract
RVPEP	Right Ventricular Pre-Ejection Period
RVSTIs	Right Ventricular Systolic Time Intervals
SEM	Standard Error of the Mean
STIs	Systolic Time Intervals
VSD	Ventricular Septal Defect
VVI	Single-chamber ventricular demand pacing mode
Vmax	Maximum velocity

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PART ONE

INTRODUCTION

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INTRODUCTION

Introduction

(i) Why study the right ventricle ?

There is increasing recognition of the importance of the right ventricular contribution to cardiac output. In its most extreme form, RV infarction (as in 50% of inferior myocardial infarctions[1-2]), may cause a distinct syndrome of cardiogenic shock with high jugular venous pressures but without pulmonary oedema[3]. In other catastrophes such as peri-infarction ventricular septal defect, RV function is both of prognostic significance[4], and can be observed to improve after successful surgical repair[5].

A large population of young adults is emerging who have had sucessful repairs of complex congenital defects in childhood. Not only was RV function of paramount importance in deciding their fitness for surgery, but there is increasing interest in estimation of RV function to determine which patients should be intensively followed to see if repair really was adequate[6,7]. At least one author has already used Doppler echocardiography to assess results after a modified Fontan operation[8]. RV ejection fraction is highly after-load sensitive, and usually improves after repair of congenital defects[6,9,10,11], or after vasodilator treatment of left ventricular dysfunction[12-14].

Right ventricular function is of importance during cardiac surgery. "Loading" of the RV during weaning from bypass is a frequently-used manoeuvre, with high filling pressures being often required. There is increasing concern that the RV is inadequately protected during cardioplegia[15,16], unlike the left ventricle(LV), and that this may contribute to postoperative morbidity and mortality[17].

RV function is being increasingly studied in chronic obstructive airway disease(COAD). A low RV ejection fraction is associated with a high chance of progression to cor pulmonale and a reduced life expectancy[18,29]: this is of particular importance because these patients live longer and are improved symptomatically on long-term domiciliary oxygen[19]. Many bronchodilators are also vasodilators, and so have complex actions on RV function[20].

In addition, the RV has become more interesting to physicians specialising in cardiac arrythmias because of the recognition of the syndrome of RV cardiomyopathy[21] and dysplasia associated with ventricular tachycardia. Although still an uncommon cause of sudden death, most Departments of Cardiology are reviewing several such patients, who are often young and otherwise fit.

(ii) How can the RV be studied ?

It must be admitted at once that numerous difficulties beset any study of RV function. The chamber is a difficult wedge-shaped entity which changes further on contraction[22,23]. Casts of the "normal" RV (usually in end-diastolic conditions) have been used to investigate various formulae, but their application to situations of signficant volume overload (for instance) has yet to be validated. Methods of assessing RV ejection fraction from bi-plane angiography with reference to these models have not found wide application.

The proximity of the left ventricle, around which the RV is wrapped, is also a problem. The shared interventricular septum may contribute to either ventricle's output. Disease processes may affect both ventricles simultaneously, and poor LV function raises pulmonary resistance and hence affects RV function.

Clinical and radiographic examination are at best crude instruments for assessing RV function, and serious RV disease can be present despite a normal electrocardiogram[24].

Cardiac catheterisation has provided much of the published data on RV function[25]: but it is invasive, expensive, and neither without risk nor easily repeatable. It is always difficult to know how much a stiff catheter placed across a heart valve in a low-pressure system like the right heart in itself changes the very parameters one wishes to measure. In addition, invasive investigation of RV function is insensitive, with other methods such as radionucleid study consistently producing higher figures for RV dysfunction in many medical conditions [2,4].

Pressure-volume loops offer important insights into RV function, demonstrating how different RV and LV physiology really are; they can be used to monitor the effects of changing loading conditions [26-27], and have been used during cardiac surgery[29] to look at the RV effects of cold cardioplegia. However, they require both invasive pressure monitoring and biplane angiography simultaneously, so despite being the reference standard at the moment for assessing RV function, they are unlikely to find widepsread clinical application.

Radionuclied study can produce accurate figures for cardiac output by first-pass study [29], and partly side-steps the geometry problem by relying on count-related summation methods to estimate RV ejection fraction[30-33] (although the problem of proximity to the LV remains, and subtraction techniques are necessary). The hardware involved is neither cheap nor portable. Obviously, the methods expose patients to small doses of radioactivity, so limiting repeatability. Assessment of beat-to-beat variability is difficult in both first-pass and multiple-gated acquisition studies. Dilated atria (by increasing "background" counts) and the presence of atrial fibrillation (both frequent in heart disease) further reduce the value of this method[34]. However, it has remained a valuable tool for the study of exercise effects[35].

Two-dimensional echocardiography (2D-echo) is comparatively cheap and usually portable: serial studies are easy, harmless and non-invasive. Standard views and normal ranges have been proposed[36-40]. However, the problem of geometry persists, and measurement of RV ejection fraction remains difficult. There is not even an "easy" measurement such as fractional shortening, as has been used in the LV [41-42]. Further, multiple views are required for accurate assessment, and this is often difficult to achieve in the elderly or in patients with respiratory disease.

Echocardiographically-guided Doppler imaging of blood flow has many advantages in the non-invasive appraisal of RV function. Pulsed Doppler has been used to assess RV inflow velocities and assess age-, rate- and respiration-induced changes[43]; this work is in early stages. The finding that regional pressure gradients exist in the RV[44], as they do in the LV, complicates matters; although only a few millimetres of mercury pressure in magnitude, they further illustrate the complexity of the problem.

Estimations of RV systolic function are much easier, and have already found clinical uses. For estimates of Pulmonary Artery(PA) pressure, the method of Yock [45] and Hatle [46] utilising tricuspid regurgitant velocity offers good agreement with invasively measured values [46]. However, beat-to-beat variability is difficult to study: right atrial pressure is assumed to be an arbitrary constant (which it certainly is not in more than very mild tricuspid regurgitation), and sensitivity is insufficient to study the effect of interventions. Even with very sensitive machines, tricuspid regurgitation is not detectable in everyone. Nonetheless, clinically useful estimates of PA pressure can be obtained [47-50].

An alternative approach is to time ventricular outflow and to study the RV outflow waveform. Systolic time intervals (STIs) have come a long way since Weissler[51,52] and Hirshfeld [53] pioneered their use in the early 1970s. RV STIs were originally measured using pulmonary valve (PV) movement[54]; but whereas this is broadly satisfactory in children in whom imaging is usually easy, it is much harder to get reliable images in adults. Considerable variation was found in correlation with invasive methods[55-63]. It is also often difficult to time the end of RV systole using this method [64]. However, the use of pulsed wave (pw) Doppler ultrasound allows great accuracy even when the valve leaflets cannot easily be seen[65-67] and in addition creates new parameters such as the time-to-peak flow or acceleration time (AT)[68,71], which are themselves useful. "Rules-of-thumb" e.g. that an acceleration time of <100ms almost always means significant pulmonary hypertension emerged[64,65,67,71].

(iii) Rationale of this study

RVSTIs require further development. Firstly, the range of normality has been inadequately explored. Many "normal ranges" were obtained from studies on patients referred for suspected heart disease[54,61,73]. The effects of age (outside infancy), sex, beat-to-beat variation and inter-personal variation have not been adequately studied.

Are RVSTIs sufficiently constant within individuals and from beat-to-beat for studies on interventions?

Is between-person variation sufficient to make a normal range of limited application anyway?

What are the effects of age, heart rate and sex?

Part One of this study therefore set out to determine normal ranges for all the commonly-used RVSTIs and to study their variability within and between subjects.

In addition, the effect of RV loading conditions requires investigation because of the steep Frank-Starling curve in the RV[74] and the importance therefore of RV preload. One major determinant of RV preload is the PR interval[77], and correct timing is important for RV output [74,75]. One would wish to have access to a model that would change the PR interval on a predictable basis, whilst keeping other variables almost unphysiologically constant.

Complete heart block, in which there is complete atrio-ventricular (AV) dissociation with continuing "disconnected" atrial activity, provides an approximation to this ideal. There is continuous variation of the atrioventricular interval combined with a very constant ventricular rate supplied by an electrical pacemaker.

Of course, this situation is not just of academic interest. There is increasing disenchantment with single-chamber ventricular pacing without any attempt at atrial synchronisation, and increasing interest in the benefits of dual chamber pacing[74,76,77]. The North Atlantic Society for Pacing and Electrophysiology (NASPE) has already laid down guidelines which include the use of dual-chamber pacemakers in most of such cases[78]: but it would be fair to say that many fewer such devices are implanted in the UK, largely for economic reasons, and the debate is far from over.

Important questions remain. Most research attention has been focused on effects on the left ventricle: but does variation in the AV interval significantly affect RV output?
Is there an "optimum" PR interval for most patients?
Can one still perceive the effects of atrio-ventricular variation in the presence of aberrant ventricular excitation such as an artificial pacemaker produces?
How does the effect on the RV compare with the fairly small changes reported in left ventricular function?[79] (The wire is, after all, in the right ventricle).

The second part of this study therefore looked at 30 patients with apparently normal left ventricular function, ventricular demand (VVI) pacemakers, and complete heart block with continuing atrial activity, to study intra-subject changes in RVSTIs as variation in AV interval occurred spontaneously.

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HISTORICAL DEVELOPMENT OF SYSTOLIC TIME INTERVALS

Historical development of Systolic Time Intervals (STIs)

(i) Early development of systolic time intervals

Early studies on the left heart

The Frenchman Marey [80] is credited with the first graphic recordings of the arterial pulse in man, as far back as 1860. His contemporary, Garrod [81], noted the inverse relationship between heart rate and duration of systole, and this was confirmed by others [82-84]. The classic studies by Wiggers [85,86] in the 1920s greatly added to understanding of the timings of the cardiac cycle, and of the relationship of systole and diastole to the heart rate. Katz and Feil [87,88] applied electronic recording methods and explored variability in atrial fibrillation and hypertension; and Blumberg studied a wide range of cardiac disorders [89]. Coblentz [90] gave the first modern description of STIs in 1949, demonstrating the links between electrical and mechanical activation, backed up a few years later by Braunwald [91]. However, all these descriptions were of largely theoretical interest, with little practical application.

Weissler and associates first foresaw and developed the clinical potential of STIs, by a series of seminal papers on their studies in normal individuals and then in patients with heart disease [92-94]. They explored the effect of digoxin, beta-adrenergic agonists and beta-blocking drugs on left ventricular function by these methods [95]. Electrical activation of the ventricles was taken from the onset of the QRS complex of the electrocardiogram, onset of ejection was taken as the beginning of the rise of the carotid upstroke, and the end of ejection was determined from aortic valve closure on a phonocardiogram.

Although open to criticism now, as there is a delay between the onset of systole and the rise in the carotid waveform, these careful studies on the left heart laid the foundations for future development, set out normal ranges, and remain the most-quoted papers in the whole field.

Early studies on right ventricular STIs

Although the earliest papers on STIs contained some descriptions of right ventricular STIs (RVSTIs)[90,91], the difficulty of non-invasively recording right ventricular (RV) systole retarded their development. In addition, right heart function was thought to be much less important. Leighton et al [96] produced a pain-staking study of RVSTIs, and their relationship to left ventricular (LV) STIs, in 1972. They used invasive methods, studying pulmonary artery (PA) waveform, and used intracardiac phonocardiography to accurately fix the pulmonary component of the second heart sound (P2). LVSTIs were determined non-invasively, by Weissler's method. Twenty-seven patients (of whom only five were normal - most were under investigation for cardiac murmurs) underwent cardiac catheterisation, and timings were made at rest using catheter-tip transducers to minimise any errors. Atrial pacing was used in each patient to study the effect of heart rate. They found that RV ejection time (RVET) was longer than LV ejection time (LVET) in each individual (as had been previously found in animals [97]); that the effect of deep inspiration was measurable though small in RVSTIs and unimportant in LVSTIs; that RVET and LVET were strongly negatively associated with heart rate but that the pre-ejection periods were not; and they were the first to suggest that RVSTIs could perhaps be developed to predict PA pressure, demonstrating a moderate correlation of the RV pre-ejection period (RVPEP) with the pulmonary artery diastolic pressure.

(ii) The assessment of PA dynamics using STIs

Studies assesing PA pressure from RVSTIs using pulmonary valve movement

However, RVSTIs would be of little practical use if their measurement required invasive investigation, as PA pressure could also be directly measured by that technique. Following description of pulmonary valve imaging by Gramiak and Nanda[98] in 1972, Hirschfeld[99] used the method to measure RVSTIs on 11 normal children (aged 3-14 yrs) and compared them with LVSTIs obtained by imaging the aortic valve.
Ingeniously, he compared these values (the first non-invasively determined "normal range") with those obtained from 15 children who had transposition of the great arteries. He found a LVET/RVET ratio of 0.8 and a LVPEP/RVPEP ratio of 1.26 in normals, with these figures being approximately reversed in Transposition.
He concluded (correctly) that pressure and vascular resistance were the main determinants of STIs.

It seemed logical, then, for him to go on and later that year to assess the pulmonary vascular beds of 62 young patients with congenital heart disease [100]. He enlarged his series of "normals" to 45 (still mostly children), describing the effects of ageing on RVPEP and RVET (minor in his age range) and on the ratio RVPEP/RVET (no effect). All of his 62 patients with congenital heart disease were catheterised, and pulmonary artery pressure and cardiac output were measured, and from these determinations pulmonary vascular resistance was estimated. The ratio RVPEP/RVET was found to moderately correlate with pulmonary artery diastolic pressure (PADP), although the scatter was fairly broad. Association with pulmonary vascular resistance (PVR) and mean PAP were less good. He concluded that for the first time, useful estimates of pulmonary artery pressure and resistance could be made from non-invasive methods.

Nanda and Gramaik[101] went on to study adult patients. They performed cardiac catheterisation on 63 adult patients with a a variety of cardiac disorders (25 had mitral valve disease, 12 had ischaemic heart disease, 16 were in atrial fibrillation, etc.) and measured right ventricular pre-ejection period corrected for heart rate by a Bazzett-style[102] formula. In only 35% of their patients was a good-quality pulmonary valve echogram achieved, and they did not attempt to record pulmonary valve closure. Stevenson and associates[103] fared better when studying infants and children (95 out of 125), and noted that sedation improved the correlations considerably.

The differing chest shape of older children and adults is largely to blame for the generally poorer imaging and hence accuracy compared to infants, in whom reliable images are usual[103]. However, Silverman[104] was unable to duplicate Hirschfeld's results, finding no correlation between RVPEP/RVET and mean PAP or PVR.

Boyd[105] noted that high right atrial pressures and the presence of right bundle branch block also diminished any such association. With increasing disaffection with the technique, other pointers such as the waveform of pulmonary artery ejection (as judged from pulmonary valve movement) and depth of the "a" wave were explored[106,107] but no consensus was achieved here either[108,109].

Studies using RVSTIs to assess PA pressure using pulsed Doppler ultrasound

The situation was rescued by the arrival of pulsed Doppler ultrasound. Even if the pulmonary valve could not be clearly imaged, flow in the right ventricular outflow tract or proximal pulmonary artery could be obtained in almost every case, and it was much easier to determine the end of right ventricular ejection. Light[110] first studied PA flow using continuous wave Doppler ultrasound, but this was a "blind" technique, and in adults it could be difficult to be sure that one was not lined up on aortic flow, especially when the aorta is tortuous, as it frequently is in adults. Pulsed Doppler ultrasound can be combined with real-time two-dimensional imaging, and much greater anatomical accuracy can be achieved. The pulsed Doppler mode does carry with it limitations as regards velocity measurement, but as PA flow is usually less than 1 m/sec[111], these are usually containable.

Gardin and associates [112] studied 20 normal individuals, comparing and contrasting left- and right-sided STIs derived from Doppler measurements of aortic and pulmonary artery flow. They confirmed previous findings that LVET is shorter than RVET, and addressed the new parameter of acceleration time, or "time-to-peak" flow. This was found to be much longer in the PA (mean of 160ms in the PA vs. 98ms in the aorta) and to take up a much greater part of the ejection time in the PA. Peak velocity was higher in the aorta (0.9 m/sec vs 0.6 m/sec in the PA). These data suggested that despite the systemic vascular resistance being much higher than the pulmonary, blood was accelerated two or three times more rapidly in the aorta. No attempt was made to confirm these findings invasively.

Kitabatake[113] studied the correlation between invasive and Doppler data in 33 patients, almost all of whom had heart disease. This should be remembered when using his much-quoted range of normal values (in his patients without elevation of pulmonary artery pressure). He studied flow in the RV outflow tract (RVOT) and noted a useful inverse relationship between acceleration time (AT) and mean PAP, which improved slightly with logarithmic transformation. Even better was the ratio AT/RVET which was also inversely associated with mean PAP, and improved with log. transformation. This kind of accuracy was clearly clinically useful, and several attempts were made to duplicate his work.

Kosturakis[114] achieved similar results when studying seventeen children (age range 2/12 to 13 yrs) but could only achieve moderate correlations.

Isobe's group[115] studied 45 adults with varied cardiac disease and demonstrated similar figures to Kitibatake, but also showed that neither RBBB nor low cardiac index significantly diminished the usefulness of the technique; they also demonstrated good correlations between the ratio RVPEP/AT and mean PAP.

Matsuda and colleague[116] studied 67 patients with heart disease and confirmed previous findings; they found that an acceleration time of 90ms or less always meant a high PAP, but unfortunately this was not very sensitive as 12 of their 22 patients with mean PAPs of >25 mmHg had ATs of more than 130ms. Confirming associations with pulmonary vascular resistance and pulmonary blood flow, they found these poorer than others.

However,in Martin-Duran's series[117] of 51 patients not only were AT and AT/RVET found to accurately predict mean PAP, but PVR was also strongly negatively associated.
General agreement was reached that meaningful estimations of pulmonary flow dynamics could be made from pulsed Doppler recordings of PA flow.

As early detection of pulmonary artery hypertension is important in neonates, normal ranges for neonates[118,119] and even for the human foetus[120] were constructed.

Attempts were made to quantify intracardiac[121] and extracardiac[122] shunting by the ratios of LVSTIs and RVSTIs, and Hatle[123] and Marx[122] went one stage further and produced good estimates of PAP from such data. Amid renewed enthusiasm, Hsieh et al[124] looked at RVSTIs derived from M-mode and Doppler and demonstrated their essential identity, showing clearly that Doppler ultrasound was much better at pinpointing end-systole.

Lighty[125] and Panadis[126] cleared up some of the confusion of different "normal ranges" by showing that the position of the sampling beam in the pulmonary artery substantially altered the AT and peak velocity measured.

(iii) PA pressure estimated from the velocity of tricuspid regurgitant and other high-velocity jets of blood

Studies assessing PA pressure from continuous wave Doppler ultrasound

In parallel with these developments, Hatle et al[69,127] found that PAP could also be measured from the velocity of jets of blood across ventricular septal defects. Using a modification of the Bernouille equation that became widely accepted [69], she found that transeptal jet velocity could be used to estimate pressure drop across the defect, and therefore if left ventricular systolic pressure was known (via cuff blood pressure) right ventricular systolic pressure could be estimated with degrees of accuracy which were clinically useful. In general, high velocity jets across VSDs meant low or normal RV pressure, and hence a good prognosis.

Going one stage further, she showed [69] that the velocity of tricuspid regurgitant jets, which had been noted to be present in a majority of normal individuals[128,129], could be added to either a notional right atrial pressure or a clinical estimate of the jugular venous pressure to give PA systolic pressure. de Prada[131], Yock[132], Currie[133] and Berger[134] rapidly confirmed Hatle's findings, with correlation co-efficients generally in the region of >.9 ; the method has become accepted as the best and most accurate technique for non-invasively measuring PAP where tricuspid regurgitation can be detected by Doppler ultrasound. Fortunately, the higher the PAP, the more likely it is that tricuspid regurgitation will be detectable. It became apparent that many people[135] (perhaps as many as 40% of normal populations tested [136]) also had pulmonary regurgitation; similar logic could be applied to these jets to estimate PA diastolic pressure and mean PAP[137], and impressive correlations were again found.

(vi) Reasons for continued interest in RVSTIs

Have these CW Doppler techniques rendered RVSTIs obsolete ?

At first sight it might appear as though these latter methods of non-invasively measuring PAP have totally superseded the previous, more cumbersome ones. However, this is not so. TR and PR are not detectable in "useable" amounts in everyone, and even when they are detected, complete "envelopes" allowing confident estimation of pressure are not always available. Clinical estimates of right atrial pressure are crude and unreliable, and accuracy is improved when a notional figure of 10 mmHg is taken for RA pressure ! When the right atrial pressure is very high the velocity of right-ventricular-to-right-atrial jets falls (because the pressure difference is less) and one can only say that the pressure is "at least" a given figure. Whilst this is

indeed often sufficient for clinical work, Hatle and Yock's method is insensitive to small changes in PAP and is unsuitable for analysis of beat-to-beat variability. Using a formula involving squaring the velocity[69] means a non-linear relationship, and a difference of, say, 1 m/sec due to a poorly- aligned Doppler beam may involve an error of 30 mmHg.
Severe TR distorts right atrial mechanics [104] and then the right atrial pressure certainly does not stay unchanged during ventricular systole !

Thus I believe that RVSTIs still have a useful place in the assessment of pulmonary artery pressure and pulmonary vascular resistance, remain the only non-invasive method of determining beat-to-beat effects, and remain useful for longitudinal studies. The advent of pulsed Doppler has made the widespread application of the technique to adults possible, and created new useful parameters which themselves reflect aspects of RV function not readily discernible by other methods.

(v) Studies in the accuracy of measurements

Variability of measurements

Beat-to-beat variability in RVSTIs is small in normal individuals at rest in sinus rhythm [13,14] breathing quietly. Respiratory effects, no doubt partly mediated through changes in heart rate [92,137], occur with deep breathing[139], and are large when R-R' intervals vary markedly, as in atrial fibrillation[140]. In pericardial effusion, STIs have been used thus to explain the mechanism of pulsus paradoxus[141].

The study of variability has even had its comic side: one set of authors (a husband and wife team, it seems) even explored the effects of sauna on STIs (but made no effort to try to control for the large number of variables involved !)[142].

Some STIs vary with the heart rate: although there is some disagreement about RVPEP[92,93,96], RVET varies inversely with heart rate [92,93,96]. AT also varies inversely with heart rate (at least in pigs!) and Gardin suggested the use of a Bazett-style formula to correct it[143]. He found, like Weissler[92] and Leighton[96], that RVPEP/RVET did not seem to vary with heart rate, and found that AT/RVET did not do so either.

The question of consistency and inter-observer variation was addressed by Lang-Jenson[144]; he found intra-observer co-efficients of variation of around 7%, and inter-observer rates not much higher at 10.6%, for assessments of peak velocity. However (encouragingly), the figures for STIs were very much lower again at less than 2.5%, indicating how easy and accurate these measurements can be. It should be noted, nonetheless, that all his subjects were young women, who are usually very easy to study by echocardiography.

(vi) Studies in the use of STIs in pacing technology

Importance of atrial synchronisation

One situation where beat-to-beat changes have come to the fore is in complete heart block with ventricular pacing systems. Most patients with complete heart block have continuing but "disconnected" atrial activity, such that the atrio-ventricular interval (the "PR" interval) is continuously varying; electrical pacing systems can either just maintain a ventricular rate of around 70-90 bpm, or the more sophisticated ones may attempt to raise ventricular rate according to body needs by a variety of mechanisms. The most physiological way to do this is to make the ventricular pacing rate follow the spontaneous atrial rate. This approach will also keep normal atrioventricular intervals (often programmable over a range of around 50-250 ms) and, it is thought, preserve ventricular filling and function.

Although single chamber pacing (VVI) in complete heart block saves life[145] and restores life expectancy to normal[146] or near-normal[147] (depending on the presence or absence of cardiac failure and other pathology[148]), there is evidence that dual-chamber pacing improves survival in both complete heart block [149] and sino-atrial disease[150], and that this effect is more marked in patients already in heart failure[148,149].

Invasive studies on atrial contributions to cardiac output in paced patients

An impressive body of opinion now exists as to the superiority of some form of atrial synchronisation over VVI pacing. Pacing is an abnormal method of activation, and does not lead to normal contractility[151], producing an effect similar to left bundle branch block[152]; and there was, for some years, some dispute about the relative importance of pacing site and atrial contribution to cardiac output. However, the careful studies by Daggett[153], Mitchell[154], Linden[155] and Sayder[156] on dogs with surgically-induced complete heart block demonstrated that atrial contributions to cardiac output, stroke volume, dP/dtmax and myocardial segment lengths were much more important than the site of ventricular activation. They also showed that atrial function actually became more important at higher heart rates[154] but was less affected than might be supposed by fluid loading conditions[156]. This early animal work was confirmed by human studies undertaken initially by cardiac catheterisation by Samet[157] and Benchimol[158] in patients with normal hearts and in a variety of heart diseases by Karlof[159]. Myocardial oxygen consumption, coronary sinus lactate and arterial blood lactate, and coronary blood flow (all measures of cardiac work) were the same at rest in VVI and dual-chamber pacing, but cardiac output was higher in dual-chamber pacing in these and Nordlanders[160] study, confirming increased myocardial efficiency.

On vigorous exercise by bicycle ergometry cardiac output and work capacity are higher in dual-chamber pacing[161,162], and arterio-venous oxygen difference is much lower[163].

Radionuclied studies on the effects of atrial synchronisation during cardiac pacing

Radionuclieds have also been used to assess ventricular blood volume and ejection fraction (EF) in patients with pacemakers that could be programmed to VVI or dual-chamber (DDD) function. Ejection fraction is higher at rest with a physiological PR interval[164,165]. Ambulatory intra-arterial blood pressure monitoring in similar patients has also shown that mean blood pressures are higher and variations in blood pressure much less frequent in DDD pacing[166]. Patients much prefer DDD mode[166].

Why do we still implant single-chamber systems?

It might be asked, therefore, why DDD pacemakers are not routinely implanted for the treatment of complete heart block where there is continuing atrial activity.

It would be unfair to suggest that dual-chamber pacing systems are without their own problems.

Displacement of the atrial lead, which was a relatively frequent problem in early days, has been largely solved by the increasing use of active fixation atrial electrodes.

"Endless loop" tachycardias[167-170] are usually avoidable by careful programming of refractory periods[172-175].

There is undoubtedly a need for increased sophistication of programming equipment and support staff.

But the main reason is cost: at present a VVI system and wire can be bought for around five hundred pounds (with minimal programmability), whereas a DDD system and its two wires costs around fifteen hundred pounds. With numbers of elderly expected to rapidly increase in the next ten years, the cost of providing a pacing service will rise substantially.

It is often said that elderly people do not need the sophistication of high technology devices as they live somewhat sedentary lives. Needless to say, this may become a self-fulfilling prophecy! Because of fiscal restrictions, a good case has to be made; investigation of the unwanted effects of single-chamber(VVI) pacing should be part of this. Although most old people who receive pacemakers are, for the moment, likely to receive VVI systems, investigation into the effect on their health is vital.
Quality of life is as important for many old people as quantity of life.

What unwanted effects of VVI pacing have been identified, and can it be demonstrated that loss of atrial synchrony is involved ?

Unwanted effects of single-chamber pacing do occur, and are related to the "PR" interval fluctuations inherent in single-chamber pacing. An entity comprising fluctuating blood pressure, pulsations in neck veins, breathlessness and dizziness (sometimes with syncope) was described by a number of authors in the early 1970s[176-180], and the term the "Pacemaker Syndrome" was coined [181-185]. Accompanying the falls of arterial blood pressure were raised atrial pressures [186,191,192] and retrograde atrial flow into systemic and pulmonary veins, demonstrated by contrast echocardiography[187,188] and Doppler ultrasound [189,190]. Nishimura, in a series from the Mayo Clinic[193], showed that this syndrome was abolished by conversion to dual-chamber pacing. He advised careful fine-tuning of the PR interval to obtain optimal haemodynamics.

How do STIs fit into this "fine-tuning" ?

Shuster and Nanda[194] were amongst the first to foresee the potential of a non-invasive technique such as Doppler ultrasound to "fine-tune" the atrioventricular interval. Some studies looked at left ventricular filling by pulsed Doppler timings of mitral valve flow[195-198] and increments of around 20% were added to cardiac output when measuring left ventricular outflow[199-202]. Stewart[203] did suggest that perhaps looking at the differences with and without atrial synchronisation could be used to select patients for DDD pacing. Several studies (mostly measuring cardiac output by transcutaneous aortovelography rather than STIs) concluded that the optimal PR interval at rest was around 100-150 ms, but that perhaps a shorter timing of 50-100ms might be appropriate on exercise [197,198,201,203]. But little effort was made to explore the effects of "inverted" atrioventricular sequencing (i.e. P waves following ventricular activation)[205], such as occur in VVI pacing; almost all these studies were performed on dual-chamber systems, and in this mode this event cannot occur. These studies exclusively concentrate on the left heart, and no studies using STIs or flow integrals have been published on right heart dynamics in this situation.

But pacing is a right ventricular event; and it is also logical to study the right ventricle because of its lower pressures, which should make the effects of atrial timing (or mistiming) more obvious. The pressure/output curve for the right ventricle is also much steeper, making loading conditions very important. A determinant of RV loading is the PR interval.

Thus this area is still largely unexplored: the effect of varying but "physiological" PR intervals has been poorly studied in the right heart, despite the clinical importance through pacing: and the effects of inverted atrio-ventricular sequencing are unknown.

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STUDY METHODS

Study Methods

(i) Equipment

All recordings were made using a Toshiba Sonolayer SS-60a dedicated echocardiography and Doppler apparatus. This equipment allows simultaneous two-dimensional imaging and a display of steerable pulsed Doppler images. Two-dimensional echocardiograms and Doppler examinations of the valves were first obtained on all control subjects to ensure the absence of any detectable abnormality. Pulsed Doppler recordings of pulmonary artery flow were obtained at 2.8 MHz using a combined echocardiographic/ Doppler transducer, Doppler shifts being processed by Fast Fourier Transformation and displayed as frequency change versus time. The time delay between acquisition of data and its display on the FFT trace is around 5-10ms on this machine (Toshiba, personal communication).

This must be borne in mind when quoting minor changes in beat-to-beat variation, but should be constant throughout the recording. The magnitude of this change is not addressed in any other published series of pulsed Doppler data of which I am aware. Recordings were made onto silver recording paper with a speed of 100 mm/sec. There are markers on the trace corresponding to 10ms each for calibration purposes. Run speeds were checked and found to be correct with an error of $\pm$ 2%.

An electrocardiogram, the lead chosen to optimally display atrial activity, was displayed simultaneously.
A minimum of ten cardiac cycles on controls, and thirty cycles on patients with pace-makers, were recorded per patient for analysis.
Measurement of intervals was performed manually from these traces and the data so extracted entered and processed on the University of Wales mainframe computer, using a commercially available statistical software package (Minitab) for the bulk of the calculations.

(II) Selection of Controls

Controls were selected from volunteers of all age groups who were free of cardiac symptoms and signs on careful examination. All controls had normal 12-lead electrocardiograms, and normal two-dimensional and Doppler examinations.
I did not think it ethical to submit my control patients to radiological examination, especially as echocardiographic means are considerably more sensitive in detecting cardiac disease.

I believe this to be the only control series of measurements where such rigorous exclusion of abnormalities has been undertaken.

All controls freely gave informed consent to the procedure.

Three of eighty would-be controls were excluded: in one case becasue of the clinically unsuspected finding of moderate aortic regurgitation, and in two cases because the proximal pulmonary artery could not be imaged despite repeated attempts.

(iii) Selection of paced patients

Patients with complete atrioventricular block with single-chamber ventricular-inhibited pacemakers were considered for study if they had continuing co-ordinated atrial activity, and adequate images and Doppler signals could be recorded from the proximal pulmonary artery.
Patients with clinically apparent congestive cardiac failure were excluded from the study.
Patients with valvular heart disease apparent clinically or on two-dimensional echocardiography were excluded also.
Patients with ischaemic heart disease were allowed into the study provided that left ventricular function appeared normal on two-dimensional echocardiography.
Of 55 patients initially screened, 25 were excluded because LV or RV function did not appear normal on two-dimensional echocardiography. Tricuspid regurgitation, where present, was also used to screen for pulmonary hypertension, and velocities of > 3.0 m/sec were considered abnormal; however, all such had already been excluded on the two-dimensional echocardiographic appearances. No patients were excluded because of failure to obtain adequate images.
Thirty such patients were recruited and intensively studied.
All patients freely gave informed consent to the procedure: the study had been approved by the Ethical Committee of the Leicester Hospitals.

(iv) Recording techniques

All patients were examined in a darkened soundproofed room after ten minutes quiet rest on a couch. The proximal pulmonary artery was imaged using a short-axis parasternal [Fig 2] view, and a 1cm "window" for pulsed Doppler was positioned in the centre of the pulmonary artery trunk [Fig 3], just beyond the pulmonary valve leaflets, under two-dimensional echocardiographic control. This position was chosen because of its reproducibility and to enable the use of pulmonary valve leaflet motion artefacts in timing [Fig 4].

This position was then adjusted to find the highest velocity and the longest acceleration time of any sample (as Panadis et al[126], Lighty et al[125]).

Filters were adjusted to include motion artefacts from the pulmonary valve leaflets to assist timing. In fact, unlike Matsuda et al[116], but in concert with the majority of authors, we found no difficulty in timing the end of RVET, taking the return to baseline as its end[113,114,115, 117,118].

Using PV motion artefacts to time end-systole draws support from Hsieh et al, who demonstrated an excellent correlation between M-mode and Doppler-derived estimates of timing [91].

A single-lead electrocardiogram, the lead chosen to optimally display atrial activity, was recorded simultaneously on the same paper trace.

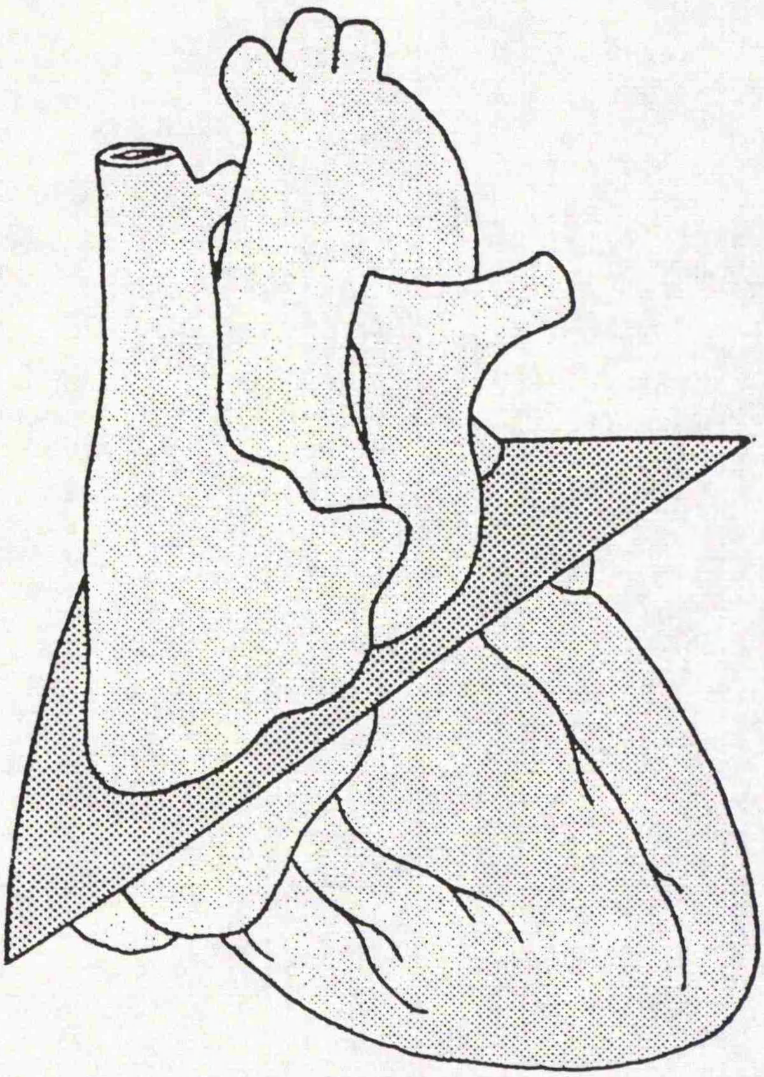

Fig. 2

IMAGING PLANE

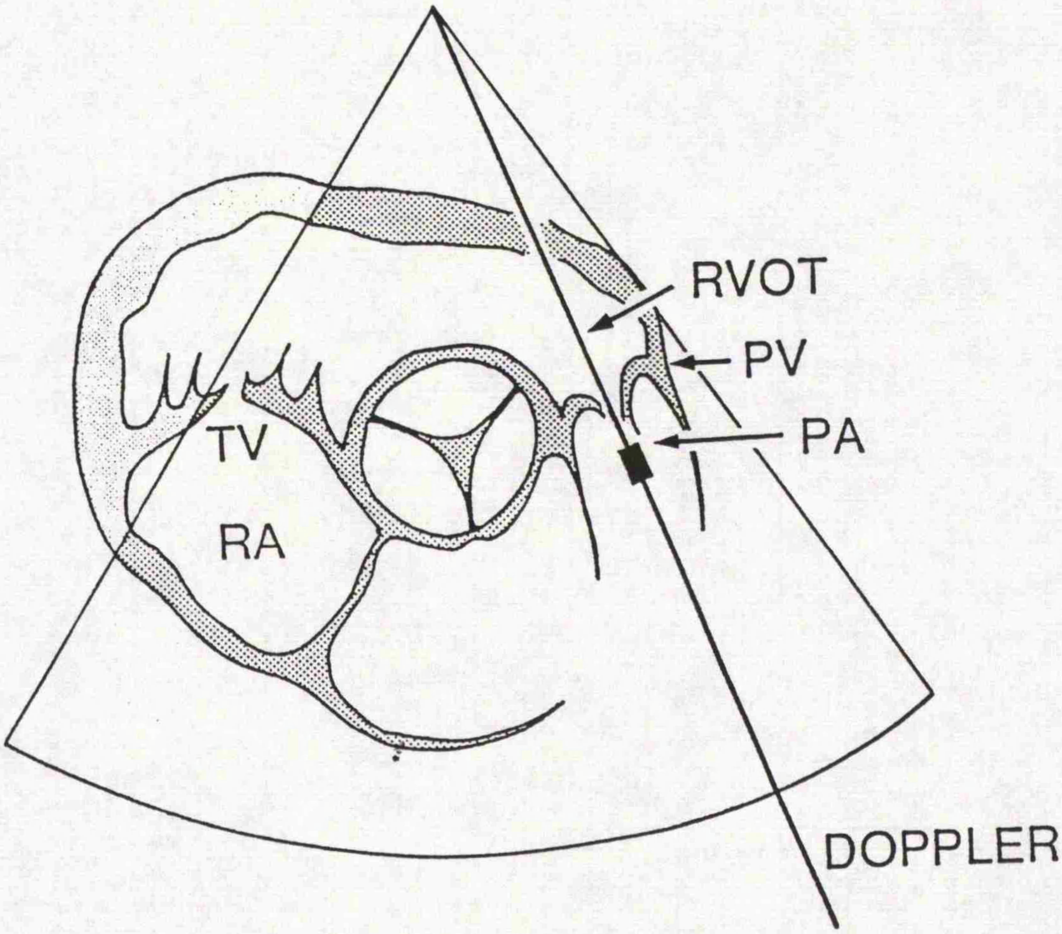

Fig. 3

DOPPLER SAMPLE POSITION

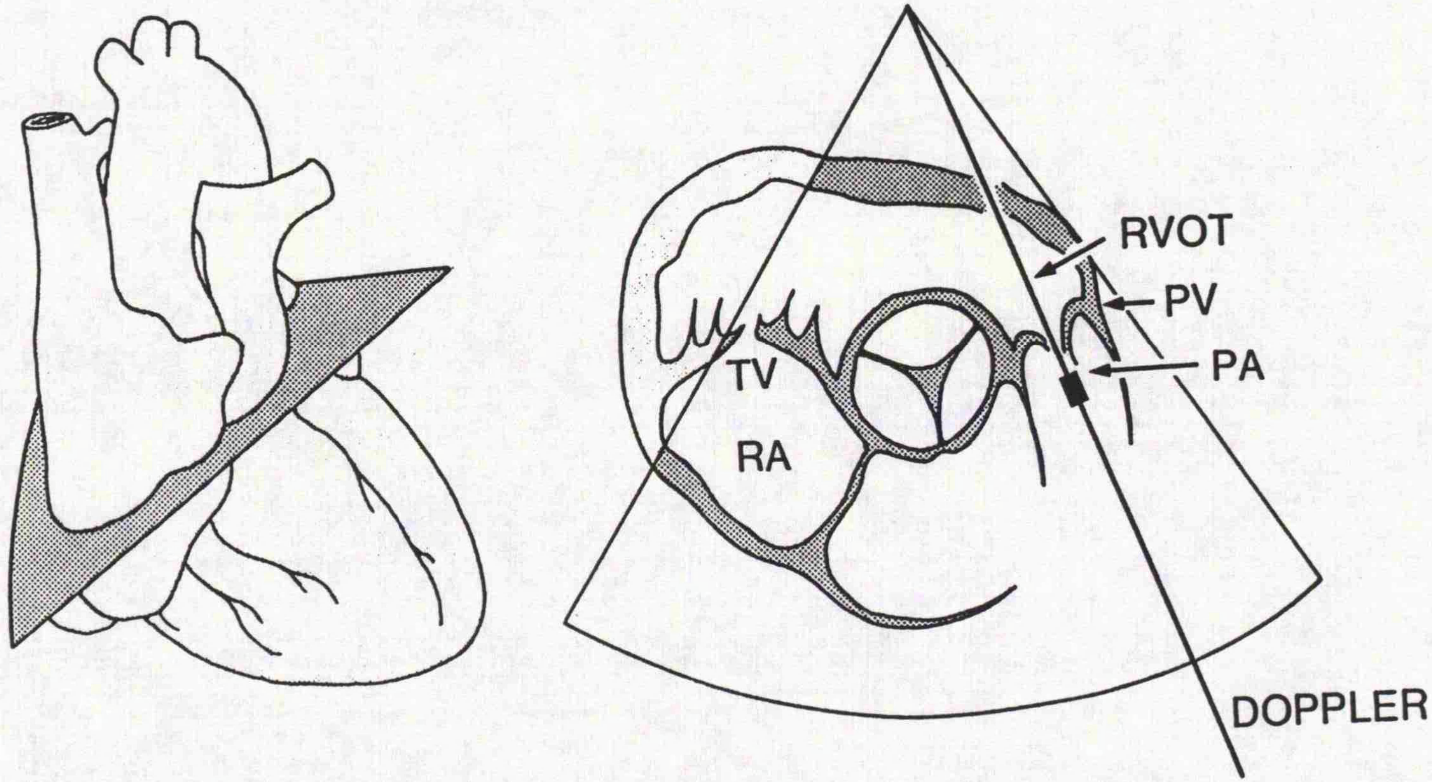

Fig. 4

IMAGING PLANE

Extra-systolic and immediately post-extrasystolic beats were excluded.
The effects of the previous QRS complex on the subsequent filling associated with the next PR or PF interval must be considered.
As paced rates were 70/min throughout the study, and the mean heart rate of the normals was also 73 beats a minute, the groups are broadly comparable; in all paced patients, the P-Pi interval was much shorter than the R-Ri interval.

All recordings were made with the subjects in relaxed end-expiration, without previous hyperventilation. This was done to eliminate the effect of thoracic movement on right heart blood flow, and to keep the angle of incidence of the Doppler beam to the direction of flow constant.
There is, in fact, good evidence that respiratory alterations affect right heart function: inspiration has been shown to increase RV ejection fraction (as assessed by radionucleid angiography) by about 6%; the Valsalva manouvre decreases forward flow into the pulmonary artery [208] and slows RV transit time [207] and PA pressure rises [209].
During respiration, inspiration produces negative intra-thoracic pressures and increases blood flow from the great veins into the RA and RV: simultaneously, pulmonary veins dilate as the lungs expand, causing a fall in PA pressure and pulmonary vascular impedance (i.e. a fall in RV afterload).

I believed the best data would be obtained with constant beam position (important especially for AT and PAVmax and ratios that include AT) and removal of as many other variables as possible, so I used relaxed apnoea. I am not therefore in a position to comment on how respiration would affect the changes discovered in the paced group, although I do not believe they would be materially altered.
This must be borne in mind when interpreting my data. Some previous authors obtained data in relaxed apnoea, and some during quiet breathing; most authors do not say. Most of the children's studies make no comment, but we presume no attempt was made to control breathing in young children.

No controls or patients were excluded because of failure to comply with these instructions.

(v) Recordings

From the paper traces heart rate, PR interval, RVPEP, RVET, AT, and Vmax (peak PA flow velocity) were measured (Fig 5). Heart rate corrections using an inverse root formula (vide supra) were attempted on RVPEP, RVET and AT. The ratios RVPEP/RVET, AT/RVET and RVPEP/AT were calculated.

Intra-observer and inter-observer variation are approximately 5-7% and are similar whether aortic or pulmonary flow is being measured[212]. Measurement of cardiac output by this method requires accurate assessment of PA diameter, which is sometimes difficult[213,214]. Measurement of systolic time intervals, however, does not require complex software nor measurement of vessel diameters, and has similar variability. Regrettably, the software available to us did not allow calculation of pulmonary flow integrals, which have been shown to correlate well with dye dilution and oximetry methods of calculating cardiac output.

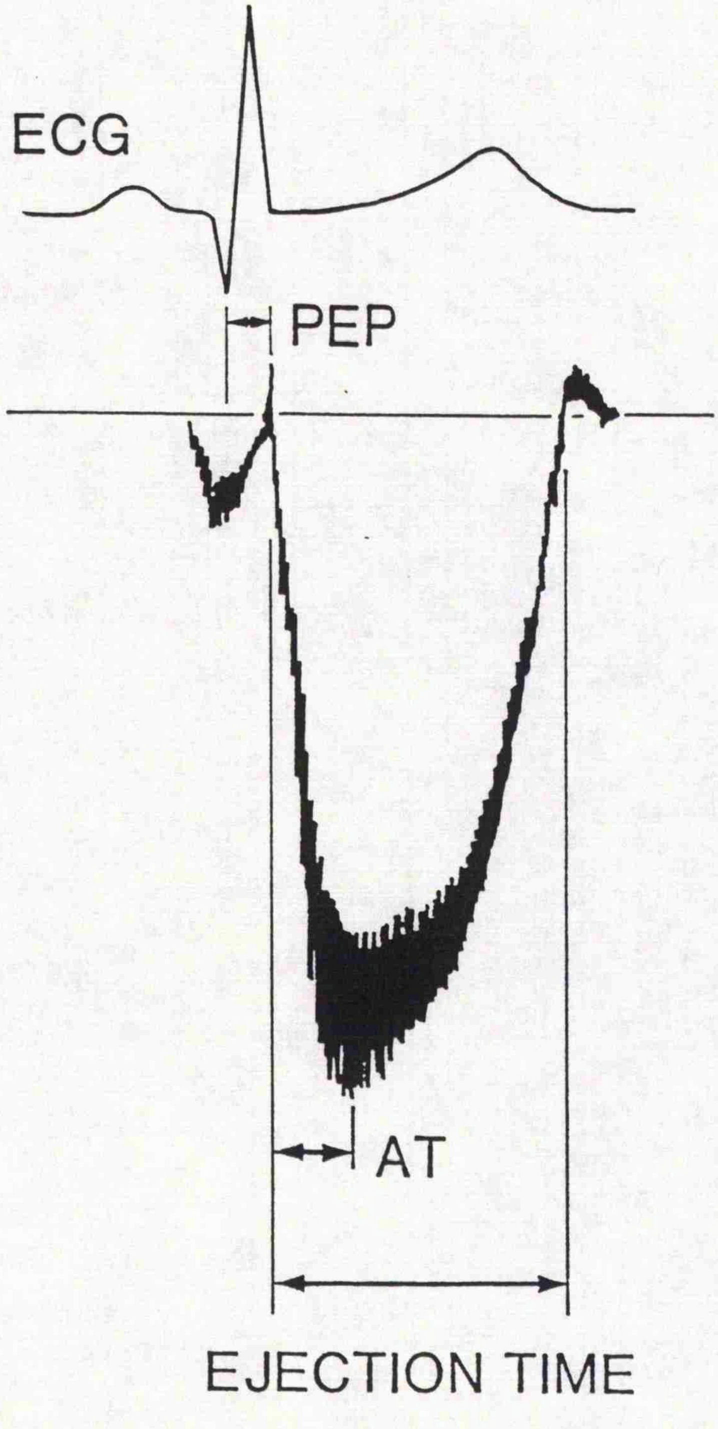

Fig. 5

MEASUREMENT OF SYSTOLIC TIME INTERVALS FROM PA FLOW

RVPEP was measured from the earliest inscription of the QRS complex (the beginning of the Q wave in controls, and the pacing stimulus artifact in paced patients) to the start of right ventricular ejection detected by Doppler. Although Benito et al [206] had difficulty here because of premature opening of the pulmonary valve, this was because most of his patients had pulmonary hypertension or constrictive pericarditis, and the effect was largely due to an inspiratory rise in right atrial pressure. I did not have similar problems.

RVET was measured from the earliest onset of forward flow in the pulmonary artery to its cessation and return to baseline zero flow. This was synchronous with PV leaflet closure in all my controls and cases.

AT was measured from the earliest onset of forward flow into the pulmonary artery to its peak. Although differing waveforms were encountered in both cases and controls, determination of the point of peak velocity was easy in all. Views were adjusted to give the longest AT of any position in each subject, although all views were parasternal short-axis.

Vmax was taken as the peak velocity recorded by pulsed Doppler. As most velocities were <.7 m/s, aliasing was not a limiting factor. In the few cases where a clean "envelope" could not be obtained because of aliasing, shifting the baseline upwards was sufficient in each.

Why other measurement possibilities were not pursued

Many other sideline and "add-on" studies were considered during pilot studies. The study as described generated huge amounts of data, most of which had to be manually processed from the traces; this took nearly one year in itself whilst doing busy clinical jobs, and a limit had to be placed somewhere. In addition, some other possibilities have already been explored in the literature, and some were found to have distinct difficulties during pilot studies.
In particular:

(i) **Simultaneous left ventricular STIs would have been interesting to study.**

However, some authors have already looked at the left ventricle [199-202], and no data existed on the right ventricle. Of the three patients in whom simultaneous studies were undertaken, changes as previously descibed in the literature (but of lesser magnitude than I demonstrate in the right heart) were seen. Because I had to accept spontaneously occurring PF intervals in the paced study, it would have been difficult to compare differences because the PF intervals would not have been identical. Our machine did not allow two simultaneous pulsed Doppler beams, but such equipment is now available, and could be so used.

(ii) **Right ventricular inflow studies on trans-tricuspid flow would have added additional information about RV filling**

During the pilot study, we found that artefact from the pacing wire in the paced patients made inflow difficult to study. In addition, several patients had holosystolic tricuspid regurgitation, and some had tricuspid regurgitation in diastole also, which would have made interpretation difficult. These problems made me abandon such studies. In addition, when the work was undertaken (in 1984-5), atrioventricular valve inflow integrals were in a much earlier stage of development.

(iii) **A further interesting side-study would have been in patients with transposition of the great vessels to view the RV as the systemic ventricle.**

Hirschfeld[99] had already done this, before and after correction by the Mustard procedure, and shown that LVSTIs and RVSTIs responded importantly to afterload. In addition, only a few sick neonates passed through the Department before and after a Rashkind procedure on their way to definitive surgery elsewhere. Too few patients with previously corrected transposition were seen to draw any conclusions.

(iv) **The pulmonary incompetent waveform could be used to study the right ventricular/pulmonary artery interaction**

Around 40% of normals have pulmonary regurgitation(PR) in previously reported series [123,136,137]. In our population only 20-25% of the normal subjects had detectable PR. As we decided to use the middle of the pulmonary trunk beyond the pulmonary valve cusps as the sampling site, a whole new set of data with a standardised sample position in the RV outflow tract would have to be generated, and resources did not permit. In addition, colour flow Doppler, which is of great use in determining the site of these small jets, was not at that time available.

(vi) Methodology of the invasive study

Invasive studies were planned on six patients undergoing pacemaker implantation for complete heart block in the face of continuing atrial activity.
Three patients were to be studied with particular reference to right atrial waveform, and three with particular reference to right ventricular waveform.

Pacing wires were placed, via the left subclavian vein, in the right atrial appendage and the tip of the right ventricle: a conventional fluid-filled catheter was passed either to the right ventricle or right atrium for pressure measurement, and a catheter-tip transducer was also placed there for accurate timing.
Pacing was initiated with an RR interval of 700ms, and the PR interval was varied from 200ms through 150ms, 100ms, 50ms, simultaneous activation, and retrograde sequencing of 50ms, 75ms, 100ms, 150ms, and 200ms.
In between measurements, dual chamber pacing in the previously described "optimal" PR interval of 150ms was done.

A minimum of twelve measurements was taken for each pressure and timing reading and mean and 95% confidence intervals were calculated for each reading for each PR interval.

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PART TWO

RESULTS ON NORMAL CONTROL SUBJECTS

DISCUSSION OF RESULTS ON NORMAL CONTROL SUBJECTS

RESULTS ON NORMAL CONTROL SUBJECTS

Results

(1) Control series

(a) Right ventricular pre-ejection period (RVPEP)

RVPEP in 77 control subjects supine at rest in relaxed end expiration had a mean of 102.7ms (median 100.2ms) with standard deviation 12.8 ms and SEM 1.46. The range was 79-133ms, 95% confidence intervals being 99.8-105.5ms.

	RVPEP
n	77
Mean	102.7ms
Variance	163.7ms
S.d.	12.8ms
St. Err.	1.5ms
Max	132.8ms
Upper Qtile	113.3ms
Median	100.2ms
Lower Qtile	92.9ms
Minimum	79.0ms
Range	53.9ms

Distribution was significantly positively skewed (see Fig 6)

Both reciprocal and logarithmic transformations substantially reduce skew although their physiological meaning is unclear.

```
RecipRVPEP
  7.5301E-03  |*                   1
  8.5573E-03  |***********        11
  9.0709E-03  |************       12
  9.5846E-03  |*******             7
  1.0098E-02  |***********        11
  1.0612E-02  |**********         10
  1.1125E-02  |**************     14
  1.1639E-02  |*****               5
  1.2153E-02  |**                  2
  1.2666E-02  |****                4

 LogRVPEP
  1.89352     |*                   1
  1.94521     |*****               5
  1.965106    |***********        11
  1.98769     |***********        11
  2.010275    |***************    15
  2.03286     |********            8
  2.055444    |********            8
  2.078029    |********            8
  2.100613    |*******             7
  2.123198    |***
```

Within-patient variation was small with tight 95% confidence limits around each subject mean (see Fig 7).

Variability between subject means was much greater than within-patient beat-to-beat variation (F=62.5, df=76, p<.001). (See Appendix 2 for plot)

Fig. 6

RVPEP
Frequency Distribution

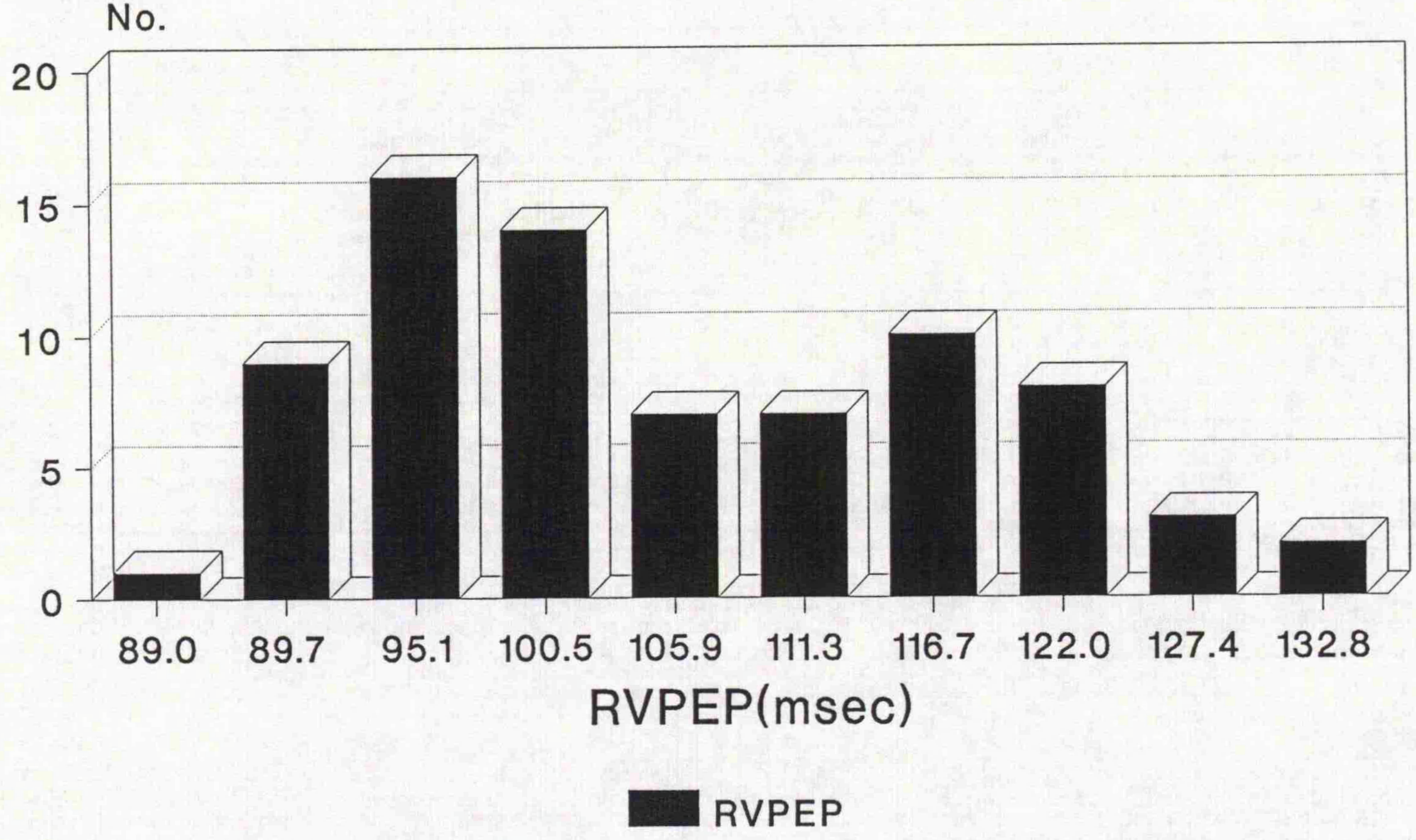
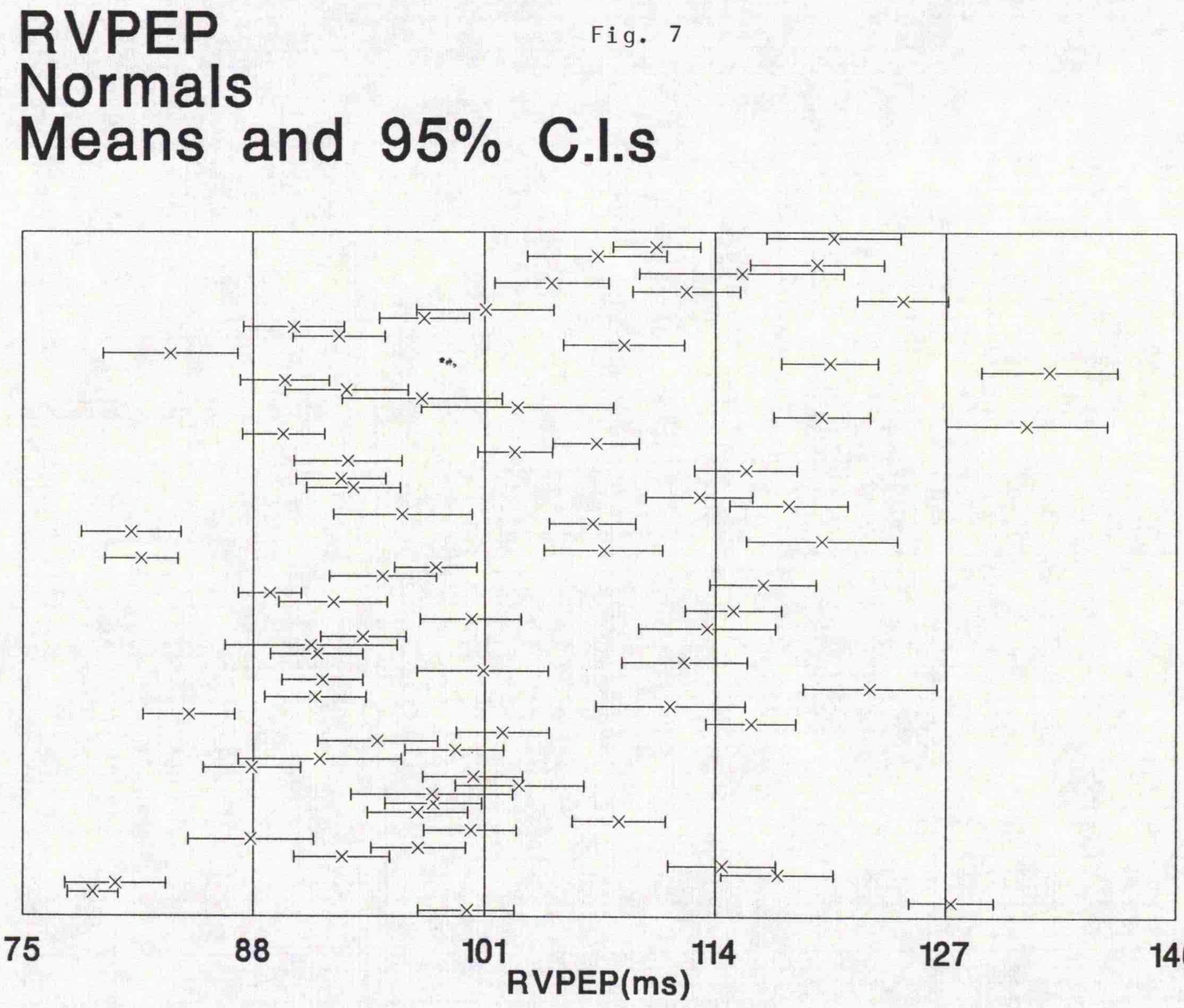


Fig. 7



RVPEP was not significantly associated with heart rate (see Fig. 8) (r = -.11, p = .43 NS). and "correction" for heart rate by the formula

$$RVPEPc(ms) = \frac{RVPEP(ms)}{/\ R\text{-}R1\ \text{interval (secs)}}$$

considerably broadened the confidence intervals.

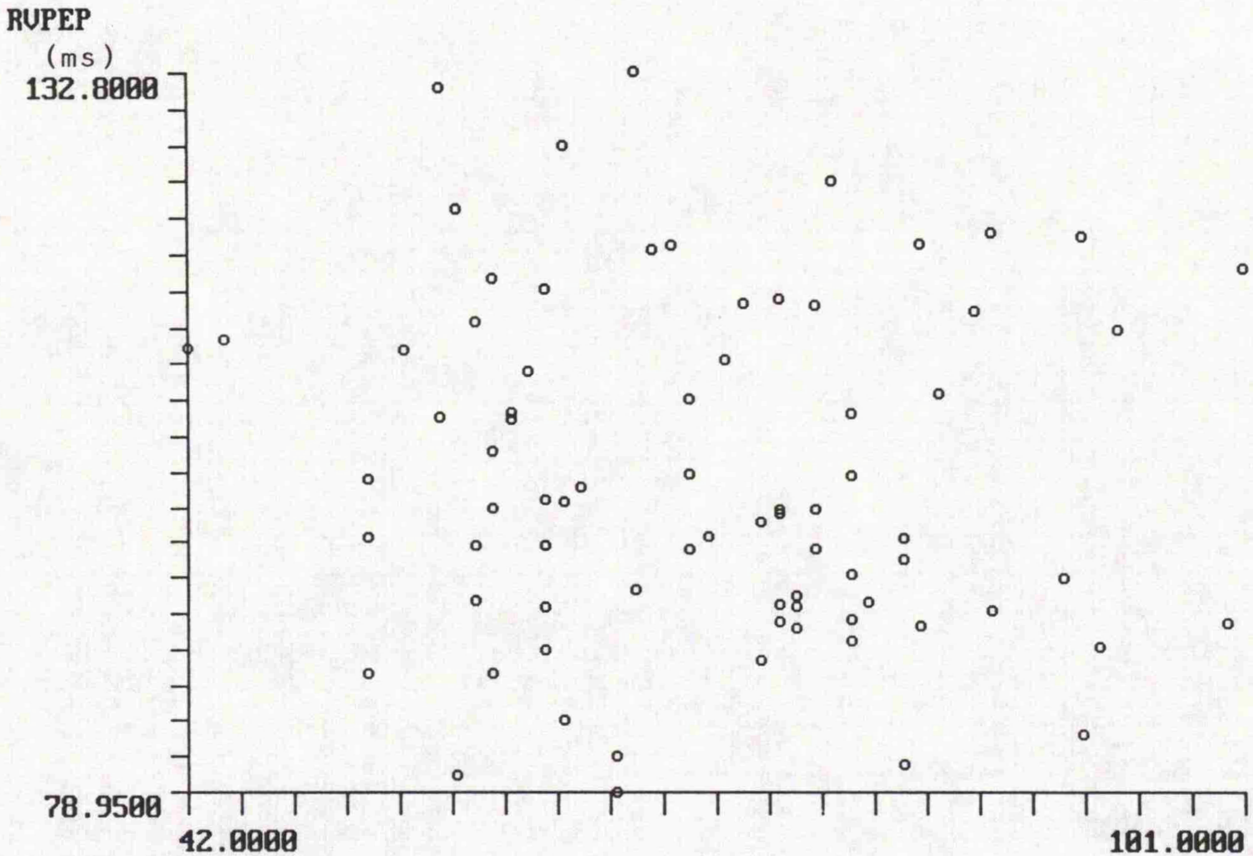
The use of inverse root formulae to "correct" RVPEP for heart rate therefore seems inappropriate.

RVPEP was weakly associated with age (r = .288, p <.05).

Somewhat suprisingly, RVPEP was not associated with the PR interval (r = .088, p = NS)

Fig. 8

RV PEP vs. RATE



(r = .07 , p = NS)

(b) Right ventricular ejection time (RVET)

Right ventricular ejection time in the 77 control subjects supine at rest in relaxed end-expiration was mean 299.5ms (median 300.8) with standard deviation 28.6ms and SEM 2.6.

The range was 227-369ms, 95% confidence intervals being 293.2-305.9ms.

	RVET	RVETI
n	77	77
Mean	299.5ms	321.6ms
Variance	818.7ms	441.4ms
St. Dev.	28.6ms	21.0ms
St. Err.	3.3ms	2.4ms
Maximum	369.3ms	373.6ms
Upper Qtile	315.8ms	337.1ms
Median	300.8ms	320.9ms
Lower Qtile	285.0ms	306.0ms
Minimum	227.3ms	279.7ms
Range	142.0ms	93.9ms

Fig. 9

RVET
Frequency Distribution

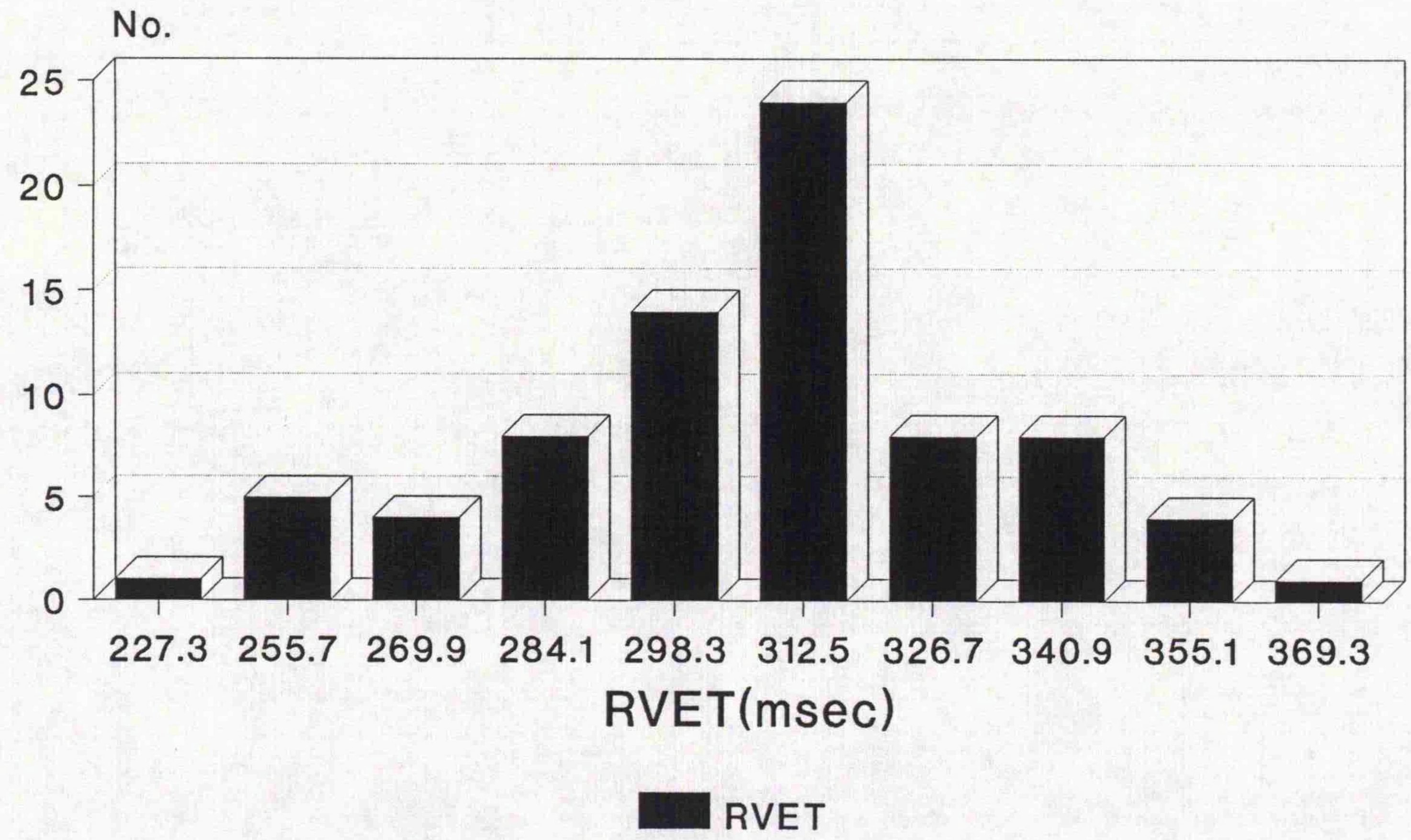
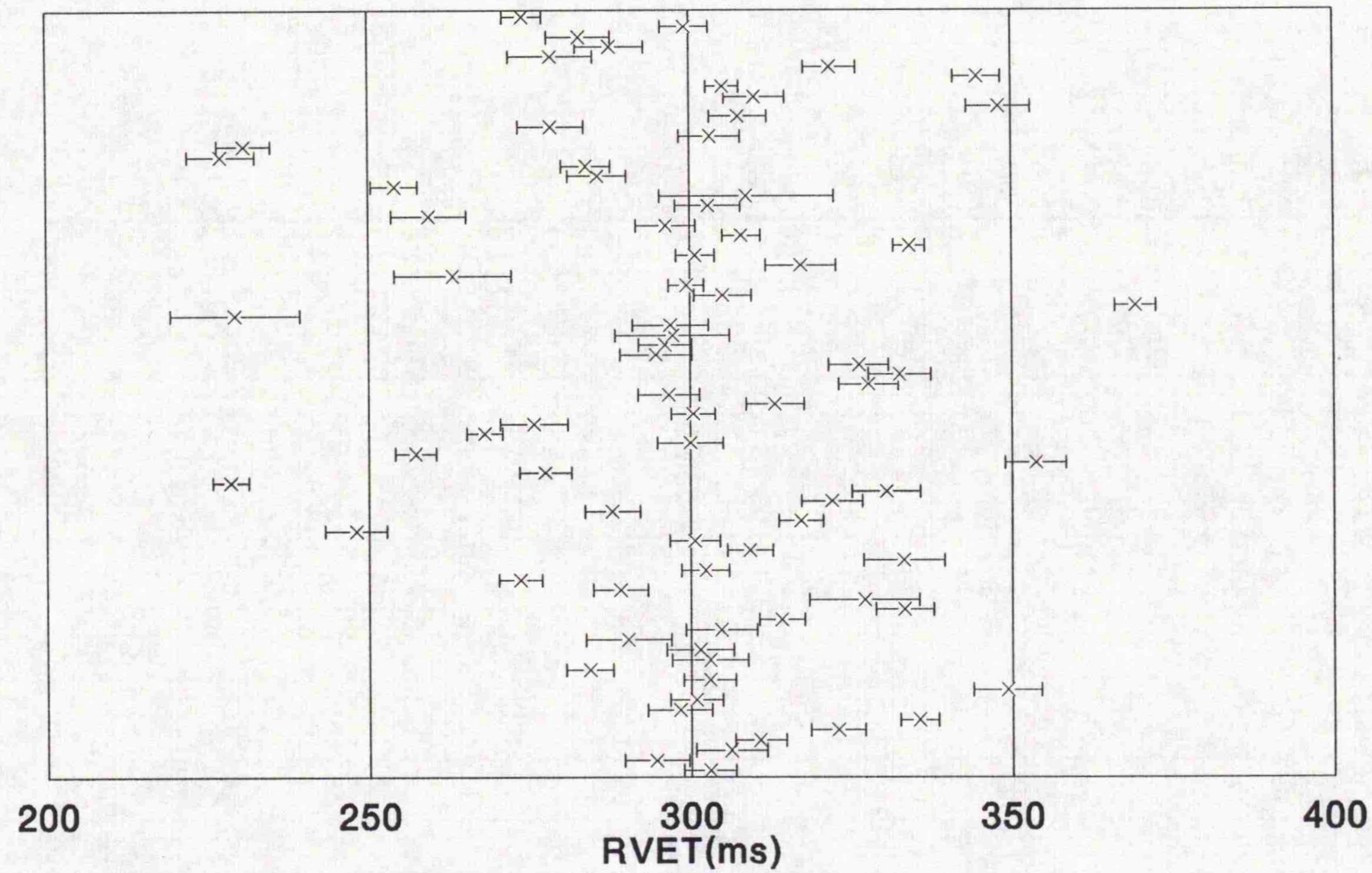


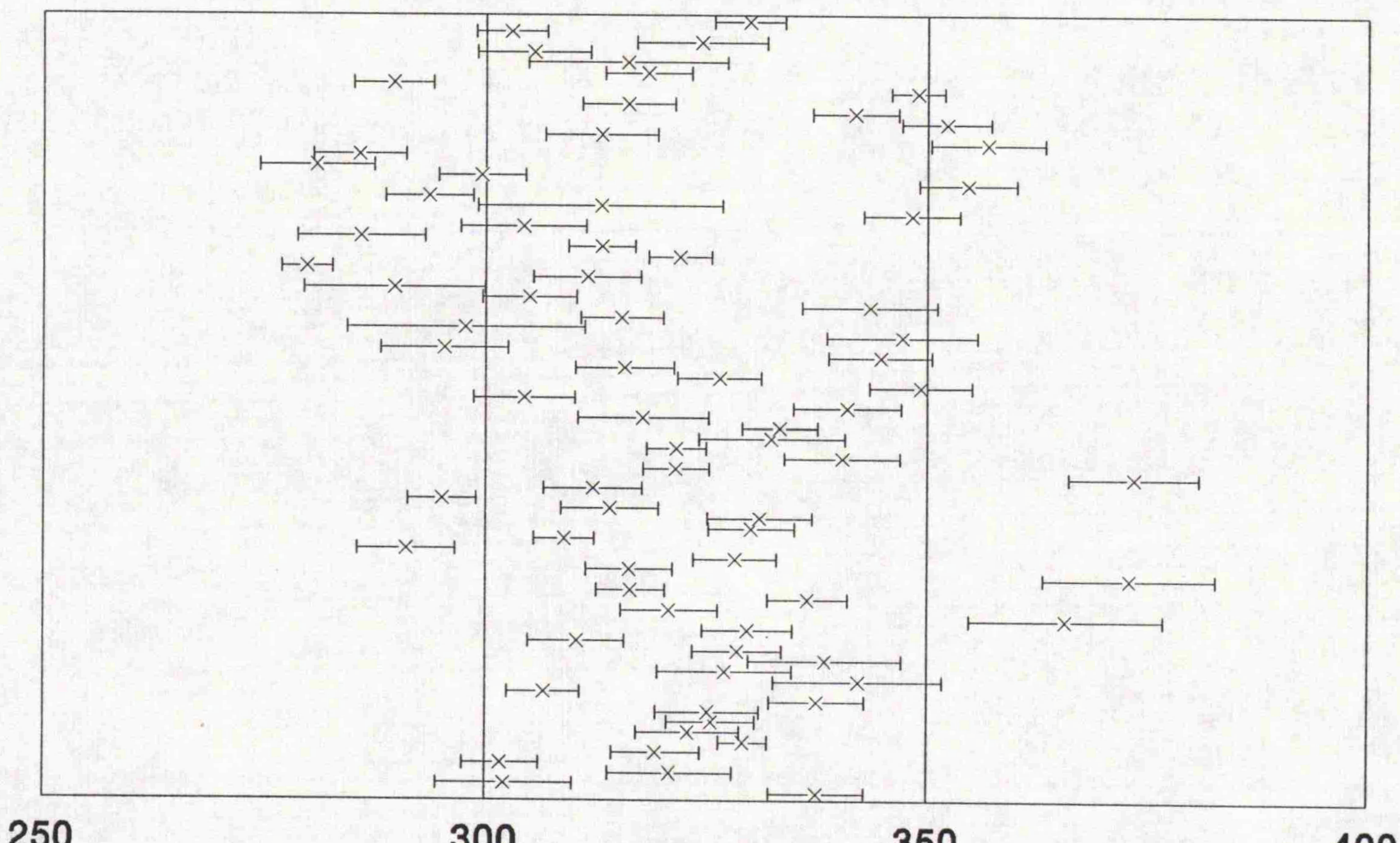
Fig. 10

RVET
Normals
Means and 96% C.I.s



RVETI
Normals
Means and 95% C.I.s

Fig. 11



Distribution was approximately normal (see Fig. 9)

The distribution of the rate-corrected RVET, RVETI, was mildly positively skewed:

```
RVETI
279.70ms |*                                  1
298.48ms |**********                        10
307.87ms |*********                          9
317.26ms |**************                    14
326.65ms |*************                     13
336.04ms |**********                        10
345.43ms |**********                        10
354.82ms |******                             6
364.21ms |*                                  1
373.60ms |***                                3
```

Within-patient variation was minor with tight 95% confidence intervals about each subject mean in both RVET (Fig 10) and RVETI (Fig 11)

Variability between subject means was much greater than within-subject beat-to-beat variation ($F=129.06$, $df=76$, $p<.001$).

(See Appendix 2 for plot)

As expected, RVET was strongly negatively associated with heart rate ($r = -.79$, $p = .000001$).
(See Fig 12 overleaf)

The equation of the regression line was

$$Y = -1.770315X + 424.7825$$

(95% CIs for $r = -.859227$ to $-.682988$)

However, use of the more familiar inverse root formula thus:

$$\text{RVETc(ms)} = \frac{\text{RVET(ms)}}{\sqrt{\text{R - R1 interval (secs)}}}$$

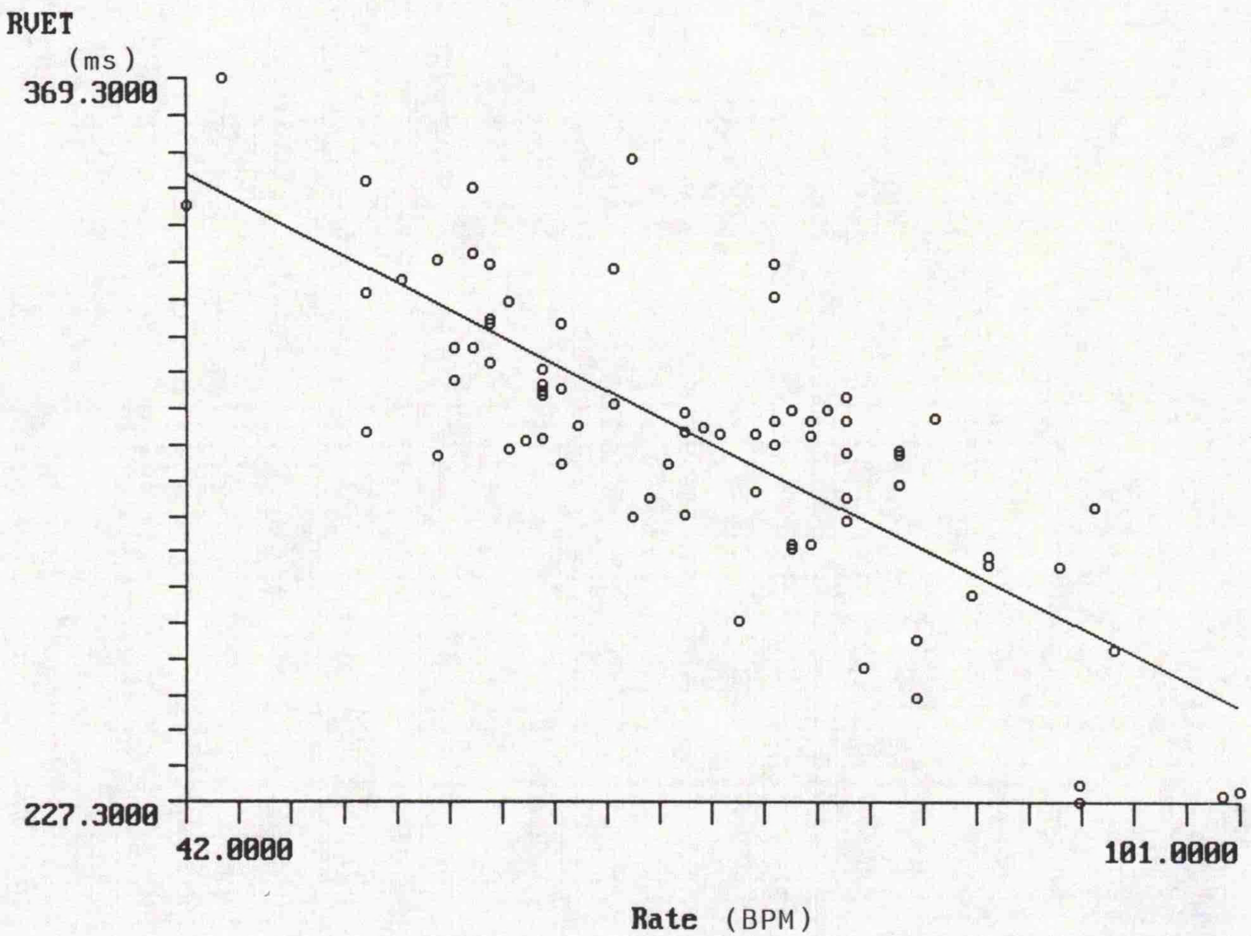
removed any signifcant association with heart rate ($r = .2$, $p = NS$).

This corrected RVET (RVETI) had a mean of 321.8ms (median 320.9) standard deviation of 21.0 and a SEM of 2.4 (i.e. a slightly tighter scatter than crude RVET). Range was 279.9-373.6ms, 95% confidence intervals being 317.0-326.5.

RVET was not associated with age ($r = -.065$, $p = NS$), the PR interval ($r = .21$, $p = NS$) or RVPEP ($r = -.083$, $p = NS$).
An association with acceleration time (AT) was confirmed ($r = .55$, $p < .001$).

Fig. 12

RVET vs. RATE



(r = -.79, p< .000001)

(c) <u>Acceleration time (AT)</u>

Acceleration time in the 77 control subjects supine at rest in relaxed end-expiration was a mean of 135.4 ms with standard deviation 23.2 ms and SEM 2.64 ms. The range was broad at 91-197ms, 1st and 3rd quartiles being 115.8ms and 151.1ms.

	AT
n	77
Mean	135.4ms
Variance	537.1ms
St. Dev.	23.2ms
St. Err.	2.6ms
Maximum	196.9ms
Upper Qtile	151.1ms
Median	135.6ms
Lower Qtile	115.8ms
Minimum	91.1ms
Range	105.8ms
Centile 95	175.9ms
Centile 5	99.8ms

Fig. 13

Acceleration Time
Frequency Distribution

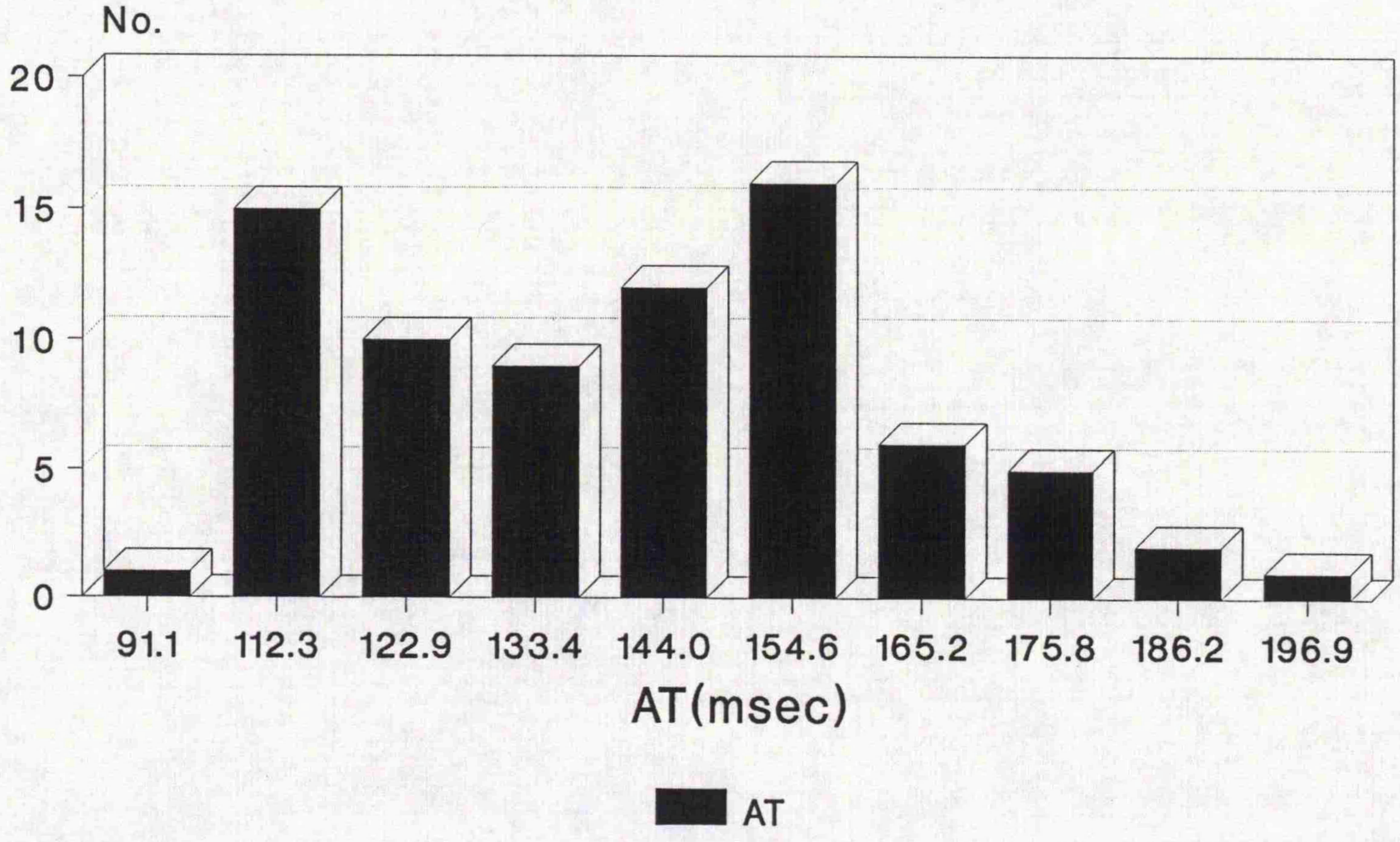
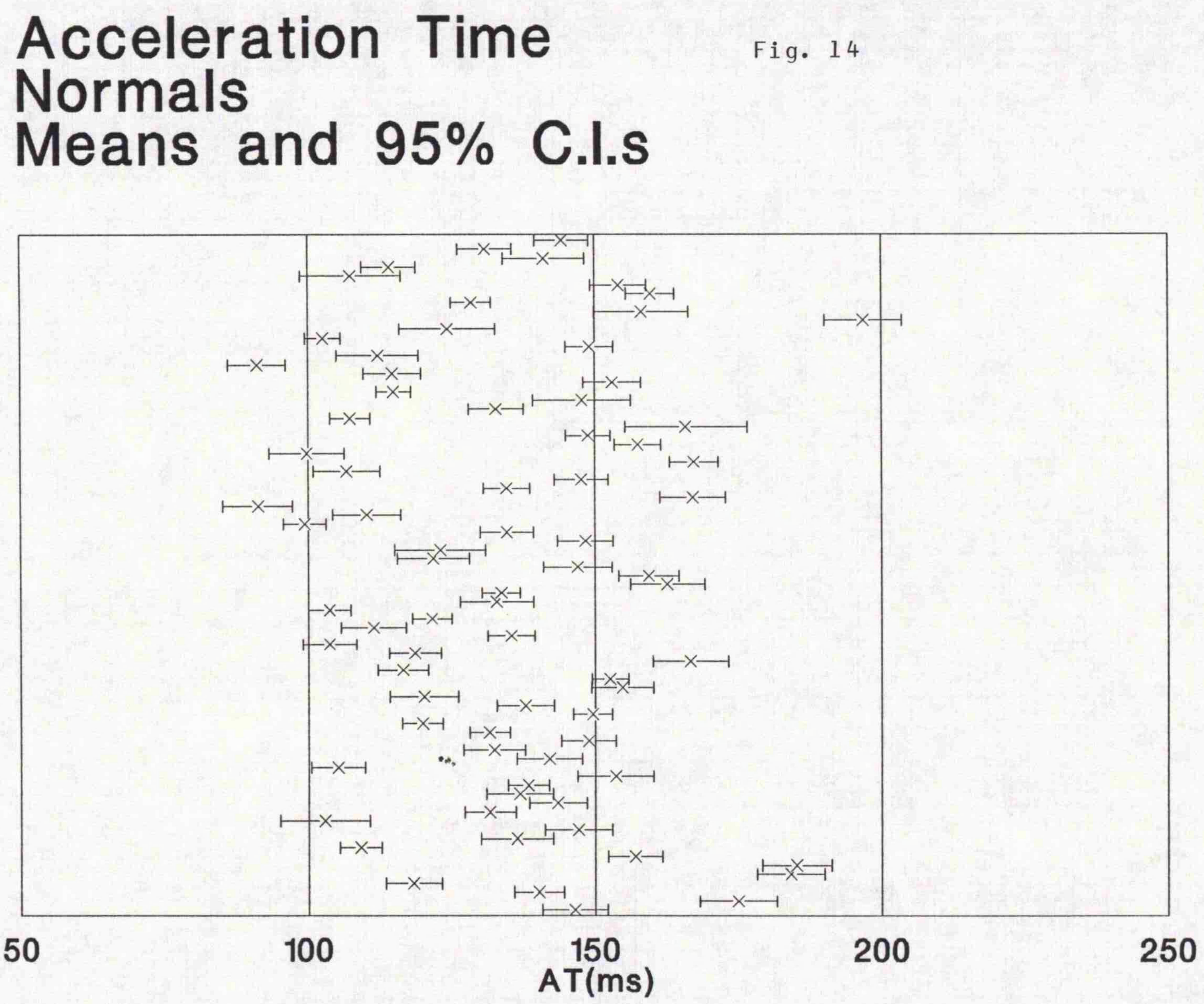


Fig. 14


Acceleration Time
Normals
Means and 95% C.I.s
50
100
150
200
250
AT(ms)

Distribution was significantly positively skewed (see Fig 13) (mean 135ms, median 134ms):

Logarithmic, but not reciprocal, transformation did reduce the skewness of the distribution:

```
LogAT
1.959709 |*                    1
2.026616 |********             8
2.06007  |*********            9
2.093524 |*********            9
2.126977 |*********            9
2.160431 |************        12
2.193885 |***************     15
2.27338  |**********          10
2.260792 |*                    1
2.294246 |***                  3
```

The fifth centile of our population with respect to this measurement was below the "lower limit" of 100ms at 99.8ms.

Four controls had acceleration times less than 100ms, previously thought to indicate abnormality, and a further four had acceleration times of less than 105ms. Careful review of the clinical and echocardiographic data did not reveal any evidence of heart disease in any of these.

Scatter around subject means was tight (see Fig 14).

Within-subject beat-to-beat variability was much smaller than the difference between subject means ($F=73.27$, $df=76$, $p<.001$).

(See plot in Appendix 2)

AT was negatively associated with heart rate but the scatter was broad ($r = .44$, $p = .000065$).

(See fig 15 overleaf)

The regression equation was:

$$Y = -.800609X + 192.1629$$

(95% confidence intervals for r were -.6037 to -.2386)

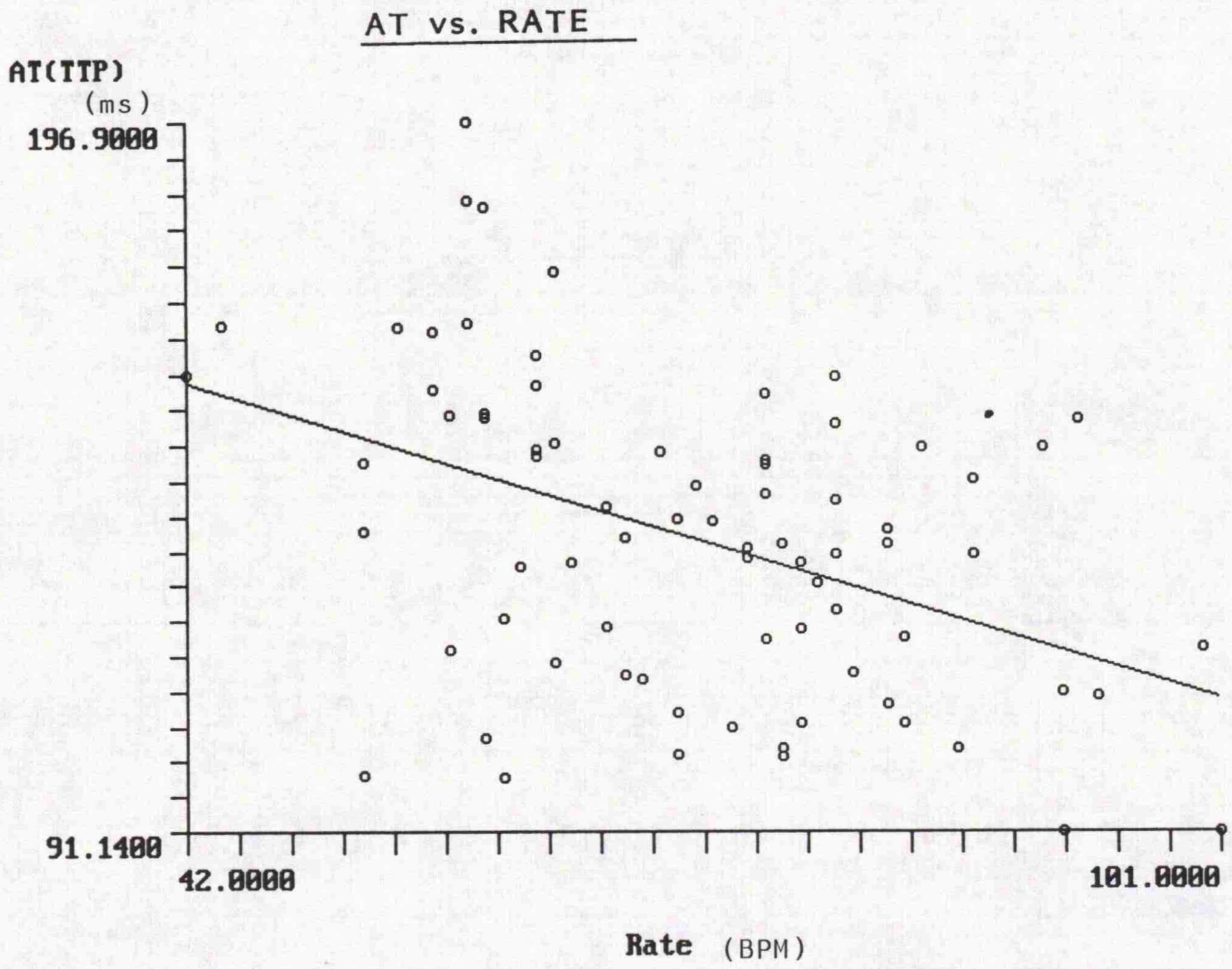
"Correction" for heart rate by dividing the AT by the root of the R-R1 interval in seconds removes an association with heart rate ($r= .1$, $2p=.38$). However, there is no improvement of scatter, with the breadth of confidence intervals hardly changing:

	AT	ATI
Median	135.6ms	145.5ms
Centile 95	175.9ms	183.1ms
Centile 5	99.8ms	110.2ms

Median difference of ATI from AT was 10.5 (95% C.I.s 2.9-17.6).

AT fell with age but the association was weak ($r = -.26$, $p <.05$).

Fig. 15



(r = -.44, p< .0001)

(d) RVPEP/RVET

The ratio RVPEP/RVET was calculated for each beat and each patient.

The mean figure for the 77 control subjects supine at rest in relaxed end-expiration was .35 (median .33) with standard deviation of .06 and SEM .00067. Range for the 77 controls was broad at .24-.53, and 95% confidence intervals much less so at .33-.36.

	RVPEP/RVET	RVPEP/RVETI
n	77	77
Mean	.347	.321
Variance	.354	.0025
St. Dev.	.059	.05
St. Err.	.0067	.0058
Maximum	.53	.46
Upper Qtile	.37	.36
Median	.33	.31
Lower Qtile	.31	.28
Minimum	.25	.23
Range	.46	.23
Centile 95	.46	.42
Centile 5	.26	.25

Fig. 16

RVPEP/RVET
Frequency Distribution

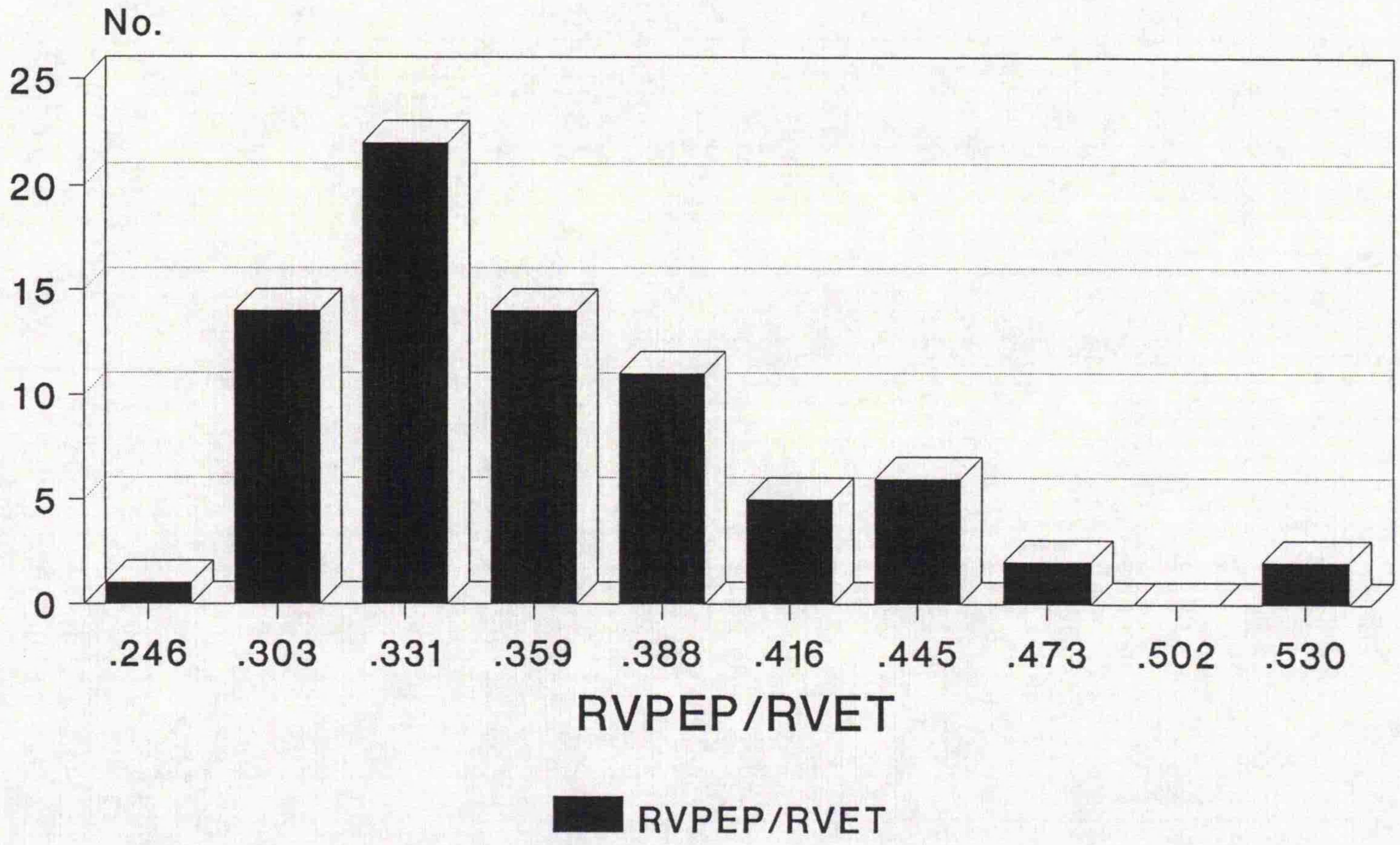
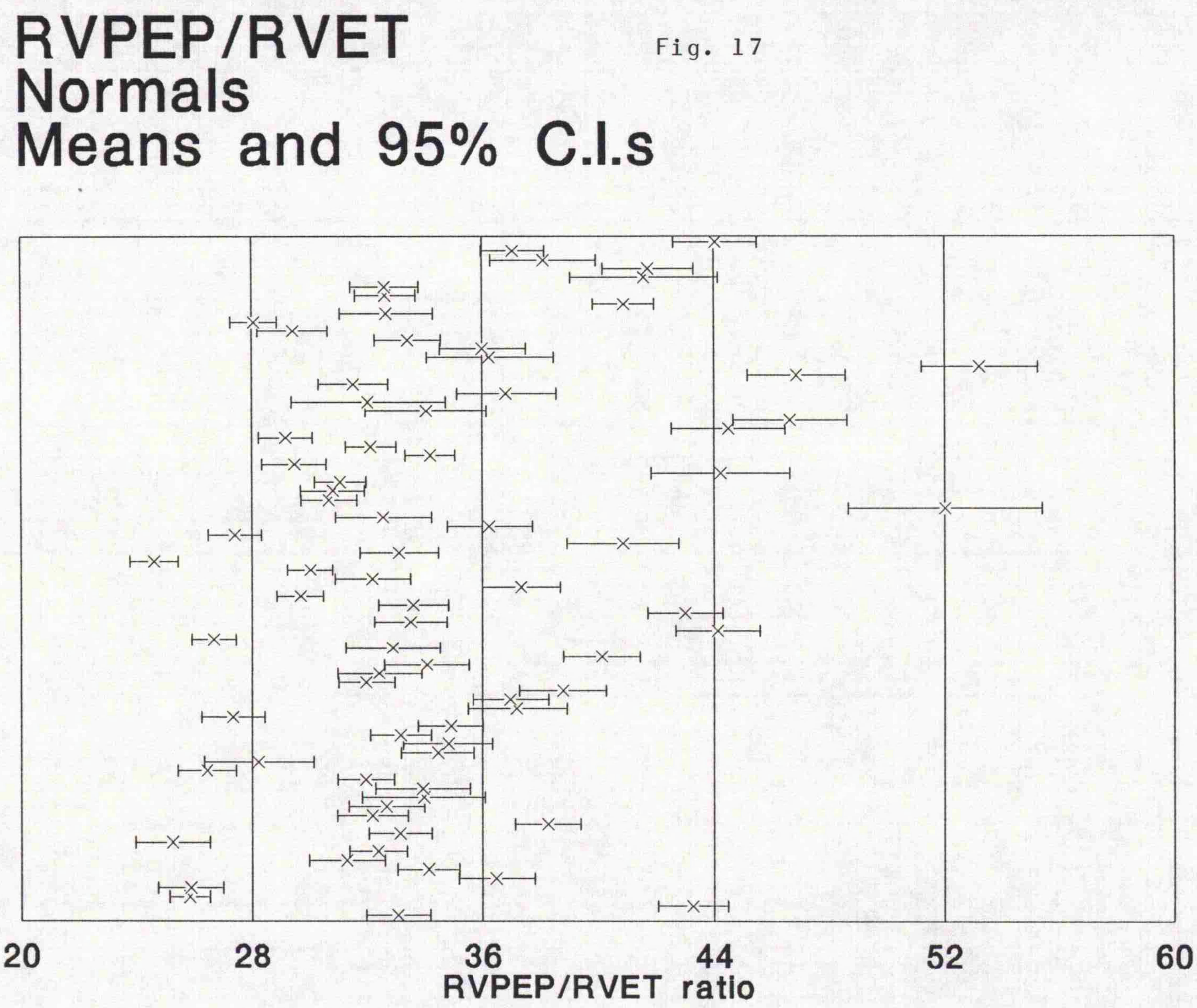


Fig. 17



RVPEP/RVET
Normals
Means and 95% C.I.s
20
28
36
44
52
60
RVPEP/RVET ratio

b280W

Distribution was markedly positively skewed (see Fig 16)

Within-patient variation was minimal with tight 95% confidence intervals for each subject: differences between subject means were much greater than intra-subject variations ($F=67.52$, $df=76$, $p<.001$). (See plot in Appendix 2)

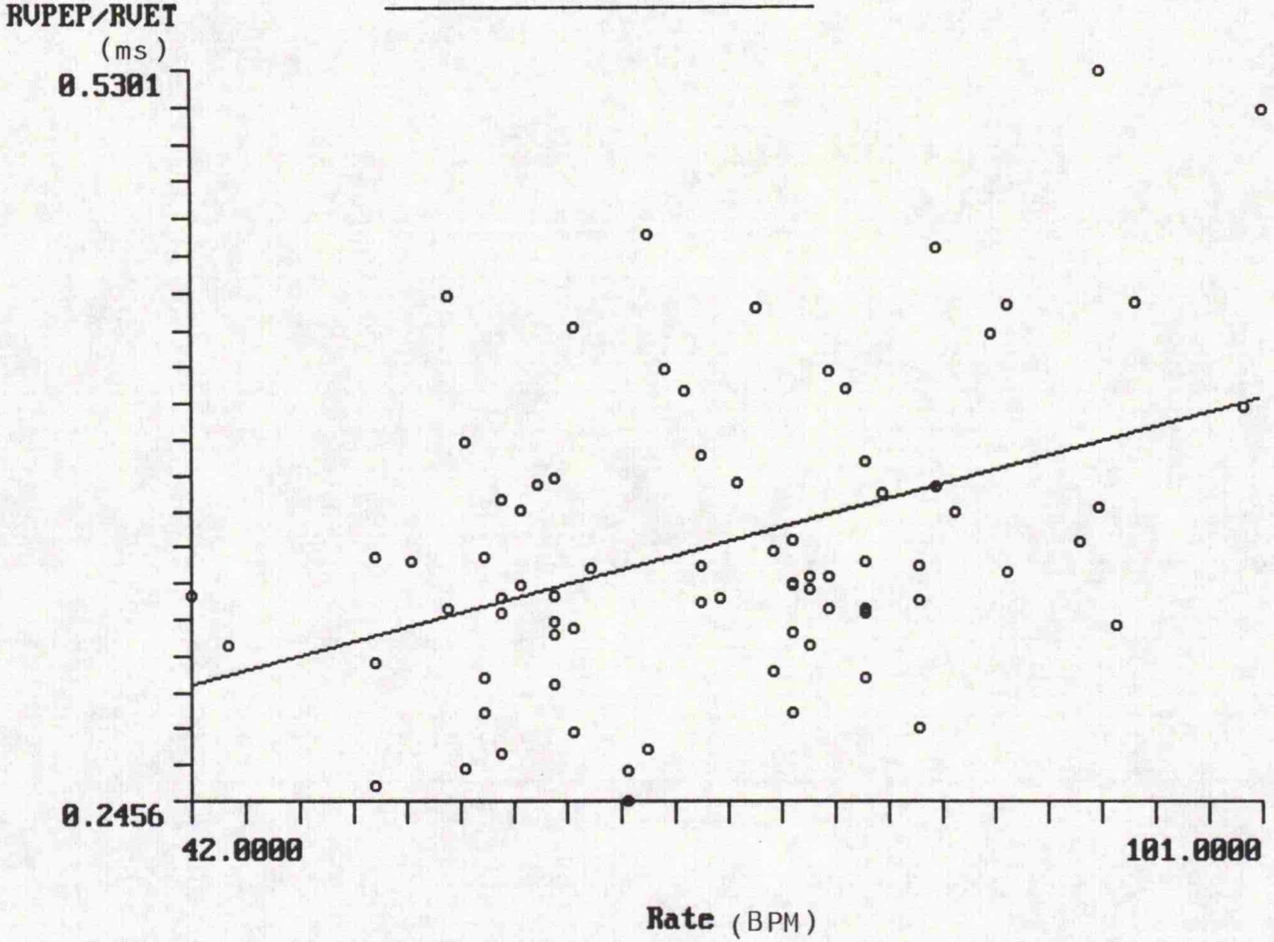
Despite previous claims to the contrary, calculation of this ratio did not remove an association with heart rate ($r = .41$, $p = .000198$).
(See Fig 18 overleaf)
(Regression equation $Y = 1.915818E-03X + .2106963$)
This is as expected as RVET is strongly influenced by heart rate and RVPEP is not.

One could correct the RVET for rate (using RVETI) and construct the ratio RVPEP/RVETI (see above).
This ratio is not related to heart rate ($r = -.154$, $2p = .1818$) but has not been validated.

RVPEP/RVET was weakly associated with age, with a similar association ($r = .29$, $p < .05$) to that of RVPEP with age.

Fig. 18

RVPEP / RVET vs. RATE



(r = .41, p< .0002)

(e) AT/RVET

The ratio AT/RVET was calculated for each beat and each patient.

The mean value of AT/RVET for the 77 control subjects supine at rest in relaxed end-expiration was .452 (median .455) with standard deviation of .064 and SEM of .00072.

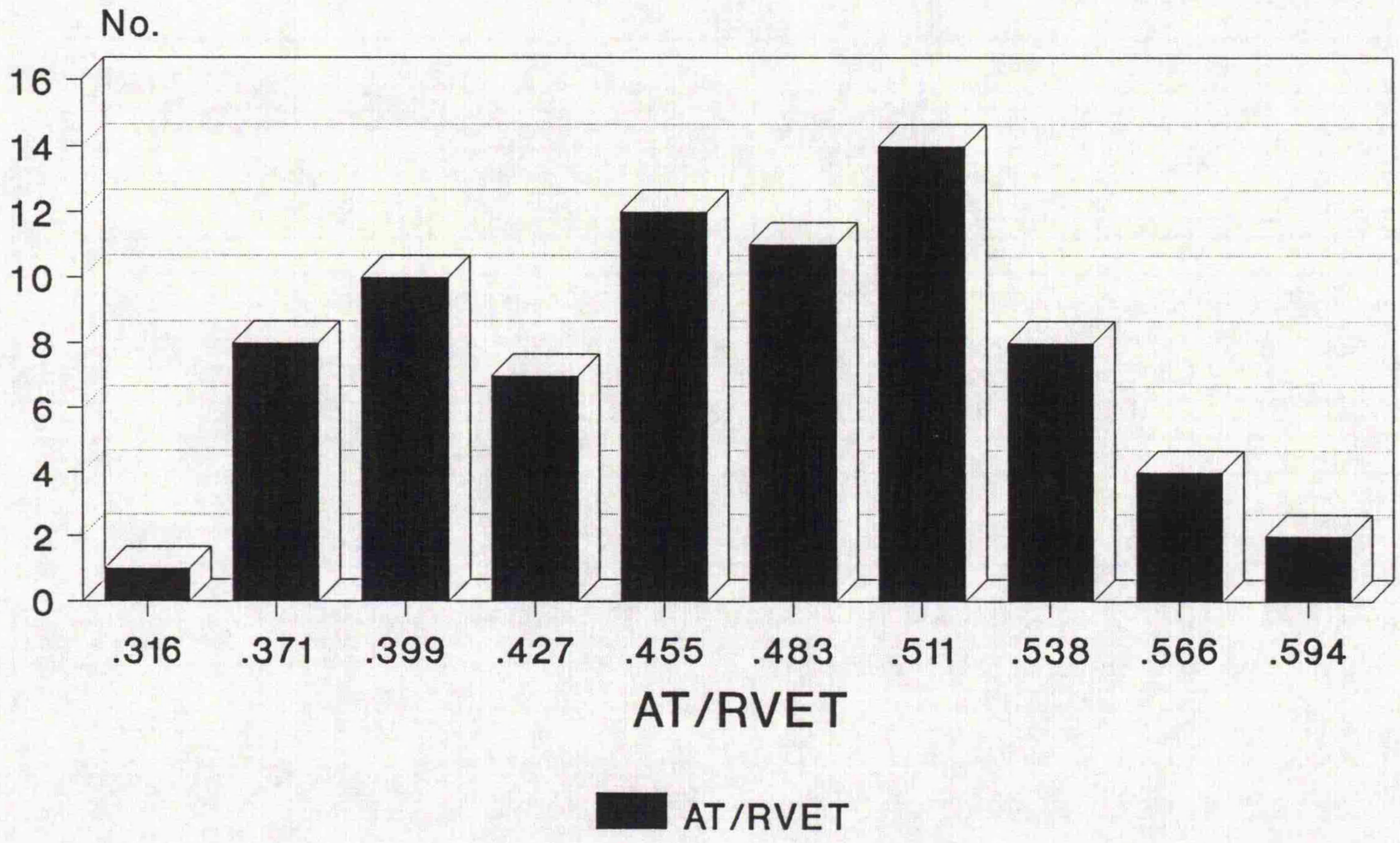
The range was .316-.595, with 95% confidence intervals .43-.56

AT/RVET	
n	77
Mean	.452
Variance	.403
St. Dev.	.063
St. Err.	.0072
Maximum	.59
Upper Qtile	.49
Median	.46
Lower Qtile	.40
Minimum	.32
Centile 95	.56

The distribution was mildly negatively skewed (see Fig 19), as for AT, but approximately normal (mean .452, median .451).

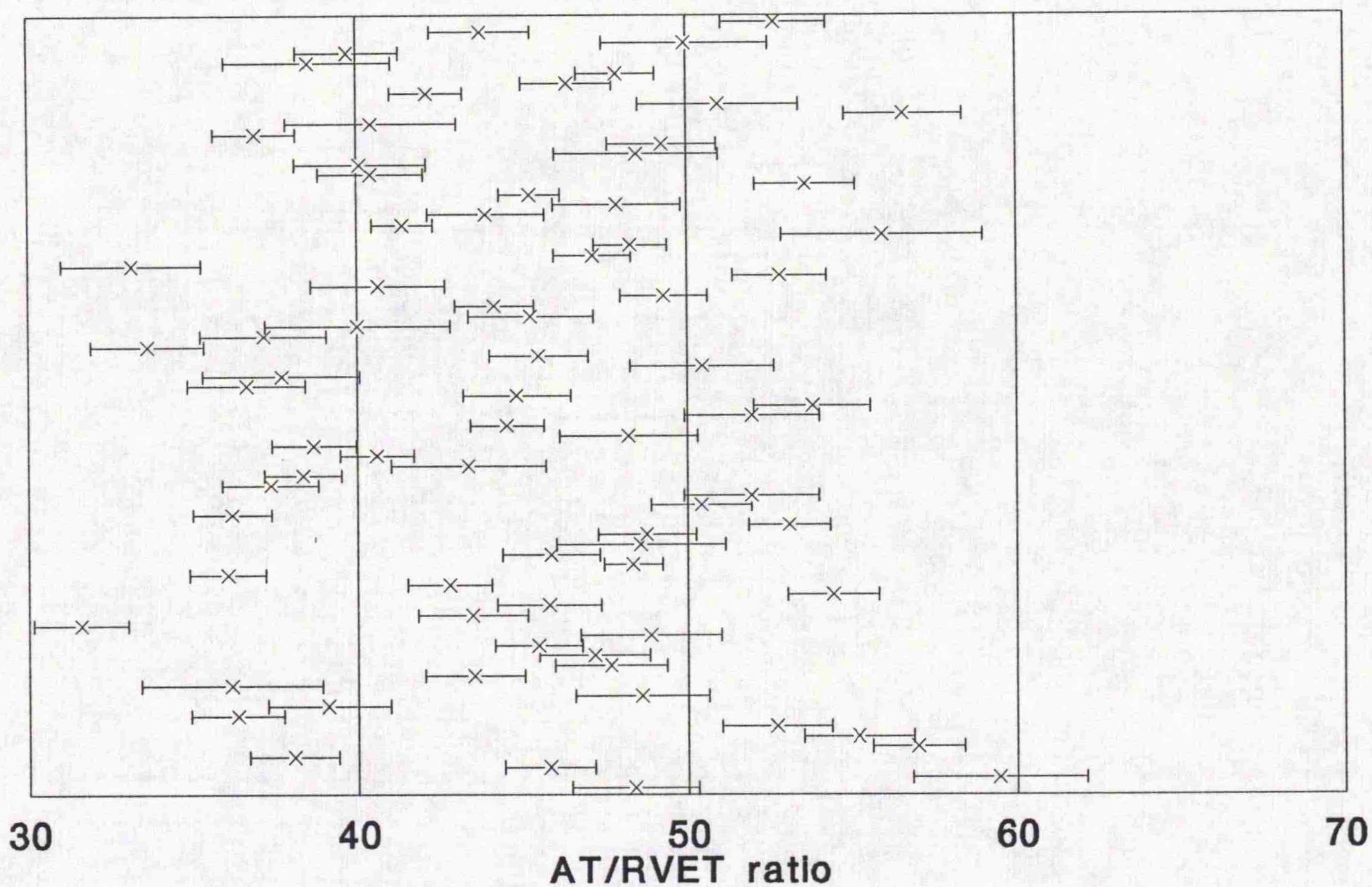
Fig. 19

AT/RVET
Frequency Distribution



AT/RVET
Normals
Means and 95% C.I.s

Fig. 20



Within-patient variation was small with tight 95% confidence intervals about each subject mean (see Fig 20): beat-to-beat variability was much smaller than the difference between subject means ($F=53.41$, $df=76$, $p<.001$).
(See plot in Appendix 2)
Calculation of this ratio appeared to remove any significant association with heart rate ($r = .008$, $p = .94$), and this ratio should therefore be useful in a wide range of circumstances.
(See Fig 21 overleaf)

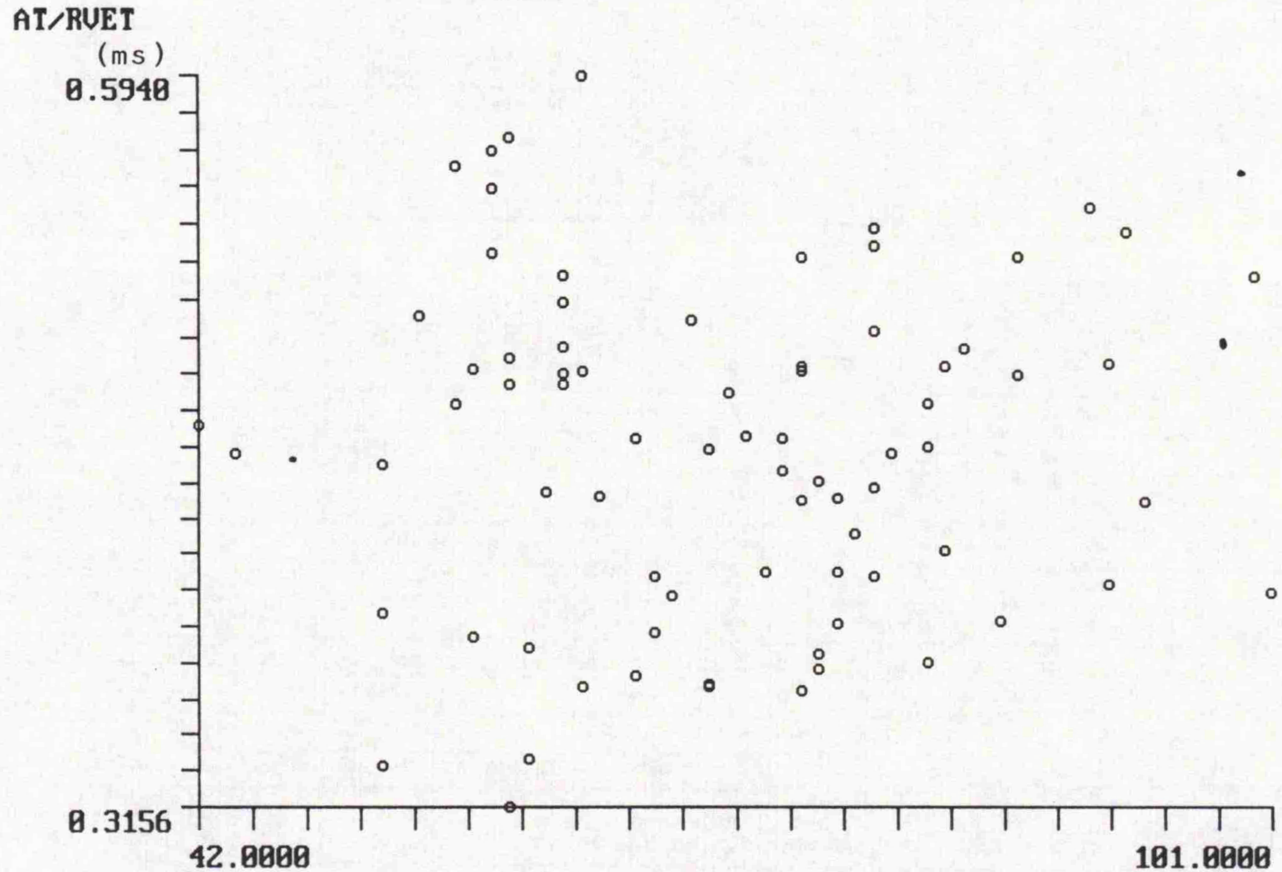
One could argue that dividing AT by RVET is just another way of correcting the AT for rate, as RVET and rate are so strongly associated, and indeed the correlations are similar;

AT/ root R-R interval	vs	AT	$r = .84$	$2p < .0001$
AT/RVET	vs	AT	$r = .83$	$2p < .0001$

AT/RVET was weakly associated with age ($r= .29$, $p < .05$).
[AT/rootRR vs age $r = .33$, $2p < .0036$]

Fig. 21

AT/RVET vs. RATE



(r = .008 , p = NS)

(f) RVPEP/AT

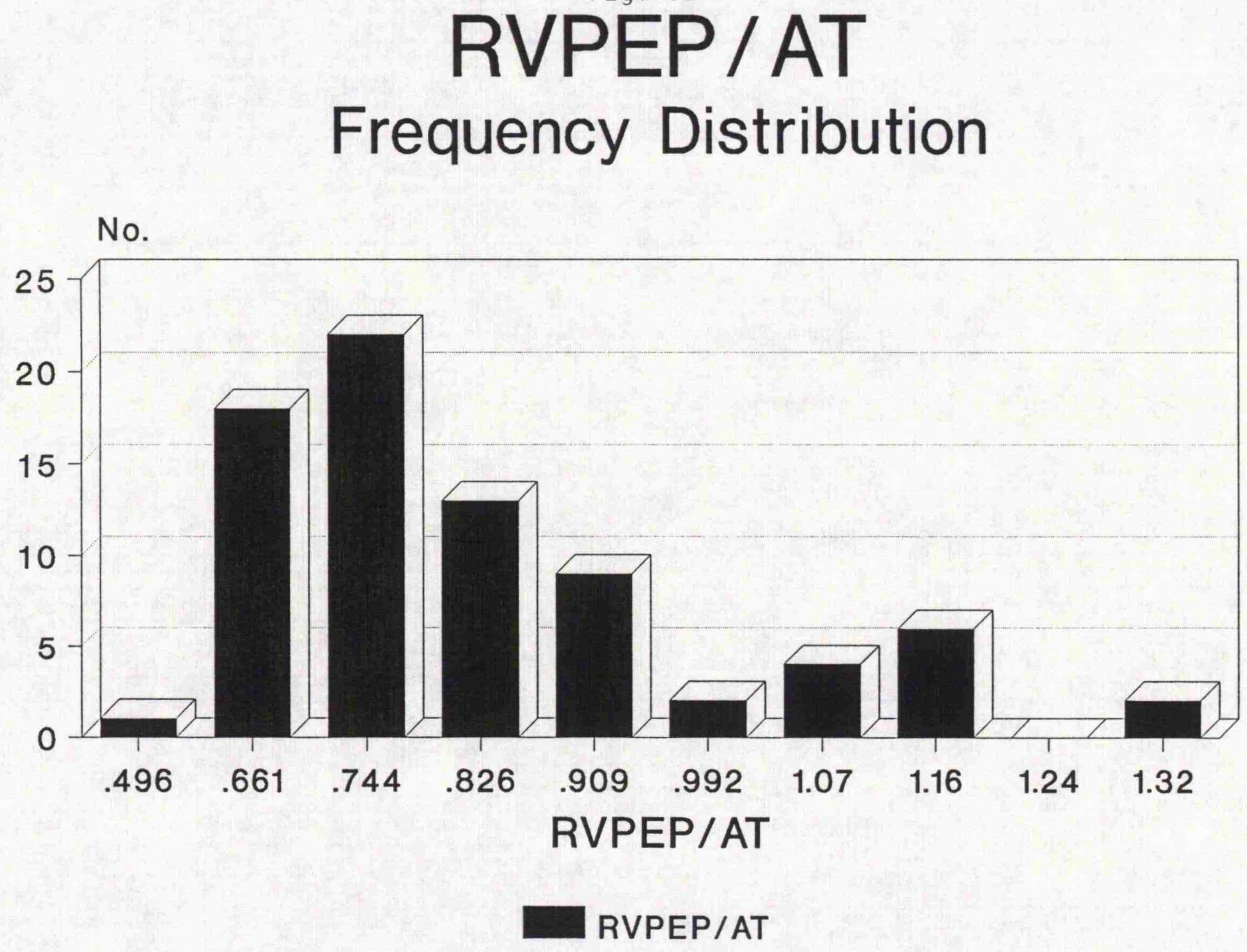
The ratio RVPEP/AT was calculated for each cycle and each patient.

The mean value for the 77 control subjects supine at rest in relaxed end-expiration was .79 with standard deviation .18 and SEM .021; 1st and 3rd quartiles were .67 and .88.

The range was very wide at 0.50-1.35.

	RVPEP/AT	AT/RVPEP
n	77	77
Mean	.79	1.34
Variance	3.31	.071
Std. Dev.	.179	.266
Std. Err.	.02	.03
Maximum	1.32	2.01
Upper Qtile	.87	1.51
Median	.73	1.37
Lower Qtile	.66	1.15
Minimum	.50	.76
Range	.83	1.26
Centile 95	1.12	1.78

Fig. 22



RVPEP / AT
Frequency Distribution
No.
25
20
15
10
5
0
.496
.661
.744
.826
.909
.992
1.07
1.16
1.24
1.32
RVPEP/AT
RVPEP/AT

The distribution was strongly positively skewed (mean .791, median .779): (see Fig 22).

Both logarithmic and reciprocal transformations substantially "normalised" the distribution, and it might therefore be better to routinely calculate AT/RVPEP instead (mean 134, median 137.5: standard deviation 26.7, SEM 3.04: 95% confidence intervals 128.8-140.7).

```
AT/RVPEP
 .7563486  | *                          1
1.008480   | ***********               11
1.134545   | ****                       4
1.260611   | ************              12
1.386677   | *************             13
1.512742   | *****************         17
1.638808   | *********                  9
1.764873   | ******                     6
1.890939   | ***                        3
2.017004   | *                          1
```

Within-patient variation was small with tight 95% confidence intervals around each subject mean ($F=48.39$ $df=76$, $p<.001$).
(See plot in Appendix 2)

With either ratio, significant though weak associations with heart rate ($r = .31$, $p = .006$) and age ($r = .41$, $p < .001$) persisted; as RVPEP is not associated with heart rate, and AT is, this is as expected.

Both ratios were strongly associated with RVPEP/RVET ($r = .765$, $p < .000001$), as they share RVPEP and AT is a fraction of RVET.

(g) Vmax

Vmax, the peak detected velocity in the pulmonary artery in systole in mid-vessel just beyond the pulmonary valve, was measured with each cardiac cycle and a mean calculated in each patient. Care had been taken to place the Doppler sample such that the largest value for Vmax and the longest AT were taken to indicate optimal positioning. In almost all cases this was centrally in the vessel.

	PA Vmax	RecipPAVmax
n	77	77
Mean	63.1	1.78
Variance	506.2	.0168
St. Dev.	22.5	.13
St. Err.	2.57	.0149
Maximum	144.7	2.16
Upper Qtile	68.8	1.84
Median	57.5	1.76
Lower Qtile	49.2	1.69
Minimum	40.2	1.60
Range	104.5	.556
Centile 95	115.4	2.06

Median value for PA Vmax in the 77 control subjects lying supine in relaxed end-inspiration was 57.5 cm/sec. The distribution was strongly positively skewed (mean 63.09, median 57.5 cm/sec): (see Fig 23)

Scatter around subject means was tight, with inter-personal variation being much greater than beat-to-beat variation (see Fig 24).

PAVmax was not associated with any of the values or ratios thought to reflect RV function, and was not associated with sex, heart rate or age.

Fig. 23

PA Vmax
Frequency Distribution

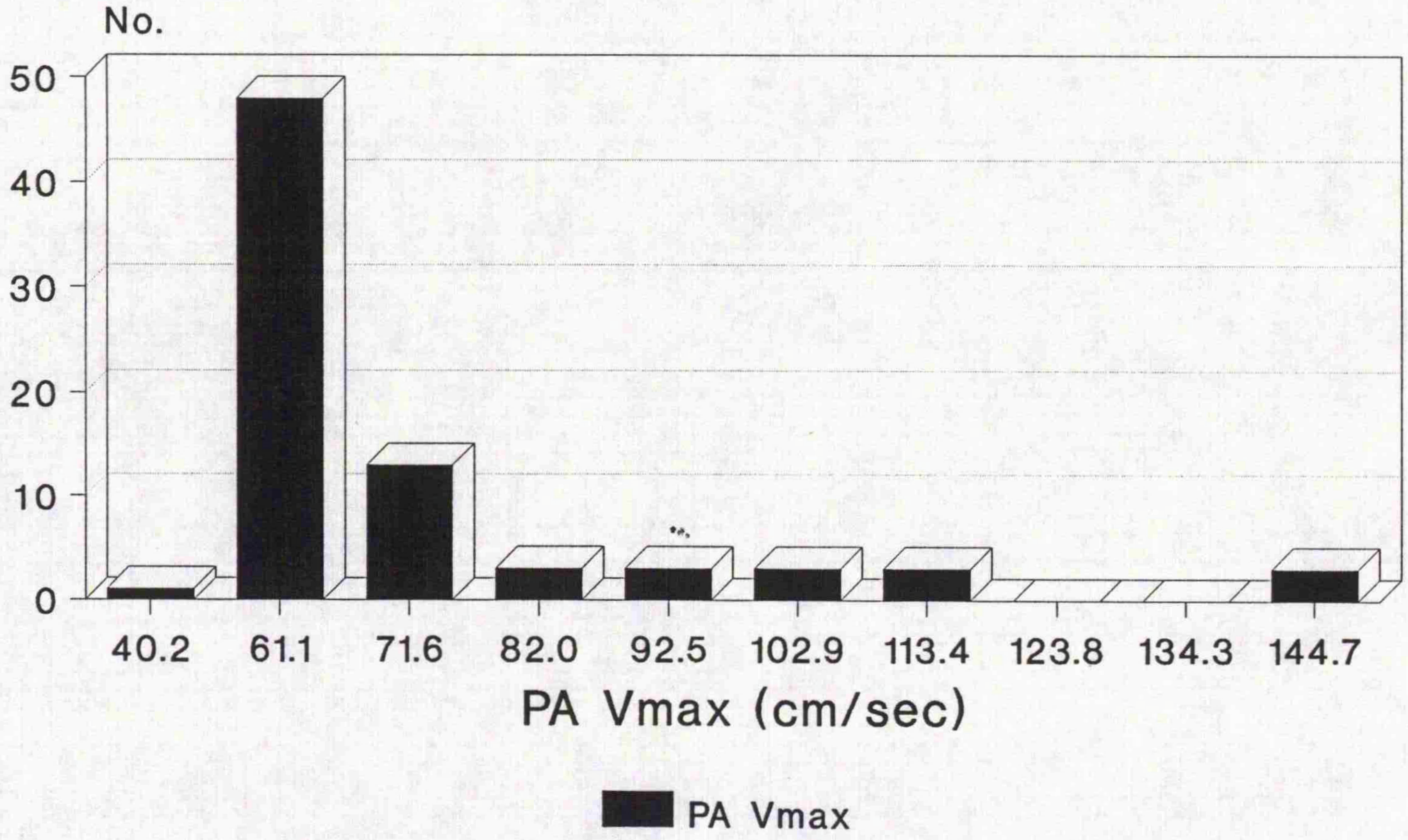
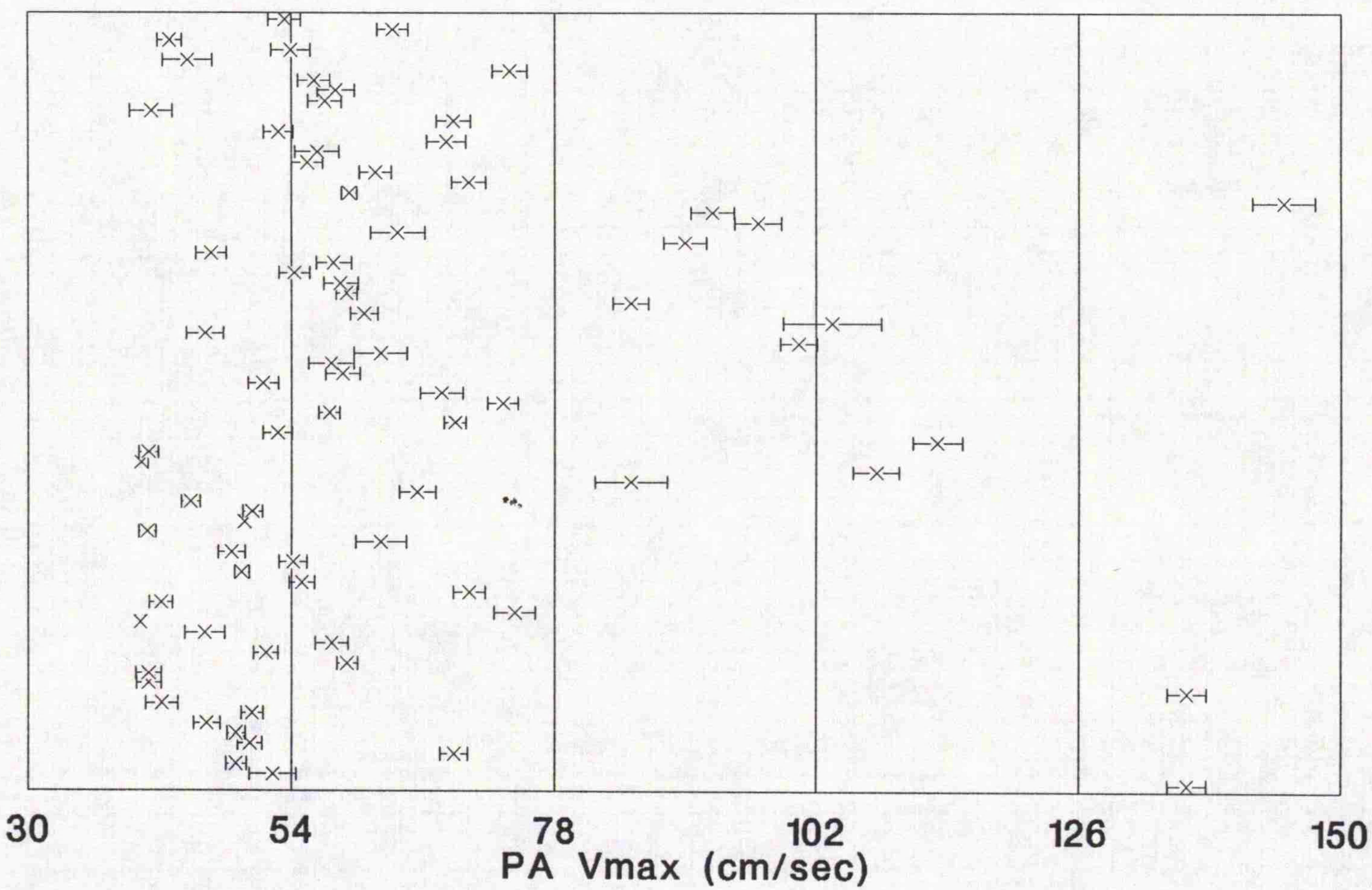


Fig. 24

PA Vmax velocity
Normals
Means and 95% C.I.s



DISCUSSION OF RESULTS ON NORMAL CONTROL SUBJECTS AND COMPARISON WITH PREVIOUSLY PUBLISHED SERIES

Discussion of results on normal subjects and comparison with previously published series

(1) RVPEP

Utility and problems of the measurement - critique of previous series

RVPEP was suggested by Kosturakis[114] as a good index of both systolic and diastolic pulmonary artery pressure in his population of 17 children with congenital heart disease who underwent cardiac catheterisation. However, his impressive associations (RVPEP vs systolic PA pressure $r = -.82$, $p<.001$, RVPEP vs diastolic PA pressure $r = -.7$, $p<.001$) could not be confirmed by subsequent work. Curtiss[215], using PV movement for timing, found different mean values in children with high and normal PA pressures, but the overlap was too great for the measurement to have any clinical value. Isobe[115] came to much the same conclusion using Doppler-derived values. Interest in the measurement continued, however, as part of the ratio RVPEP/RVET[100].

Early measurements of RVPEP used simultaneous ECG and pulmonary valve(PV) echogram recordings; the onset of electrical systole was taken from the earliest part of the QRS complex, and pulmonary valve opening was taken as the end of RVPEP. The latter is sometimes difficult to accurately time because the valve opens with atrial systole in some patients. Leatham[216] used full opening of the PV in his paper, and this accounts for his longish figure of 120ms or more. Riggs[217] studied 85 normal children and young

people (ages 2 months to 21 years) and, using the onset of pulmonary valve motion, arrived at a mean (± s.d.) figure of 109ms (11ms), and Torlicki[218], studying 25 "controls" (unspecified), 101ms (15.8). These figures are in good agreement with mine (102.7ms ± 12.8).
Hirshfeld's series of 45 subjects, mostly children[100], were measured from "the first part of the QRS complex, usually the Q wave", and the earliest onset of electrical activation may therefore have been measured differently. His figure of 67ms (± 14.9) is lower than most estimates.

Shiraishi's neonatal series[118] is clearly not comparable, although it is interesting to note that the figure for newborns was 94ms at birth falling over one month; the heart rates of his children were, as expected, rapid at 117-142.

Nanda[101] presents data on 22 patients with a broad age range (16-61 yrs, mean 42), but almost the only thing they had in common was a normal PA pressure: all were being evaluated for suspected heart disease. He does not present raw RVPEP data, but only as RVPEPc (i.e. "corrected" for heart rate, which is, as we have seen, is less than satisfactory). His point of interest is the stress on the opening slope of the PV, a measurement not taken up by other authors as too subjective.

Two authors, Leighton[96] and Curtiss[215], present data from invasive investigations. In both cases, catheter-tip transducers were passed to the pulmonary artery and measurements were made at rest and during atrial pacing. This introduces other factors of catheters being in place across heart valves, and whether the abnormal site of atrial activation due to atrial stimulation would affect STIs. Curtiss had 13 "controls" but his population is unsatisfactory: 4 had systolic murmurs, 5 had reverse splitting of the second sound, 1 had complete right bundle branch block, 1 had mitral regurgitation, 1 had undiagnosed chest pain, and 2 had a documented patent ductus arteriosus. Both of these studies, measuring pressure change rather than flow, come to similar figures; 80ms ($\pm$ 17) in Leighton's study and 86ms ($\pm$ 15) in Curtiss's.

Two authors offer adult data obtained non-invasively using pulsed Doppler. RVPEP was measured from the earliest onset of the QRS complex on the ECG to the earliest detected forward flow into the pulmonary artery. Isobe[115] studied 32 normal controls (although we are not given their ages), and found a mean RVPEP of 99ms ($\pm$ 21), similar to mine. Kosturakis's[114] patients were all very young (age 4-22yrs) and said to be "normals" (although no data on this is given).

His figure of 88ms ± 3ms suggests a very tight scatter of results not achieved by most investigators. His range of 72-104ms is, however, enclosed by mine.

Comparison of our figures with previous investigators' figures

```
Leighton   |              <------------x------------>
Curtiss    |                          <----x---->
Shiraishi  |                                   <---x--->
Hirschfeld |          <---x--->
Riggs      |                                                <-x->
Torlicki   |                                           <---x--->

CHEESMAN   |                                               <--x-->
           |
--------------------\---------\---------\---------\---------\---
                    60       70        80         90       100
                                                    (msec)
```

Mean and 95% CIs for published series of "normals" with respect to RVPEP

I believe that I present the most carefully checked series of "normal" individuals from a wide age range. My mean of 103ms is similar to Isobe[115], Riggs[217] and Torlicki[218], and two standard deviations either side suggests a working range of 77-128ms. It is possible that lower mean figures obtain in children (there were none in our study), but within my age-range there was no significant association with age. Shirashi[118] also studied the effect of age, but only within the neonatal period, when large changes in pulmonary vascular resistance are known to occur.

Relationship to heart rate

There is some disagreement in the literature about the relationship of RVPEP to heart rate. Riggs[217], in his cross-sectional study of 85 children, found a strong inverse relationship ($r=-.71$, $p<.001$) over a very wide heart rate range (50-185 beats per minute). He offers a regression equation to "correct" for heart rate of

$RVPEPc = 108.9-0.369(HR)$ or $RVPEPc = RVPEP + .369(HR)$

Nanda[101] converts his data by means of a inverse root formula:

$$RVPEPc(ms) = \frac{RVPEP\ (ms)}{\sqrt{R\text{-}R\ interval(secs)}}$$

but does not offer any validation.

Curtiss[215], however, found no relationship at all, but Hirschfeld[100] found an inverse relationship. Sundberg[219], studying LVPEP in 19 normal adults using pulsed Doppler, found none. Spodick[220] and Cokkinos[221] also found no relationship in their studies. Leighton[96] studied 27 patients invasively and found no relationship between resting heart rate and RVPEP: on 4 normal volunteers, however, when he proceeded to do an atrial pacing study, he found that there was an immediate rise in RVPEP at the start of pacing, even when the pacing rate was only just above sinus rate, and that there was also a rate-related further rise, although LVPEP did not

change. This is curious: pacing catheter position and pacing-induced conduction delay (i.e. early Wenckebach effects) may have been additional variables.
A regression equation was suggested of

RVPEPc = 0.7(HR) + either 35 or 12 depending

on whether the patient was in expiration or inspiration at the time. It must be remembered that these calculations arise from only 4 (albeit highly-studied) subjects.

I did not find any significant association between RVPEP, measured with pulsed Doppler, and heart rate on a population basis. I did not think it ethical to subject my 77 control subjects to atrial (or oesophageal) pacing. 95% confidence limits around each subject mean were tight, with between-subject variability much greater ($F=62.53$, $df=76$) than intra-subject variability, despite widely differing heart rates. I cannot support any form of "correction" for heart rate from my data, although it is possible that at much higher rates (as in childhood) there is a real effect.

Somewhat to my suprise, the PR interval did not affect RVPEP, although it is known to affect RV loading conditions.

Future prospects

It is difficult to know how useful this measurement really is. The data available are mostly drawn from pre-Doppler days when the newer variables such as Acceleration Time and direct measurements of flow were not available. Correlations with PA pressure and resistance are modest in most investigators' hands. The lack of variation with heart rate might be an attraction, or perhaps the measurement might be useful where it is genuinely difficult to decide on the end of the ejection period, possibly in combination with AT (vide infra).

My normal ranges for these intervals and their combinations are the first comprehensive ones.

(2) RVET

Utility and problems of the measurement - critique of published series

Right ventricular ejection time (RVET) is longer than simultaneously-measured LVET[96]. Measurements, whether using PV motion, or Doppler timings of pulmonary artery systolic forward flow, are essentially identical[124]. It is difficult in adults (although often easy in children) to accurately time the moment of PV closure on an M-mode echocardiogram, and the valve may move after that. One author gave up in disgust[117].

Measurement of RVET using pulsed Doppler is complicated by the differing waveforms[114,222] that can exist. In fact, these cause more problems when attempting to measure "time-to-peak" flow or acceleration time. End-systolic flow reversal[222] has also been cited as a problem, but I found no difficulty in measuring end-systole in any subject.

The raw RVET, corrected for heart rate, is negatively associated with PA pressure [100,113,114,215,217], but overlaps between patients with normal and raised PA pressure are such that RVET alone is not a clinically useful predictor[113,114] and Riggs[217] found the relationship non-linear with a broad scatter.

No good longitudinal studies exist: Mishra[223] and Wassir [224] present serial measurements of RVET in pulmonary hypertensive patients during calcium blockade therapy, but invasive validation is lacking.

Length of systole may also be affected by the contractile state of the myocardium; Gardin[112], using pulsed Doppler, demonstrated that RVET was significantly shorter in patients with congestive cardiomyopathy than in his control subjects. Changes in the LVET were of similar magnitude.
LVET, as a measure of systolic function, has been used to find an optimum "PR" interval during dual chamber pacing [155], but this effect has not before been explored in the right heart.

Comparison of my figures with previous investigators' figures

My figure for a mean value of RVET of 300ms ($\pm$ 28.6) and that for RVETI of 321.77 ($\pm$ 21.04) is in good agreement with most authors:

Isobe	[115]	317ms ($\pm$ 33)
Gardin	[112]	315ms ($\pm$ 23)
Martin-Duran	[117]	280ms ($\pm$ 84)
Kitibatake	[113]	304ms ($\pm$ 38)
Hirschfeld	[100]	276ms ($\pm$ 43)
Curtiss	[215]	344ms ($\pm$ 27]

Kosturakis's[114] figure of 385ms ($\pm$ 32) seems out of line; he studied children, but the reasons for the discrepancy are unclear; Riggs[217] found a modest positive association between RVET and age, even after correcting for heart rate, but no other author does, and the difference is still in the wrong direction. I found no association with age at all, over the range 17-84 yrs in my 77 subjects.

```
Isobe      |                     <----x---->
Gardin     |                   <----x---->
Martin     |
 -Duran    |----------x----------------->
Kitabatake |       <------------x----------->
Hirschfeld | <-----x----->
Curtiss    |                                  <------x------>
           |
CHEESMAN   |                 <--x-->
           |
-----------\--------\--------\--------\--------\-------\-----
          270      280      300      320      340     360
                                   (msec)
```

Mean and 95% CI plots for published series of RVET in "normal" subjects

Relationship to heart rate

RVET is strongly negatively associated with heart rate, and the relationship is linear in humans[96,94,100,217] and in pigs[143]. Various regression equations have been produced, but an inverse root formula of

$$\text{RVETc(ms)} = \frac{\text{RVET (ms)}}{\sqrt{\text{R-R interval(secs)}}}$$

has gained widespread popularity.

From my data, I confirm a strong negative association between RVET and heart rate ($r=-.79$, $p<.001$); calculation of RVETc by the above formula removed this association.
As an alternative, our regression equation is

$$Y = -.35x + 176$$

Unlike acceleration time and peak velocity, RVET is resistant to distortion by beam alignment[125], and is probably the easiest right ventricular systolic time interval to measure using Doppler ultrasound.

Future propects

RVET is likely to remain as an useful index of RV systolic function because of the wealth of literature surrounding its history and its predictability: the relationship to heart rate has been worked out, although regression equations are probably preferable to Bazett-style approximations. It is resistant to distortion by beam alignment, and I do not believe the problems of end-systolic flow reversal are serious. Although flow velocity integrals are of considerable interest, the software is not universally available.
This normal range should be a useful contribution to the continued use of the measurement.

(3) RVPEP/RVET

Utility and problems of the measurement - critique of published series

Weissler[92-94] first popularised LVPEP/LVET as a clinically useful ratio because he found no relationship to mean heart rate in 90 normal individuals, and an inverse relationship to cardiac output, stroke volume and ejection fraction. He found the ratio a better predictor of these measurements than either LVPEP or LVET alone: he also found that infusion of inotropic agents "improved" the ratio in patients with heart failure proportionally to improvements in cardiac output. Leighton, studying 27 patients with normal pulmonary artery pressures at rest, found that RVPEP was not associated with mean resting heart rate, but RVET was: he did not study the ratio but it would be expected from his findings that RVPEP/RVET would be related to heart rate. In Hirschfeld's [99,100] series of 45 normal young people neither age nor heart rate were related to the ratio. There was a significant association between RVPEP/RVET, PA pressure and pulmonary vascular resistance in his invasively studied group, but the pulmonary hypertension had to be moderately severe (systolic >70mmHg, diastolic >50mmHg), or the pulmonary vascular resistance markedly raised (>8 Wood units), for there to be a clear separation from normal individuals.

In Riggs's study[217] RVPEP/RVET was significantly but non-linearly related to PA pressure, but scatter again was broad; however, he again found only a small association between the ratio and heart rate or age. Shiraishi's neonatal findings were interesting in that the ratio declined sharply within a few days of birth, mainly due to a marked fall in RVPEP [118]. Kosturakis [114], using pulsed Doppler, confirmed that patients with pulmonary hypertension had higher ratios than patients with normal PA pressures, but found that sensitivity was poor (58%) and specificity worse (33%).

In Isobe's series[115] neither RVPEP nor RVET was significantly associated with heart rate: in 45 adults with pulmonary hypertension, RVPEP/RVET was not a useful predictor of raised pressure. Although Wasir[224] and Mishra[223] did find a fall in the ratio when calcium antagonists were given to patients with pulmonary hypertension, there was no invasive confirmation of pressure reduction, and most of the change was a fall in RVPEP.

Comparison of my figures with previous investigators' figures

My mean figure for RVPEP/RVET of .347 (±.06, range .24-.53) is similar to Kosturakis's (.35 ± .035) and Isobe's (.36). Riggs does not quote a mean figure, but most patients in his series with ratios up to .35 had normal PA pressures. Scatter was broad in most studies. Hirschfeld's figure of .24 (range .16-.30) is shorter than most because his range for RVPEP is short.

```
Kosturakis|                 <------x------>
Isobe     |          <---------------x-------------->
Shiraishi |      <---x--->

CHEESMAN  |                   <-----x----->
          |
-------------\-----\----\----\----\----\----\----\----\----\------
            .30   .31  .32  .33  .34  .35  .36  .37  .38
          Means and 95% confidence intervals for published
                 series of RVPEP/RVET
```

Future prospects

RVPEP/RVET has been all but abandoned as a clinically useful index of PA pressure. Its original attraction (that is was not significantly related to heart rate) was been disputed (because a majority of authors find RVPEP not to be rate-related), and although associations exist between the ratio and PA pressure however measured, sensitivities and specificities are too poor for widespread clinical application.

(4) <u>Acceleration time</u>

Utility and problems of the measurement - critique of published series

The advent of pulsed Doppler measurements in the pulmonary artery trunk enabled a new measurement to be determined. The time-to-peak flow (TTP) or acceleration time (AT) can be calculated regardless of waveform [116] and correlates inversely with PA pressure. Care needs to be taken, however, in aligning the beam to produce the longest value for this measurement, as errors of up to 50% can be made if multiple views are not used and the maximum value sought [125,126]. AT is much longer in the right heart than the left [112]. AT has been found to be inversely associated with pulmonary artery pressure [143] but the relationship was found by most investigators to be non-linear [113,115,116]; logarithmic transformation is helpful, and Isobe[115] proposes a regression equation of

$$AT(ms) = -198(\log \text{PA mean pressure in mmHg}) + 387.$$

Gardin[143] found that in the steep part of the curve, with values less than 100ms, the relationship became linear and suggested this value as a "cut-off" for suspicion of high PA pressures.

However this measurement in its crude state presents several difficulties. Apart from measurement error described above, most authors find a wide range and broad scatter of data around their means in normal subjects.

Comparison of our figures with previous investigators figures

Matsuda	[116]	110ms (± 30)
Martin-Duran	[117]	143ms (± 30)
Gardin	[112]	159ms (range 125-185)
Shiraishi	[118]	101ms (± 21]
Kosturakis	[114]	151ms (± 25)
Isobe	[115]	144ms (± 16)
Kitabatake	[113]	137ms (± 24)
Lighty	[125]	143ms (± 24)

It is possible that some of the above differences are due to beam alignment, as various authors used the RV outflow tract, PA artery proximally and distally, etc.

My mean figure of 135 (± 23.19) is similar to most of the above authors', and my range similarly broad at 91-170ms. The distribution was mildly positively skewed, and a median figure of 136ms with upper and lower quartiles of 116/151 describe the population. Four of my control subjects had acceleration times of <100ms without detectable cardiac abnormalities, and another four had acceleration times <105ms. The normal range may thus be broader than previously described.

```
Shiraishi |       <--x-->
Gardin    |                                  <--x-->
Matsuda   |          <---x--->
Martin-   |
 Duran    |                         <-----x----->
Kosturakis|                             <----x---->
Isobe     |                            <--x-->
Kitibatake|                      <----x---->
Lighty    |                          <---x--->

CHEESMAN  |                        <---x--->
          |
---------------\----\----\----\----\----\----\----\----\---------
             90   100  110  120  130  140  150  160  170
                                            (msec)
           Mean and 95% CI plots for published series on "normal"
                subjects for acceleration time
```

Relationship to heart rate

Gardin [143] noted that AT was significantly heart-rate-dependent in his pacing study in pigs. Isobe[115] did not find any relationship at rest, and Kosturakis[114] did not improve his correlation with PA pressure by heart rate correction. However, I agree with Gardin's[143] data and find a weak association with heart rate ($r = .44$, $p < .001$). He also suggested that as both AT and RVET are inversely associated with heart rate, calculation of the ratio AT/RVET might make the measurement rate-independent as well as being physiologically interesting.

Future prospects

Acceleration time is a useful measurement. The correlations with PA pressure and resistance are reasonable, although the association is probably non-linear. Most of the time the value is easy to measure, although it is clearly important to optimise beam position and sample location. It can, like RVPEP (or possibly, with RVPEP) be used when the end of RVET is difficult to time (infrequent though that may be).

The relationship to heart rate is still somewhat problematic. Although I find a modest correlation, scatter is too broad to apply a simple corrective formula. This must be borne in mind when applying it to clinical situations.

A rule-of-thumb seems to have grown up that a value of less than 100ms (or slightly more) usually means that PA pressure or resistance is elevated. Although I did not feel it ethical to perform invasive studies to measure PA pressure on my half-dozen subjects with values of <105ms, I have no reason to suspect any abnormality in any. This notional figure may have to be reviewed as a guide.
The above normal range, although a little wider than some others, illustrates the breadth of normality in a wide age-range.

(5) AT/RVET

Utility and problems of the measurement -critique of published series

Several authors comment that expressing AT as a function of RVET improved predictive accuracy of PA pressure as well as removing the association with heart rate [111,113,117,143], although Kosturakis found no advantage over crude AT[114]. Isobe[115] and Kitabatake[113] note that the relationship is still inverse and non-linear. Because it contains AT, the ratio is dependent on the beam position, as before.

I also find no significant relationship to heart rate ($r = -.007$, p=NS) and beat-to-beat variation was minimal ($F= 53.41$, df 76, $p<.001$).

Comparison of my figures with previous investigators' figures

My mean figure of .45 $\pm$ .064 is similar to most other authors:

Kosturakis	[114]	.438 $\pm$ .051	
Isobe	[115]	.45 $\pm$ .05	(range .32-.62)
Kitabatake	[113]	.45 $\pm$ .05	
Martin-Duran	[117]	.44 $\pm$ .7	
Panadis	[126]	.49 $\pm$ .08	
Okamoto	[111]	.46 $\pm$ .03	
Shiraishi	[118]	.52 $\pm$ .05	

It will be seen that one thing this ratio does seem to achieve is a remarkable degree of unanimity amongst various investigators! Most also find scatter much less broad than for crude AT.

```
Shiraishi  |                                                  <--x--
Kosturakis |           <---x--->
Isobe      |              <----x---->
Kitibatake |                <--x-->
Martin-    |
 Duran     |-----------------x-------------------------------------
Panadis    |                          <-----x------>
Okamoto    |                   <---x--->

CHEESMAN   |                <--x-->
-------------\--\--\--\--\--\--\--\--\--\--\--\--\--\--\----
           .39   .41   .43   .45   .47   .49   .51   .53
           Mean and 95% confidence intervals of published series
                of AT/RVET
```

Future prospects

This seems a good and useful ratio: the inverse relationship to PA pressure is better than with crude AT in most authors' series, and the lack of association with heart rate is an added bonus. It is relatively easy to measure in most patients whatever the waveform, and has not been shown to alter with age outside the neonatal period.

My range for normality is very similar to most other investigators'. I find no important associations with age or rate. It is also interesting as a reflection of the proportion of ejection occuring in early systole, and future studies should possibly look at proportions of flow integrals.

(6) RVPEP/AT and AT/RVPEP

Utility and problems of the measurement
-critique of published series

The attraction of this measurement is that in a situation where it is difficult to determine the exact point of end-systole (as may occur with end-systolic flow reversal), an estimation can still be made of the PA pressure.
Isobe[115] is its principal supporter: his mean figure for RVPEP/AT was .7 ($\pm$ .07, range .37-1.02), which is similar to mine (mean .79 $\pm$ .18).

He found impressive associations with mean PA pressure (RVPEP/AT vs PA mean pressure $r = .93$, $p<.001$) and offered a regression equation of

$$\text{RVPEP/AT} = .023\,(\text{PA mean pressure}) + .48$$

This work needs to be confirmed by other investigators.

Comparison of Isobe's and my figures

However, the distribution of RVPEP/AT in my normal control subjects was very markedly positively skewed and I should rather be quoting the median figure of .74; my range is very broad and similar to his (.49 to 1.34). Inversion of the ratio substantially "normalises" the distribution, as does logarithmic transformation: reciprocal transformation is easier, with a mean of 1.347 and median of 1.372 ($\pm$ .027), and contains the same clinical information. However, validation studies are awaited.

(7) PA Vmax

Utility and problems of the measurement

Peak velocity in the pulmonary artery trunk is lower than that simultaneously measured in the aorta (Gardin's data: mean PA Vmax .62 m/sec, aorta .92 m/sec[112]) and the same is true in cardiomyopathy[143], although PA Vmax is lower in these patients (as is aortic velocity, although the fall in aortic velocity was greater than the fall in PA Vmax). Gardin did not measure PA pressure directly, and studies of PA Vmax against PA pressure are awaited. He went on to demonstrate lower flow velocity integrals, as would be expected. Lighty[125] showed that beam alignment had a major influence on recorded peak velocity (varying from .66 to .96) and multiple views should be sought.

Comparison of my figures with previous investigator's figures

My mean figure of .63 m/sec (± .225) is in good agreement with Gardin's, but I find the distribution very markedly positively skewed with a median value of .575 and range of .40-1.45 m/sec. Again, logarithmic and reciprocal transformations substantially normalise the distribution and are of unclear clinical significance, unless it is shown that there is a clear relationship to PA pressure. Therefore, if crude PA peak velocity is used, non-parametric methods are mandatory in analysis.

Future prospects

Flow integrals are potentially more interesting, with measurements of stroke volume and cardiac output, but require more sophisticated software.

Measurements of peak velocity in this study showed a wide variation amongst normal subjects (even when beam alignment had been carefully checked), and were unrelated to age or rate to any important degree.

Used alone, PA Vmax is therefore of limited usefulness across a population: as a serial measurement it may find a niche; intra-personal variation was particularly small. "Normal range" for an individual may be more important than for a population.

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PART THREE

RESULTS AND DISCUSSION OF RESULTS ON PACED PATIENTS

Results and discussion of results on paced patients

Introductory notes

Advantages of paced patients as models for studying RVSTIs

One model for examining the effect of differing PR intervals on right ventricular systolic time intervals would be complete heart block. Assuming continuing atrial activity and a very constant heart rate maintained by an artificial electrical pacing system, the constantly varying "P-R" interval would provide a means of examining the effect of atrioventricular timings on RVSTIs.

The "PR" interval here would be measured from the onset of the P wave to the pacing stimulus artefact: this would constantly vary if there was complete atrioventricular dissociation.

In addition, a further advantage of such a model would be that the R-R interval would be entrained by the pacing system within extremely slender limits (much more than would be the case in health).

As some RVSTIs are rate-dependent, this would be particularly important.

Effects of abnormal ventricular activation

It must, of course, be recognised that activation of the right ventricle by an artificial electrical pacemaker is a markedly unphysiological event. Even when the "PR" interval is similar to sinus rhythm, as during dual-chamber (DDD) pacing, right ventricular ejection fraction[151] and RV dP/dtmax[156] remain abnormally low. Right ventricular pacing produces a pattern of activation similar to left bundle branch block[152] although this clearly depends on the exact position of the wire tip, and any myocardial disease. Varying amounts of the His-Purkinje system are involved[152]

Although the effects of pacing on the left ventricle are relatively well studied, the chronic effects of right ventricular pacing on RV function are largely unknown, and (as in the left heart) difficult to disentangle from the loss of atrial transport, and the possibility that conducting system fibrosis (the commonest cause of complete heart block in old age) might be part of a more generalised cardiomyopathy. Animal studies do, however, confirm that chronic ventricular pacing is associated with myofibrillar disarray[172].

Certainly, life expectancy in complete heart block is improved by asynchronous ventricular pacing [145,146,147], but there is less evidence that it is returned to that expected for an age- and sex-matched population[148,149,150].

Use of the model for exploring the effects of varying PR intervals on RVSTIs

It must be recognised, therefore, that even with appropriately timed atrial contractions, ventricular function as measured by RVSTIs might be abnormal. However, as the pacing stimulus and pattern of activation will be the same regardless of the "PR" interval the effect of atrial synchrony can still be meaningfully studied on a beat-to-beat basis by Doppler. Indeed, the ability to control the important parameters within fine limits represents the best opportunity in clinical medicine without resorting to the previously decribed invasive techniques [153,157,158,159].

No such data on RVSTIs exists in human subjects. Previous attempts to measure left ventricular output in paced patients have used integrals of mitral valve inflow[198] or aortic valve outflow [201,202]. Whilst these give evidence that PR timing is important for optimal cardiac output, and suggest that (at rest at least) a figure for the PR interval of around 150ms is best [191,192,198], no attempt is made to look at the effects on the two ventricles separately. However, artificial cardiac pacing is primarily a right ventricular event, and an attempt to look at right heart function in this situation seems eminently worthwhile.

Age differences

A further difference between the paced and control groups was age. [Fig 25].

Young people constitute only a small percentage of the total population who have permanent pacing devices in situ. We wanted to study the effects of RVSTIs throughout all age ranges, so the control group has a wide age spread.
However, most patients with pacing devices are over age 60, and our paced population is representative of them.

Unavoidably, therefore, the mean ages of the two populations are quite different. This should be borne in mind when comparing them. The mean age of paced patients was 69yrs ($\pm$12.73) as against 39.5yrs ($\pm$16.2) for the controls ($p<.001$). However, as we have already seen, correlations between most RVSTIs and age are weak or non-existent, and between-patient variability is actually greater in younger rather than older patients.

AGE COMPARISON OF CONTROLS AND PACED PATIENTS

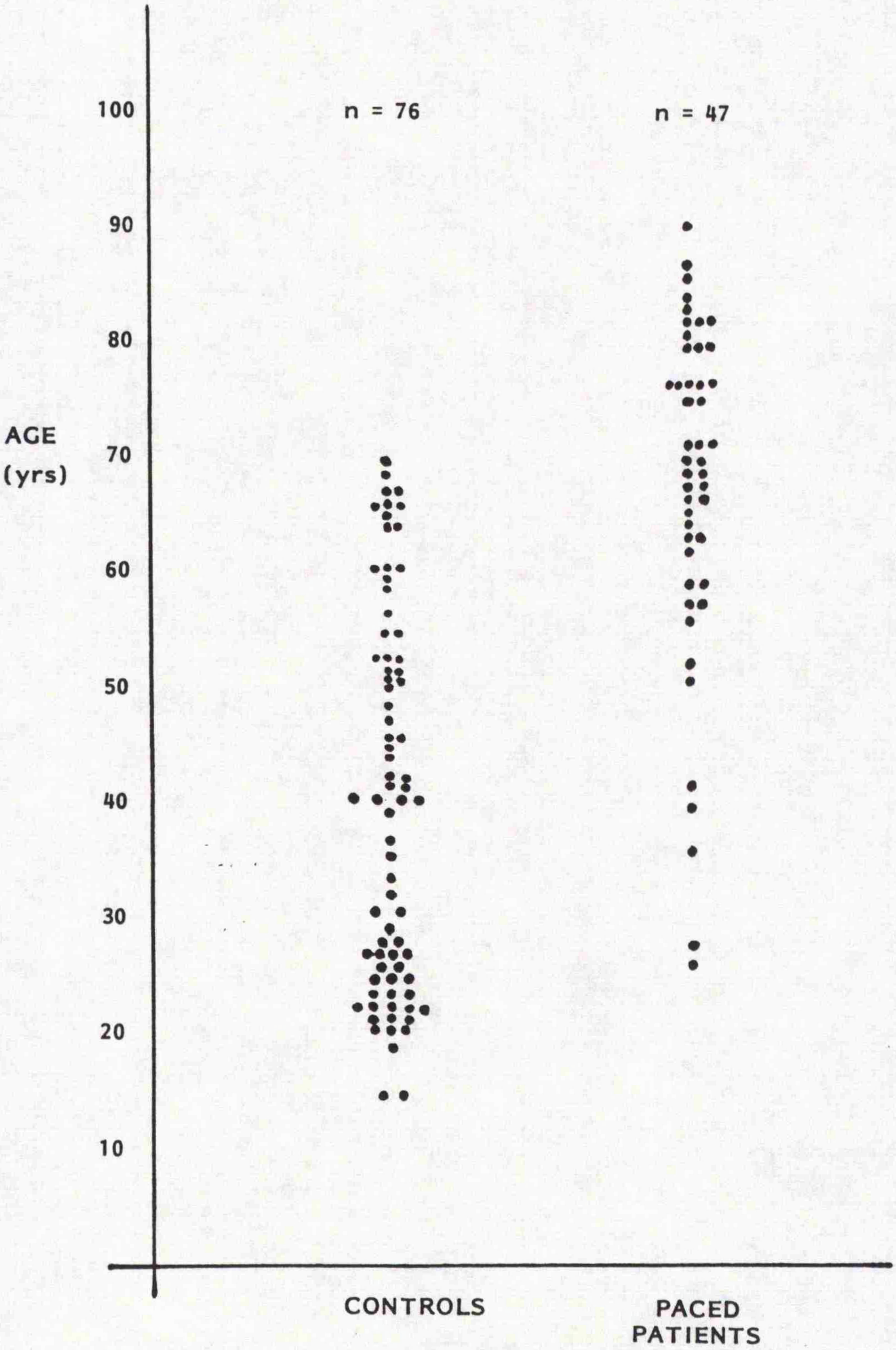


Fig. 25

Results

Differences between controls and paced patients

Descriptive statistics for RVSTIs for the sum of all recorded beats in paced patients are easy to calculate and suggest an overall reduction in measures of right ventricular systolic function as compared to controls, as expected.

	Controls		Paced patients		
n	77		30		
	Mean	Range	Mean	Median	Range
RVPEP (ms)	103 (± 13)	79-100	143 (± 29)	150	45-225
RVET (ms)	300 (± 29)	227-369	269 (± 43)	270	105-380
RVETI (ms)	322 (± 21)	374-278	293 (± 47)	296	113-408
PEP/ET	.35 (± .09)	.24-.53	.55 (± .16)	.53	.13-1.56
AT(ms)	135 (± 23)	91-136	91 (± 25)	90	30-185
AT/RVET	.45 (± .06)	.31-.59	.34 (± .09)	.34	.13-.70
PEP/AT	.79 (± .18)	.5-1.3	1.70 (± .64)	1.65	.33-5.16
PA Vmax (cm/sec)	63.1 (± 23)	40-145	47.8 (± 15)	45	20-120

Although the mean values for the two groups are clearly different, the striking feature of the values from paced patients is the extraordinary range of results, which far exceeds that of the control subjects, despite a smaller sample size. This suggests much more beat-to-beat variability in the paced population; this is apparent from the recording traces.

Variability about the subject mean in paced patients - peak and trough effects

However, the increased variability is not at all uniform around a mean. Where PR intervals occur in "normal" relationships (hence called positive PR intervals), as in sinus rhythm, RVSTIs in fact approximate to that of the control subjects. A "peak" phenomenon is discernible with "best" values for RVET, AT and the ratio AT/RVET and PAVmax occuring at mean PR values of 100-200ms. This is similar to previous data gathered invasively in animals[141] with regard to RV function.

A peculiar "nadir" phenomenon ("worst" values for the STIs)[Fig 26], not previously reported, and of much greater magnitude than the peak phenomenon, is also manifest upon study of the traces [Fig 27] and derived data. PR intervals that are "negative" (i.e. the P wave follows rather than precedes the pacing flick) are associated with lower values in general than when the PR interval is positive.
At negative values of -50ms to -150ms, gross reductions in RVET, AT and AT/RVET occur in many patients, and the effect is at least clearly discernible in most. In some patients the effect is dramatic, with falls of 50% or more. It should be stressed that none of the patients studied had any symptoms referable to this effect, and none had symptoms suggestive of the Pacemaker Syndrome; this is in fact even more suprising when pulmonary artery forward flow virtually ceased in some patients, albeit for a few beats only.

Fig. 26

FALL IN RVET WITH "RETROGRADE" P WAVES

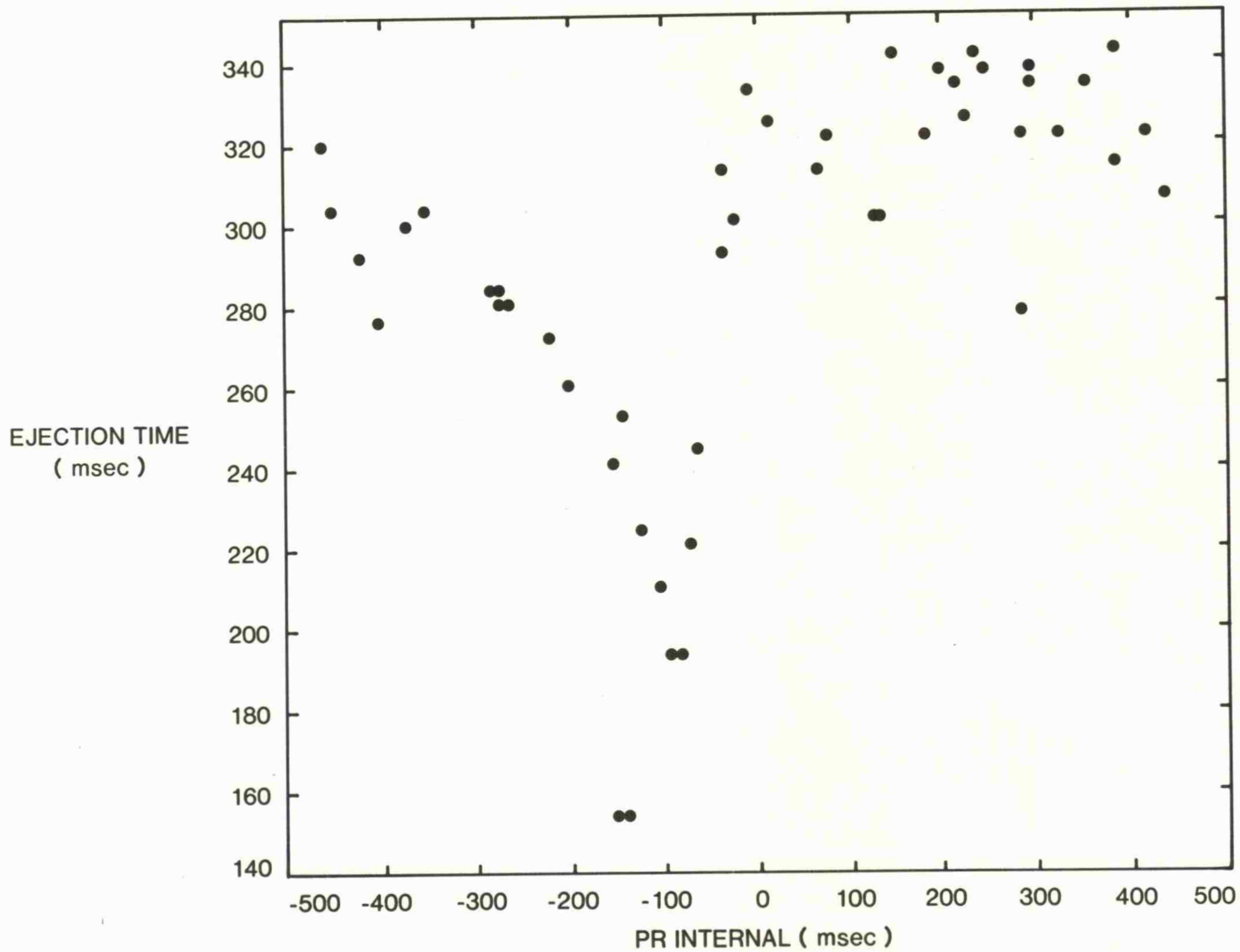
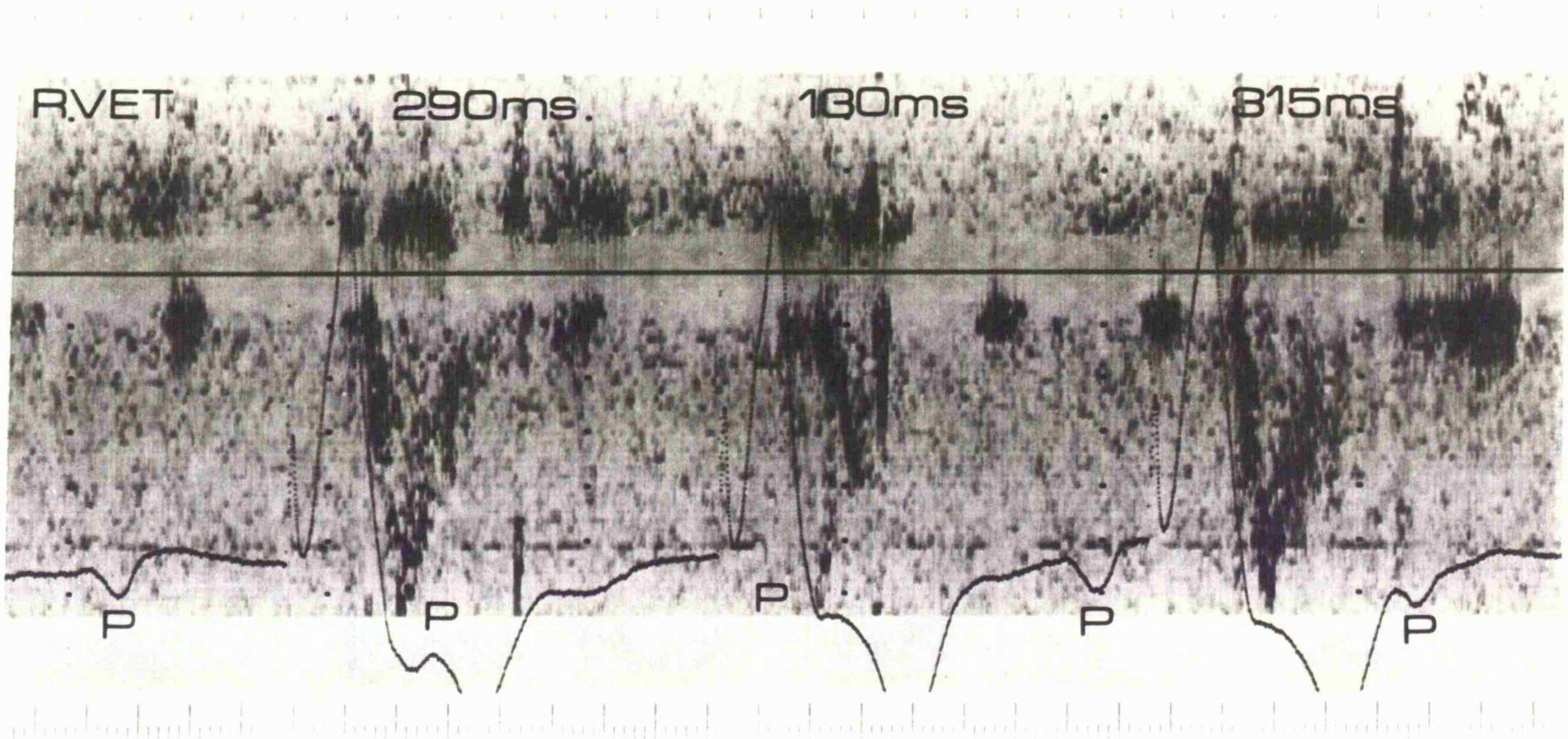


Fig. 27

SPECIMEN PA FLOW TRACE
DEMONSTRATING NADIR EFFECT



It was not possible to predict from the data nor from the previously known characteristics of the patients those in whom the magnitude of this effect would be significant.

Data analysis

(a) Construction of relative frequency curves

These nadir and peak effects are very striking in some patients and less so in others. To study the paced population as a whole requires a weighting system to reconcile the differing number of observations available on each and to construct a cumulative frequency of nadirs and peaks for the entire group.

Because I was observing spontaneous changes in PR interval I had to accept the figures for PR interval that occurred. This lead to differing numbers of observations and different sets of PR data in each subject.

For example, the first paced subject (of the 30 available) had 53 beats available for analysis, spread between PR values of -350ms and +410ms. A relative frequency of 1/(30 x 53) was put into each of his PR interval "bins".
The second subject had 45 available complexes and 4 of them occur at a PR interval of -200ms: a relative frequency of 4/(30 x 45) is therefore assigned to his PR value of -200ms (he has 3 data

points at -195ms therefore this PR interval is given a weight of 3/30 x 45, etc.). In this way, a relative frequency distribution can be built up for the entire population of subjects, with each subject having a total "weight" of 1/30 (in deference to the principle of the subject as the unit of data).

The same is then done for nadirs and peaks. For example, subject No.1 has 2 complexes attaining the lowest value of, say, RVPEP. The corresponding PR interval value receives a contribution of 1/30 x 2. Subject No. 2 has a single nadir for RVPEP, so this PR interval in this patient recieves a weight of 1/30.

The same is done for each patient and also for the nadir and peak values for RVPEP, RVET, AT, AT/RVET, RVPEP/AT and PAVmax. This method of construction of a frequency distribution gives equal weight to all subjects irrespective of the degree of replication of nadirs or peaks.

(b) Display of results

If the data is now displayed as a cumulative frequency distribution, 3 curves can be superimposed. The curve corresponding to "all observations" climbs steadily, as each data point on the curve corresponds to a PR interval actually observed.

The columns of nadirs and peaks, however, climb from the baseline in steps of 1/30s or fractions of 1/30. The steepest parts of these curves for nadirs and peaks correspond to the most rapid accumulation of numbers of nadirs and peaks, and can be compared to the speed of accumulation of "all data", as estimated from the middle curve.

The vertical difference between these curves, or degree of difference between them can be compared with the Kolmogrov-Smirnoff statistic (used for comparing relative cumulative frequencies). If there is a significant difference in the curves (such as a maximum rate of accumulation of nadirs at a different PR interval than the rest of the PR population), one can deduce that trough values for, say, RVPEP are significantly more likely to occur at this PR value. The lines cross over, and the reverse reasoning can be used to see if there is a significant difference in the rate of accumulation of peaks at one PR interval relative to the others.

(c) Results of curve comparisons

Kolmogorov-Smirnoff (KS) differences in relative cumulative frequency between nadirs/peaks and "all complexes" studied:

Measurement	No. informative subjects	Nadirs		Peaks	
		Max diff	PR	Max diff	PR
RVPEP or RVPEPc	30	.209	-85	.129	+55
RVET or RVETc	30	.483**	-20	.515**	0
RVPEP/RVET	30	.446**	+25	.483**	-20
AT(TTP)	28	.289*	+20	.251#	-15
AT/RVET	28	.236	-45	.251#	+85
RVPEP/AT	28	.210	-80	.253#	+30
PA VMax	26	.266	+55	.384**	+80

** $p < .01$ (Highest sig level tabulated for KS statistic)
* $p < .05$
# $p = .05$ approx

Results for individual RVSTIs

(a) **RVPEP** [Fig 28]

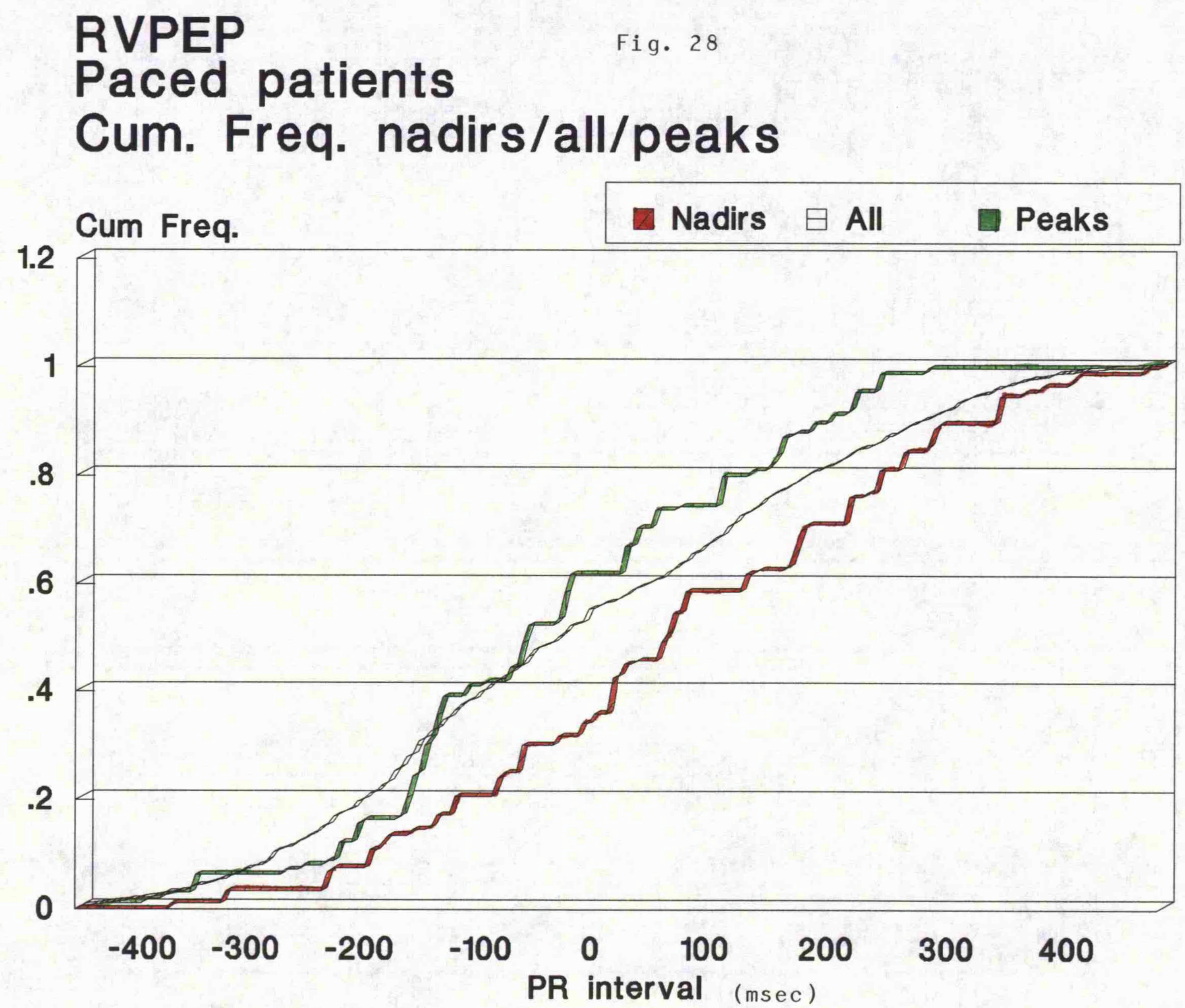
For RVPEP (or "RVPEPc"), although lowest figures were obtained at a PF value of -85ms and a peak at +55ms, the differences between the nadir and peak lines and the "all data" line are only .209 and .129 (differences in cumulative frequency) and $p > .05$ for all RVPEP observations. RVPEP did not, therefore, vary significantly with the PF interval. This is perhaps "not suprising" in view of the dubious significance of this RVSTI when ventricular electrical activation is so abnormal as in artificial pacing.

(b) **RVET** [Fig 29]

Analysis of similar cumulative frequency curves for RVET, however, demonstrates highly significant differences. All 30 nadirs (including joint ones) are confined to the interval -210ms to -20ms for PF. So, on a population basis, there was a significantly greater chance of a subject's lowest RVET occuring in this range of PF.

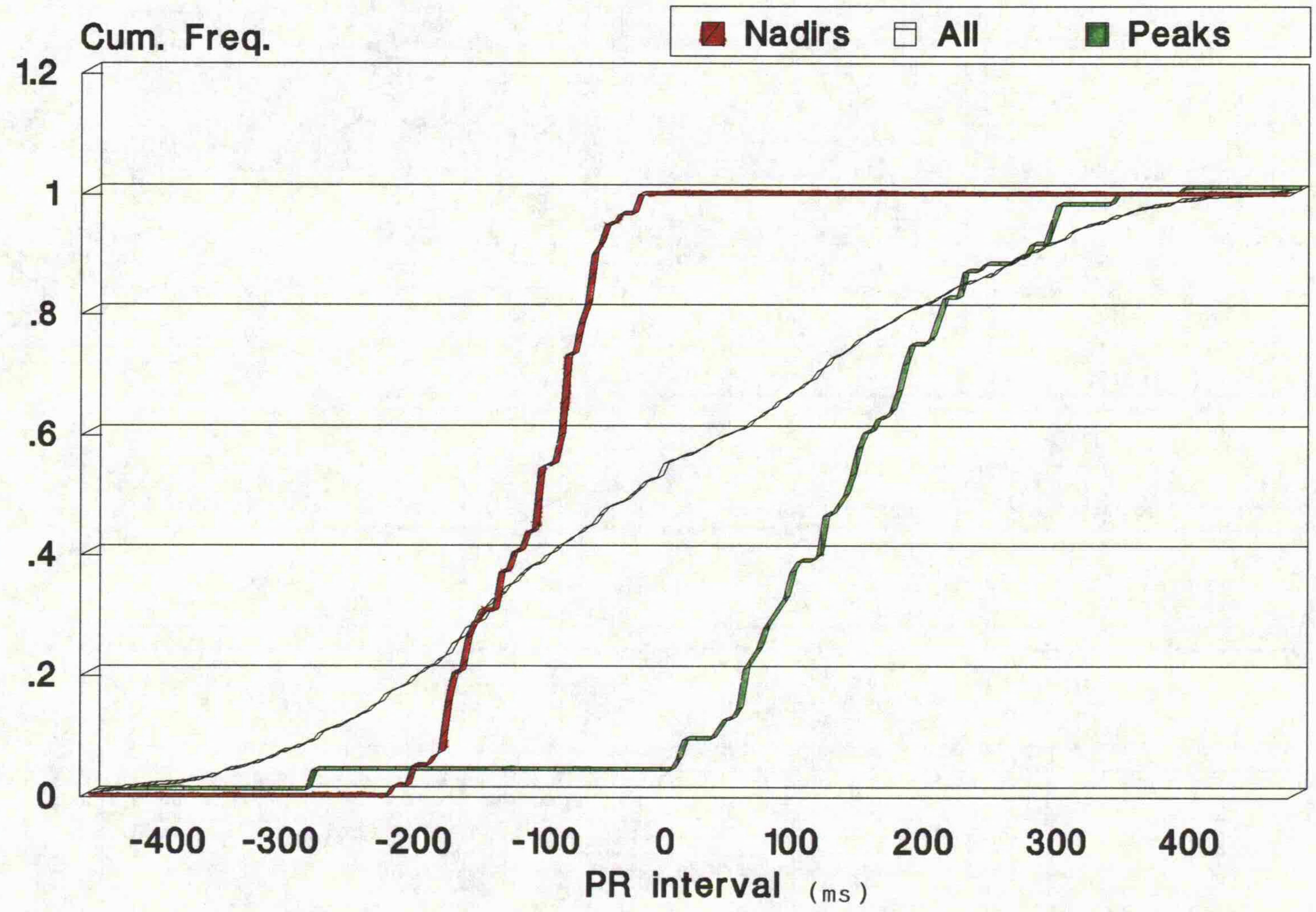
Similarly, almost all peak RVETs occur in the PF intervals 0 - +210ms, with a peak around 100-150ms. This is also apparent from perusal of most patients' scatter-plots of RVET vs PF interval.

Fig. 28


RVPEP
Paced patients
Cum. Freq. nadirs/all/peaks
Nadirs
All
Peaks
Cum Freq.
1.2
1
.8
.6
.4
.2
0
-400
-300
-200
-100
0
100
200
300
400
PR interval (msec)

RVET
Paced patients
Cum. Freq. nadirs/all/peaks

Fig. 29



Maximum differences between the nadir and "all data" lines was .483 ($p < .01$) and between the peak and "all" lines even greater at .515 of cumulative frequency ($p < .01$).

Thus, the PR interval markedly influences RVET (or RVETc): "physiological" PR intervals are associated with longest RV ejection times but "retrograde" P waves are associated with gross shortening of this measurement, reflecting marked reductions in flow.

(c) RVPEP/RVET

Analysis of the ratio RVPEP/RVET confirms a pattern approximately the inverse of RVET: this would be expected if RVET is influenced by PR interval and RVPEP is not. Peak differences of .446 for nadirs ($p < .01$) and .483 for peaks ($p < .01$) are similar in magnitude to values for RVET, and this ratio therefore appears to mean little more than the reciprocal of RVET in this situation.

(d) AT(TTP) [Fig 30]

Acceleration time (or time-to-peak flow) shows a basically similar, but less pronounced pattern. Peak differences between the nadir and peak and "all" cumulative frequency curves are .289 ($p < .05$) and .251 ($p = .05$) respectively. This shows that inverse atrioventricular sequencing significantly affects acceleration time: it is not clear whether there is an effect within "physiological" ranges for PR.

Disappointingly, neither the ratio AT/RVET nor RVPEP/AT were an improvement on crude AT: differences were non-significant at p values of around .05.

(e) PAVmax [Fig 31]

There is, however, no doubt about the difference between the peak line and the "all data" line with PA maximum velocity. The peak difference was .384 at around +80ms ($p < .01$). It would have been nice to calculate PA flow integrals on a beat-by-beat basis had the software been available at the time.

Fig. 30

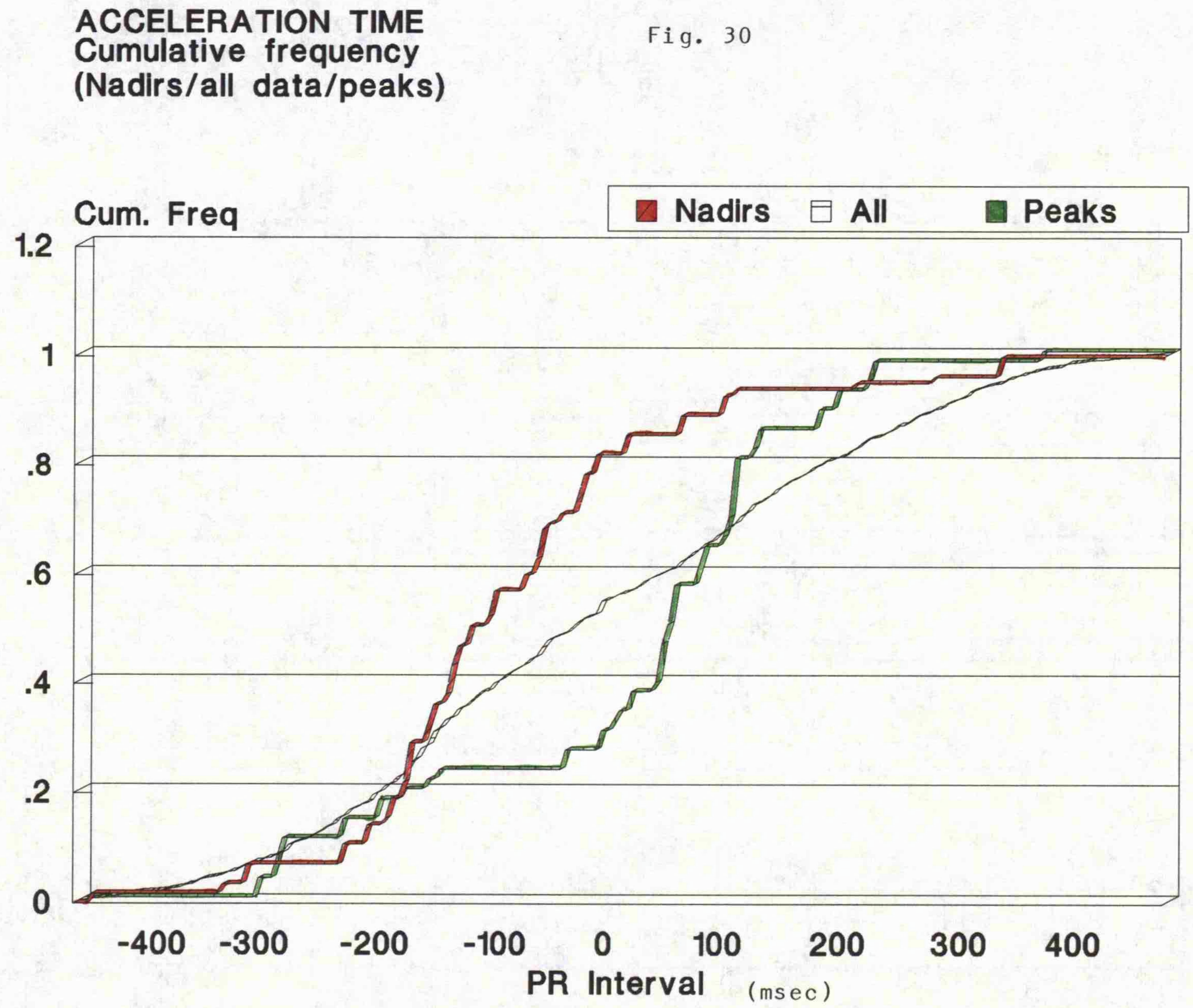
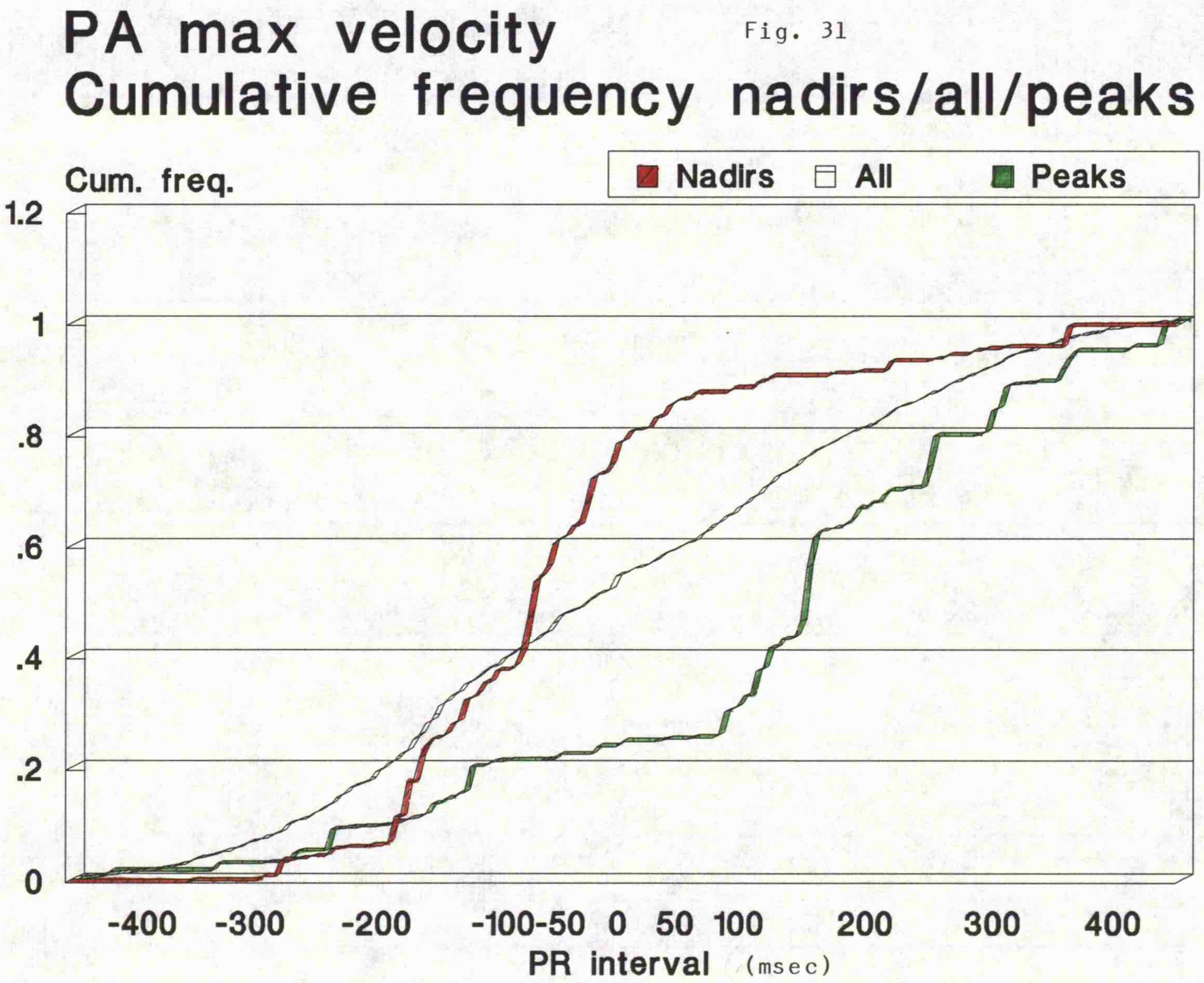

ACCELERATION TIME
Cumulative frequency
(Nadirs/all data/peaks)
Cum. Freq
Nadirs
All
Peaks
1.2
1
.8
.6
.4
.2
0
-400
-300
-200
-100
0
100
200
300
400
PR Interval
(msec)

Fig. 31


PA max velocity
Cumulative frequency nadirs/all/peaks
Cum. freq.
Nadirs
All
Peaks
1.2
1
.8
.6
.4
.2
0
-400
-300
-200
-100
-50
0
50
100
200
300
400
PR interval (msec)

By contrast, although nadirs do tend to congregate around a PR value of -100ms, significance on the KF statistic is borderline ($p = .05$ approx). Although in individual patients, therefore, the very low peak velocities associated with inverse atrioventricular sequencing are manifest, this could not be demonstrated over the entire population.

Discussion of results: - potential clinical applications (particularly to pacing technology and practice)

The continuing debate about the merits of atrial synchonisation

Although single-chamber ventricular pacing without any attempt at atrio-ventricular synchronisation prolongs life in complete heart block, survival is better in heart failure when dual-chamber pacing is used [149,150]. Dual-chamber pacing is associated with smaller end-diastolic and end-systolic chamber dimensions and a higher cardiac output.
Maximal work ability is higher and arteriovenous oxygen differences are smaller [160,161], despite no change in coronary blood flow or myocardial oxygen uptake, suggesting increased efficiency [159]. Not only is cardiac output around 30% higher whether in heart failure or not [191] but patients much prefer dual-chamber pacing [160,165].

There is some evidence that patients paced for sick sinus syndrome are more likely to end up in atrial fibrillation if VVI rather than atrial or dual-chamber pacing is used [225]. Although patients with normal-size left atria are most sensitive to loss of atrial transport [204], long-term VVI pacing is associated with larger left atria eventually [199].

**Previous studies of the deleterious effects of reverse atrioventricular sequencing
- relationship to the "Pacemaker Syndrome"**

Ogawa [182], in a classic experiment with seven open-chest dogs, demonstrated that during atrioventricular dissociation, pacing the atria after the ventricles (a "negative" PR interval) caused a fall in forward flow and ventricular filling pressures, and a sharp rise in systemic and pulmonary venous pressures. This is the basic haemodynamic situation in the "Pacemaker Syndrome", which only occurs with single-chamber ventricular pacing and continuing atrial activity.

There is less agreement about why atrial pressures (which are the probable cause of the increased incidence of atrial fibrillation and poorer output) are raised. Negative flow waves can be detected in both systemic veins (cannon waves)[185] and pulmonary veins[226], and conventional wisdom has it that these are due to atrial contraction against a closed atrioventricular valve. Clinically, the waves look like tricuspid regurgitation in the neck; pressure waves in the right atria look like those of marked tricuspid regurgitation

[180,185,226]. Blood regurgitates into the pulmonary veins also [227] but this could happen by either mechanism.

Contrast echocardiography shows "packets" of contrast echos in the inferior vena cava during negative PR intervals, but this could also be due to atrial contraction against a closed valve [186]. Pierard [187] demonstrated echocardiographic contrast refluxing into both great veins in all his patients but in only about 1/3 did he see contrast clearly moving backwards across the tricuspid valve.

It is known that mitral regurgitation can be increased by long or very short PR intervals [202], and there is even a case report of the production of mitral valve prolapse by VVI pacing [228]. But although mitral regurgitation was noted in some studies [226], others could not show the production of mitral regurgitation in any pacing mode [203].

Thus, the mechanism for high, pulsatile pressures in the atria remains in dispute.

There is no real disagreement, however, about the effect of mis-timed atrial contractions on ventricular filling. The onset of atrioventricular valve closure bears a constant temporal relationship to the P wave [198]. Although the atrial contribution to cardiac output is probably less in cardiac failure [229], and a long PR interval might be best in those circumstances [163], most studies report that left ventricular output and filling pressures are optimal in patients with normal ventricular function at around a PR interval of 100-150 ms [164,194,202,226]. On exercise in a normal adult in sinus rhythm, physiological shortening of the PR interval occurs [230], and cardiac output is higher (as assessed by continuous wave Doppler) with a shorter PR interval of 75ms on exercise rather than 150ms at rest [231].

Similar data does not exist for the right heart.

My data suggests that peak right heart output, as judged by length of ejection time and acceleration time, and by ejection velocity, also occurs at around a PR interval of 100-150ms at rest in individuals with normal ventricular function.

However, the extent of the fall in forward flow during negative PR intervals was very suprising; none of my patients had been shown to have intact retrograde ventriculo-atrial conduction, (which is only thought to occur in about 1 in 7 patients with complete anterograde heart block[232]).

This phenomenon, which appears to be of much greater magnitude than anything reported in the left heart, may be a reflection of the greater sensitivity of the right heart to loading conditions. As most patients receiving pacemakers are elderly, the fact that maximal late diastolic (i.e. atrial) flow rises with age [233] both absolutely and as a proportion of all diastolic filling (suggesting decreased ventricular compliance), may further magnify this effect.

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Invasive study on patients undergoing insertion of permanent pacing systems

The original protocol submitted to the ethical committee for this study involved invasive studies on patients (six were planned) undergoing permanent pacing implant. Because of recurrent equipment failure, only two patients could be studied. Fortuitously, one of each group was studied.

Repeated equipment malfunction, in particular the catheter-tip transducer, on which I relied for accurate timing of pressure waves, prevented the study reaching a conclusion. There were no funds available to buy any more.

I therefore include the data from this investigation for illustrative purposes only.

Method:

After the initial subclavian puncture, temporary wires were inserted via the left subclavian vein and advanced to the right atrium and right ventricular apex. A conventional fluid-filled catheter was placed in the right ventricle for pressure measurement and a catheter-tip transducer was also placed there for accurate systolic timing. A third line was placed either in the right atrium or right ventricle, for RA pressure or RVEDP measurement. Pacing was initiated with a R-Ri interval of 700ms, and the PR interval was varied from 200ms through 150ms, 100ms, 50ms, simultaneous activation, and retrograde sequencing of 50, 75, 100, 150 and 200 ms.

In between recordings at each setting, dual-chamber pacing with a PR interval of 150ms was performed for 3 minutes, to allow a return to "steady-state".

A minimum of twelve measurements was taken and mean and 95% CIs calculate for each PR interval.

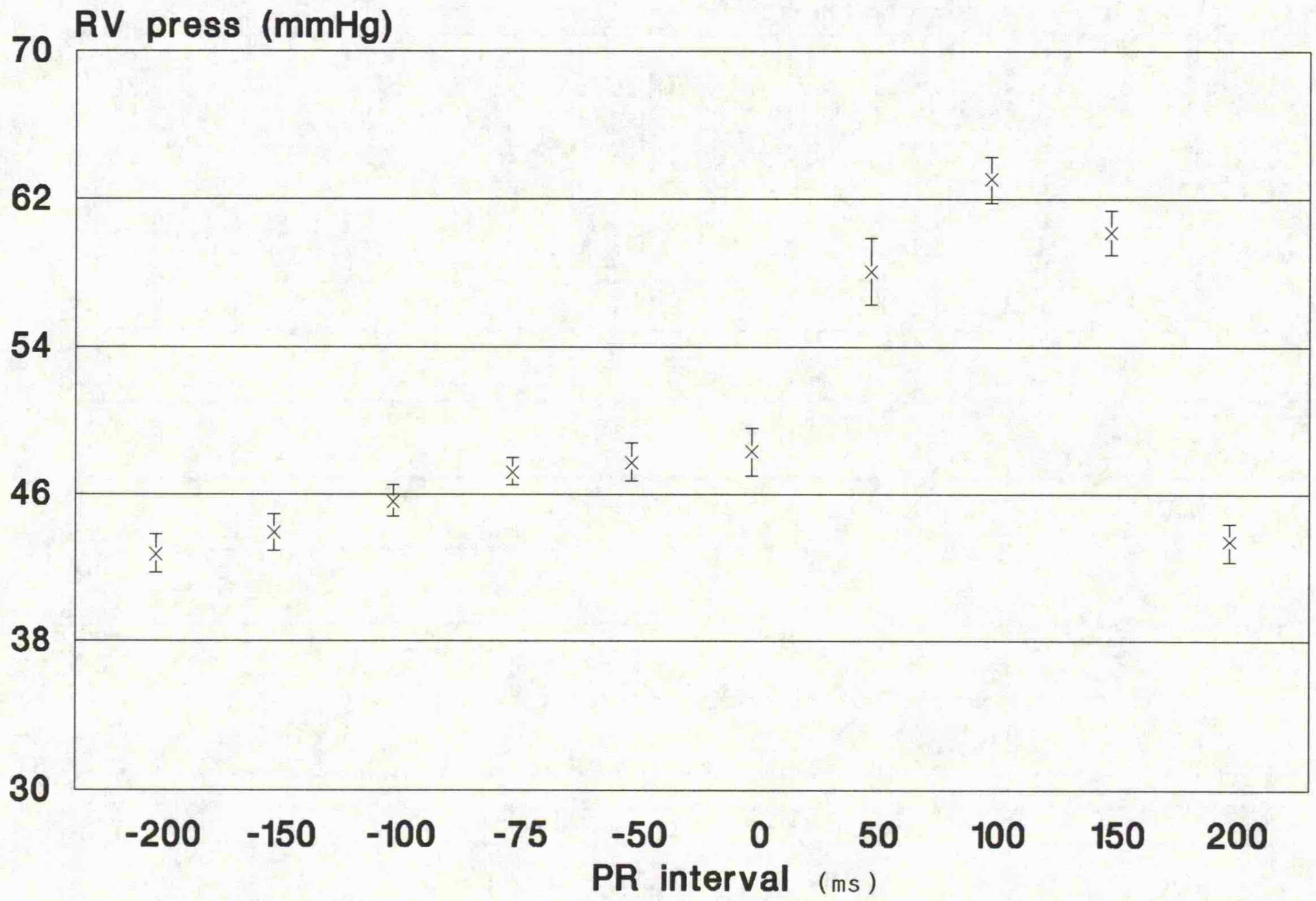
Results:

Patient (1):

PR interval (ms)	RV sys. pressure (mmHg)		RV syst. time (ms)		RVEDP (mmHg)	
	Mean	95% CIs	Mean	95% CIs	Mean	95% CIs
- 200	42.7	41.7-43.8	373	365-382	8.7	8.3- 9.1
- 150	43.9	42.9-44.9	369	361-377	8.3	7.8- 8.8
- 100	45.6	44.8-46.5	377	369-385	8.4	8.0- 8.8
- 75	47.2	46.5-48.0	370	365-374	8.8	8.3- 9.3
- 50	47.7	46.7-48.8	370	363-376	9.2	8.8- 9.6
0	48.3	47.0-49.6	368	0-375	9.6	9.2-10.0
50	58.1	56.3-59.9	391	382-401	10.4	10.4-10.9
100	63.1	61.8-64.3	426	418-433	12.7	12.2-13.1
150	60.2	59.0-61.4	401	394-408	12.8	12.3-13.4
200	43.4	42.3-44.4	383	378-386	10.6	10.0-11.1

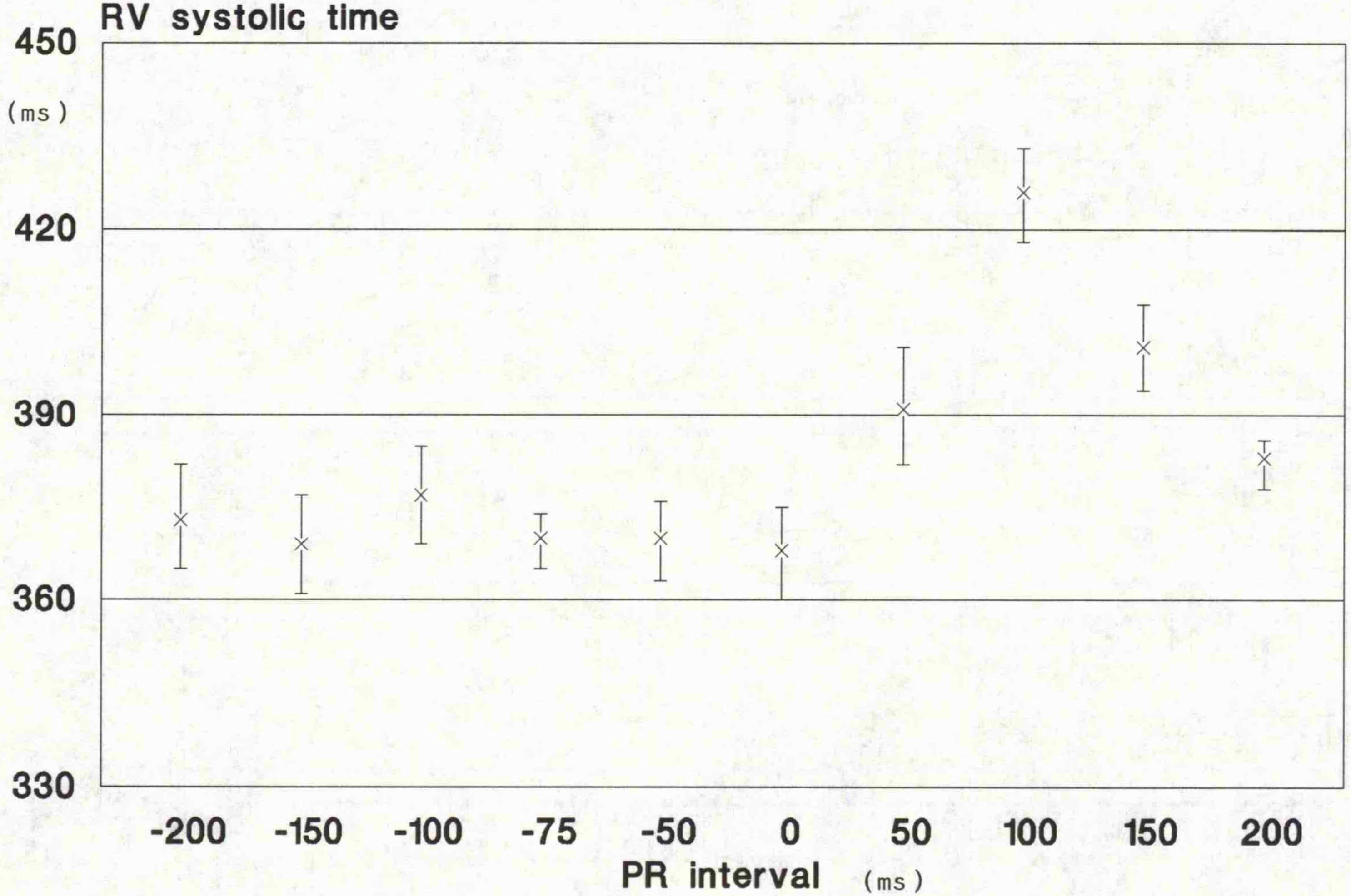
RV systolic pressure (mmHg)
Varying PR intervals
(95% confidence intervals)

Fig. 32

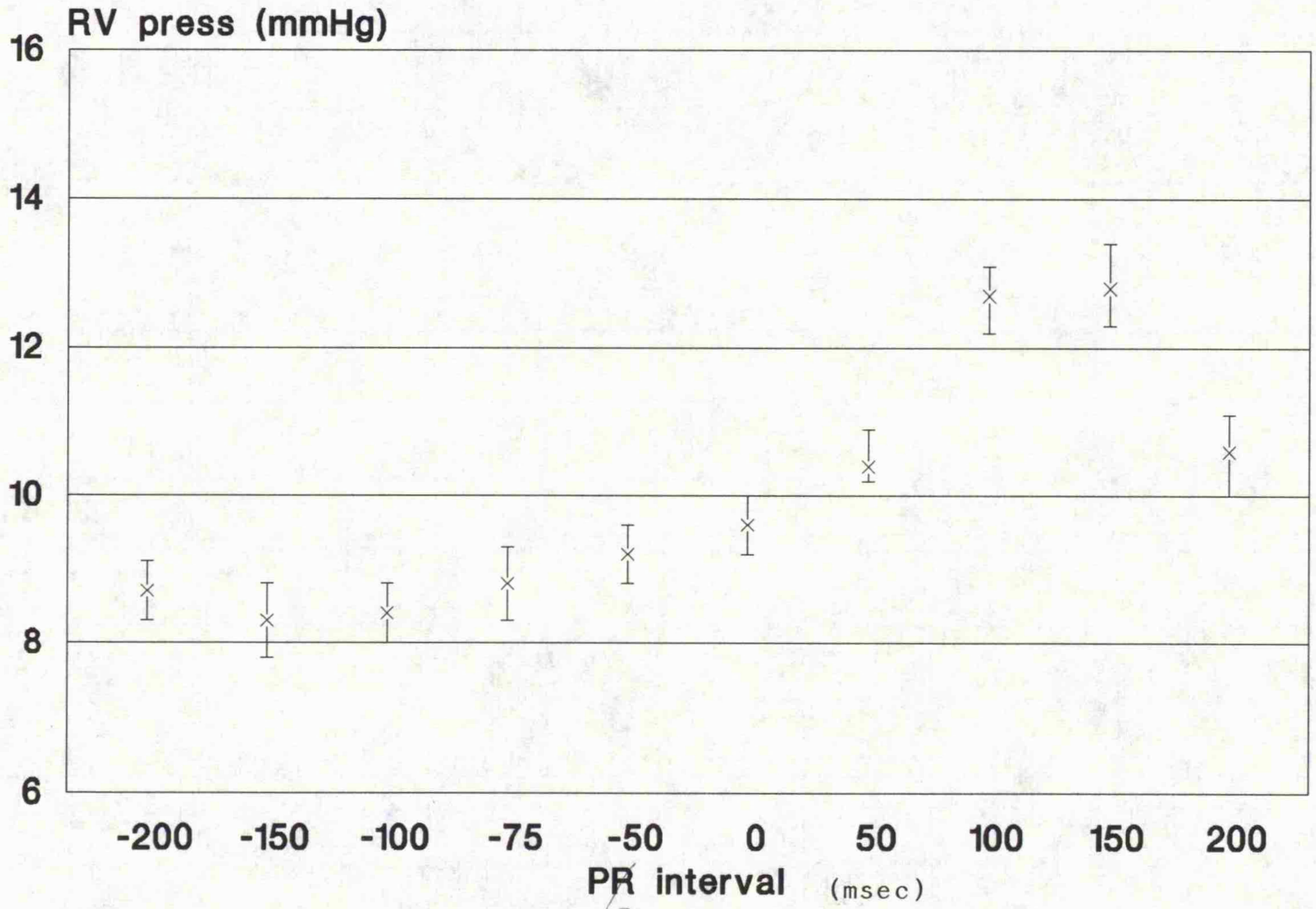


RV systolic time (ms)
Varying PR intervals
(95% confidence intervals)

Fig. 33



RV end-diastolic pressure (mmHg) Fig. 34
Varying PR intervals
(95% confidence intervals)



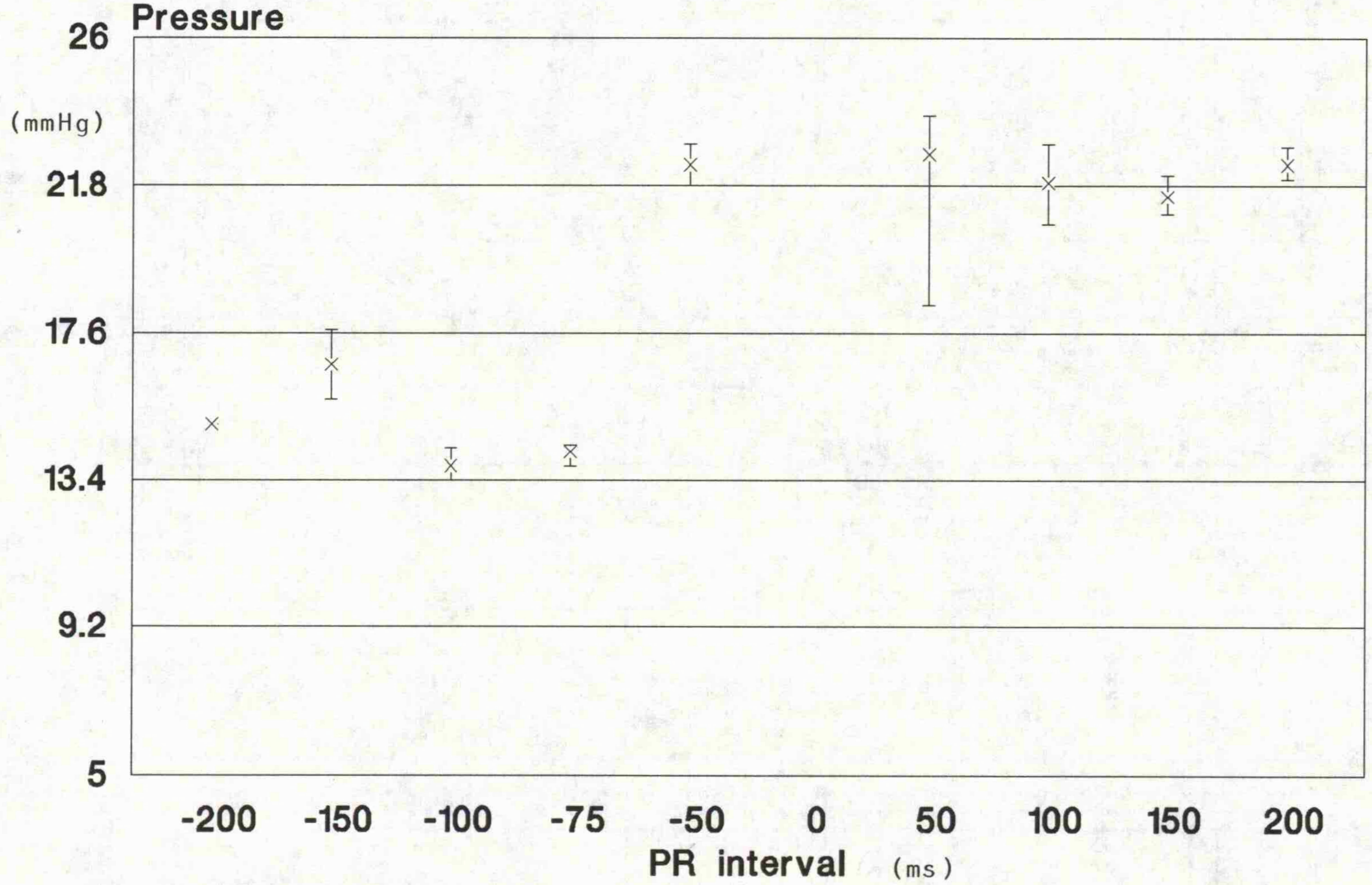
Patient (2)

PR interval (ms)	RV syst press (mmHg)		RV syst time (ms)		RA pressure (mmHg) A wave		V wave	
	Mean	95%CIs	Mean	95%CIs	Mean	95%CIs	Mean	95%CIs
-200	15.0	15.0-15.0	421	405-437			14.4	14.2-14.7
-150	16.7	15.7-17.7	402	395-409			14.5	14.3-14.8
-100	13.8	13.4-14.3	431	417-445			13.8	13.5-14.0
- 75	14.2	13.8-14.4	409	404-413			16.6	16.1-17.1
- 50	22.4	21.8-23.0	489	481-496			18.3	17.8-18.8
0								
50	22.7	18.4-23.8	409	402-415	9.9	9.1-10.6	7.3	6.8- 7.8
100	21.9	20.7-23.0	408	402-415	7.8	7.6- 8.0	6.3	6.0- 6.5
150	21.5	21.0-22.1	444	437-450	7.6	7.3- 7.9	6.2	6.0- 6.5
200	22.4	22.0-22.9	444	439-450	6.9	6.5- 7.2	6.3	6.1- 6.5

No data is recorded for the "a" wave in RA pressure at negative PR intervals, because the large "v" wave completely obscured it.

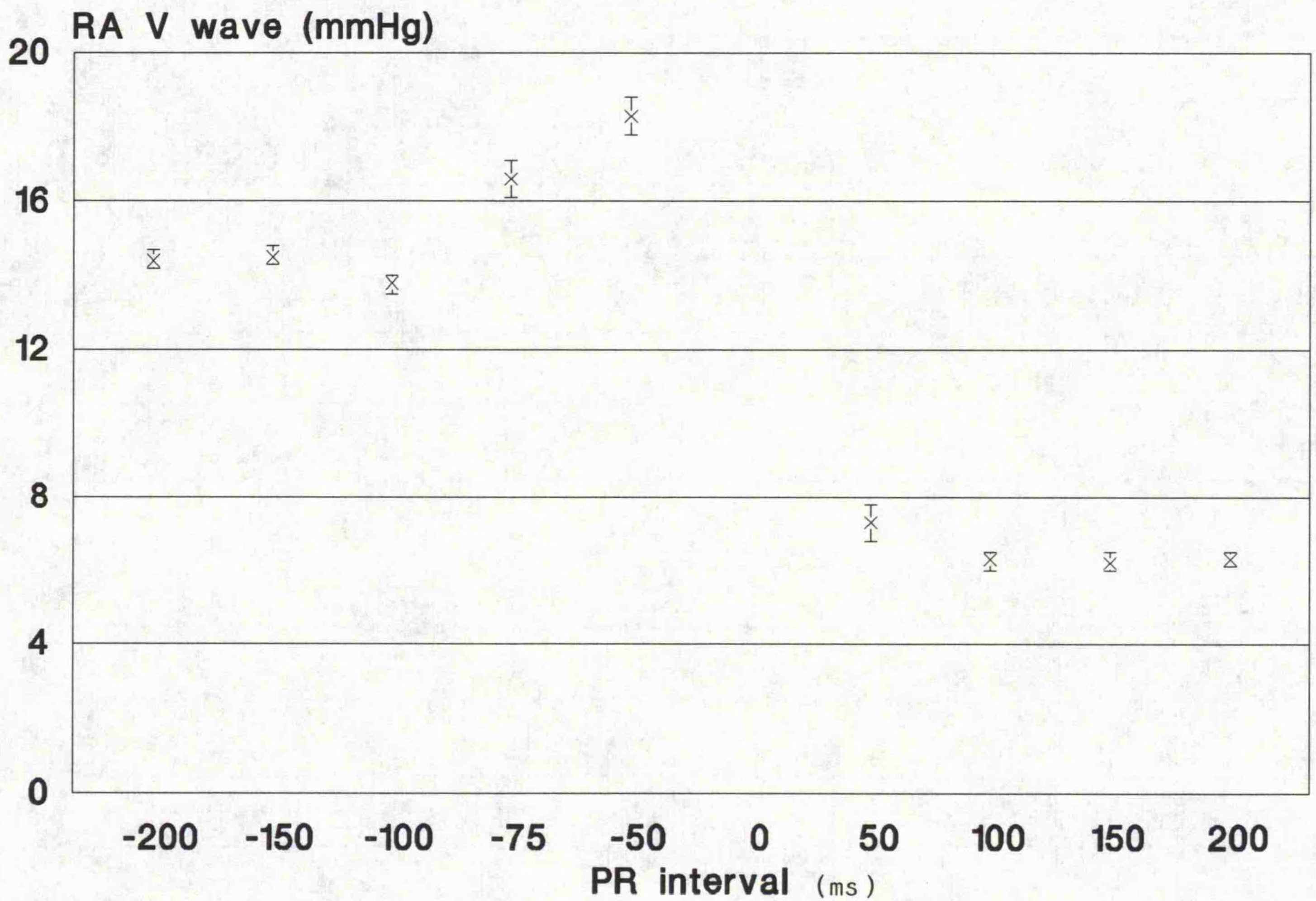
RV systolic pressure
Varying PR intervals

Fig. 35



RA pressure - V wave
Varying PR intervals

Fig. 36



Discussion

It will be immediately noted that RV systolic pressure [Fig 32, Fig 35] and time [Fig 33] were significantly less at all negative PR intervals than at positive or "normal" ones, the decrease in RV systolic pressure in both cases being about one third of the highest systolic pressure recorded. The effect of atrial systole on LV output has been previously found to be about 25-30% in most subjects with normal hearts [163], and are here documented to be the same in the right ventricle.

The RVEDP [Fig 34] and atrial pressure data [Fig 36] are very interesting. The RVEDP rises with appropriate PR intervals from a nadir of 8.3mmHg to a peak of 12.8mmHg at a PR interval of 150ms, and RV systolic pressure and systolic time rise in parallel. It looks as though RV preload is an important determinant of RV output in this patient, and that the PR interval is markedly affecting RVEDP: there is a small change with variation in "positive" PR intervals, with a peak at 150ms, but "negative" or retrograde PR intervals are all associated with much lower RVEDPs and RV systolic pressures.

Patient two offers an explanation for this. The right atrial pressure wave is normal with equal "a" and "v" waves with appropriately timed PR intervals, but when atrioventricular sequencing becomes negative the "a" wave is completely obscured by a very large "v" wave reminiscent of tricuspid regurgitation. Not only does the RV systolic pressure fall at this point, but the RA pressure becomes similar to the RV systolic, suggesting equalisation of pressures between the chambers. A plausible explanation would be gross tricuspid regurgitation.
This phenomenon can also be observed during complete heart block (see later).

CONCLUSIONS

Conclusions

The physiologies of the right and left ventricles have recently been demonstrated to be very different. Invasive measurements of RV volume and pressure reveal very disimilar so-called "pressure-volume loops" in the two chambers, reflecting the differing sensitivities of the two ventricles to loading conditions. The pressure against which the ventricle contracts to eject its contents (afterload) is the major determinant of the shape of the pressure-volume loop (PVL). The normally triangular PVL in the RV [234] is retained whatever the filling pressure (preload), and volume-loading itself does not greatly distort the shape [235]; but increasing afterload progressively changes the shape of the PVL to a left-ventricular-like "square" shape [235]. Relief of this increased afterload causes a resumption of the triangular pattern. Conversely, vigorous after-load reduction in the left ventricle, by vasodilator treatment [236] or in severe mitral regurgitation [237] causes the PVL to assume a triangular or "RV" type of curve.

(1) RVSTIs are limited but still useful: comprehensive normal ranges are presented

The timing of ejection from the ventricle is influenced by the shape of the PVL. In the LV, there is a more clearly-defined isovolumetric contraction phase, and ejection commences during rising pressure with subsequent loss of pressure and volume; however, in the right ventricle, ejection may occur during falling RV pressure, and an isometric contraction period is less well defined[234] . Afterload variation would therefore be expected to have a major effect on systolic time intervals, and it was on this premise that they were introduced for the study of pulmonary artery pressure and resistance (both measures of RV afterload). However, success has been very patchy: general associations have been confirmed between these variables and most of the RV systolic time intervals but predictive accuracies have varied from the apparently clinically usable [113-117] to studies coming to the opposite conclusion [108,109,111].

A very abnormal set of RVSTIs should arouse suspicion of seriously elevated pulmonary artery pressures, and, being noninvasive, the technique retains some usefulness. Serial studies are easy and informative, and should probably be undertaken more often.

This study describes a carefully-constructed set of "normal" values for a wide age range.

The ranges appear to be considerably wider than previously accepted for normal subjects from previous investigators' reports: in addition, many of the frequency distribution are markedly skewed: in some this can be partly compensated-for by transformations.

Means, medians and measures of dispersion are presented for all the commonly used variables.

The effects of heart rate, age and other variables are explored, and the limitations of the various "corrections" examined.

Measurements of dispersion about individual subject means show that intra-personal variation is very small, and (at least at the same "sitting") sufficiently so to allow the examination of interventions such as variation of PR intervals: inter-subject variation was much wider, and population studies are therefore more difficult.

(2) **Complete heart block is a useful model for comparing the effects of differing PR intervals, and RVSTIs can be applied to the measurement of RV systolic function in that situation**

The evidence that filling pressure affects RV systolic function is extensive, and application of RVSTIs as a study method here has not been previously undertaken. I chose complete heart block as a model because the continuously varying PR intervals cause continuously varying RV filing conditions on a beat-to-beat basis; if a permanent pacemaker is in place the ventricular response is held unphysiologically steady and allows a fairly "pure" assessment of the effects of changing the RV loading conditions.

I show that such an approach is practical, and yields positive results: variation of RVSTIs is much greater than would be expected from random intra-personal variation, and follows a distinct pattern.

Although manipulation of the PR interval by programming in a dual-chamber system is easy enough, there is no way that the effect of reversal of atrioventricular sequencing can be simulated; simply observing spontaneously varying atrio-ventricular sequencing (although generating much more "untidy" data) offers this prospect. In addition, it is of importance to clinical practice.

Right ventricular loading conditions have clinical importance. During myocardial infarction with significant right ventricular involvement, optimal RV filling pressure is around 10-14 mmHg[238] and relatively minor departures from this may produce large reductions in overall cardiac output; volume-loading in hypotension and cardiogenic shock caused by RV infarction is well-established treatment [239,240]. There is, however, some evidence that in some patients at least, too high a pressure may also be deleterious to cardiac output during RV infarction [234,240]. One possible explanation for reliance on a higher filling pressure would be decreased compliance of the infarcted area.

Age is also a determinant of compliance. The isovolmetric period and maximal late diastolic (atrial) flow both rise with age, suggesting increased stiffness of the heart [241]. Although most of the work on this subject has been done in the LV, it seems reasonable to assume that a similar process occurs in RV muscle. This would suggest that RV loading conditions are even more important in older folk for the maintenance of cardiac output. The rapidity with which elderly patients become shocked during volume depletion supports this view, although clearly other factors such as diminished vasomotor reserve, coronary and renal blood flow and concomitant disease are also important.

(3) RV loading conditions are important in pacing practice, and RVSTIs can be used to study them.

Complete heart block with ventricular demand pacing provides a situation for study of continuously varying right atrial pressures. Ill-timed atrial contractions (during or falling just after ventricular systole) cause large pressure waves in the right atrium, reminiscent of tricuspid regurgitation(TR)[185]. There has, in fact, been some considerable discussion as to whether these waves really represent atrial contraction against a closed tricuspid valve[186,189]. The point is not merely academic: asynchronous ventricular pacing, with no attempt to keep atrio-ventricular sequencing constant, is associated with atrial enlargement[183]; and this is less so in those with dual-chamber pacemakers[242]. As would be expected, patients with normal-sized atria are more sensitive to the loss of atrial synchrony[204]. The atria would be activated after the ventricles (at just the "wrong" time) if electrical impulses originating in the ventricles (be they artificial or naturally-occurring ventricular ectopic beats) were carried retrogradely up the heart's conducting system to the atria, activating that chamber. Intact retrograde ventriculo-atrial conduction can be demonstrated in around two-thirds of those undergoing pacemaker implant for sick sinus syndrome; and 14% of those with complete heart block, even if there is complete anterograde block [243]. Most patients with severe "Pacemaker Syndrome" have intact conduction.

But Ogawa's meticulous experiments [182] on seven dogs with surgically-induced complete heart block (and therefore no chance of retrograde conduction) still demonstrated marked rises in right and left atrial pressures during mis-timed atrial contractions; RV and PA pressures and cardiac output all fell at the same time. Changes in LV dynamics were less marked but still detectable, perhaps because of the differing sensitivities of the two ventricles to volume-loading.

It might therefore be asked, in the light of these findings, and my own (showing a striking fall in forward flow during mis-timed atrial contractions), whether the fall in pressure and forward flow was the result of backward flow into the atrium i.e. tricuspid regurgitation; or just poor RV loading. The literature is contradictory on this point.

Pressure waves in the RA are striking[183] and do mimic TR[191], as I demonstrate in my abortive invasive study, and there is little doubt that inappropriately short or long PR intervals can increase atrioventricular valve regurgitation[202]. "Packages" of echocardiographic contrast medium seen in the inferior vena cavae of patients[188,187] undergoing ventricular pacing could be (and were) explained in both ways, although Pierard [187] states that he clearly saw bubbles refluxing across the TV in thirteen of his patients. However, other workers could not detect AV valve regurgitation in any pacing mode [201].

Whatever the mechanism, RV loading is clearly sub-optimal during inappropriately-timed atrial contractions.
The optimal PR interval for dual-chamber atrioventricular pacing has been addressed in many studies [244,245,256,247,201,248,249]; all concentrate on LV function. There is general agreement that the PR interval profoundly affects atrioventricular valve closure. With physiological PR intervals, AV valve closure occurs towards the end of diastole [250,251]: if ventricular systole starts before atrial emptying is complete, the proportion of ventricular filling caused by atrial transport is reduced [252]. If the atrial contraction is late in diastole, ventricular systole starts with the valve cusps wide apart and regurgitation may result [251,252], especially in early systole[253,254].
If atrial systole is premature, LV filling time is reduced by the premature closure of the AV valve reducing venous inflow.

Most authors agree that during dual-chamber pacing, cardiac output at rest is optimal with a PR interval of approximately 150ms [165,201,244,246,248,249,255,256]. During exercise the PR interval physiologically shortens in a normal individual [257], and shorter paced PR intervals of around 80ms are better[244,249] The same is true in situations of cardiac stress such as in acute myocardial infarction [164,246,256] and following cardiac surgery where heart block develops [258]. Videen [164] suggests that longer PR intervals are better during chronic pacing in patients with congestive heart failure (almost all the other studies only examined patients with normal ventricular function) and this should prove to be an interesting area for future research; it may be that the flattening of the Frank-Starling curve during heart failure in the RV will mean that the atrial contribution is less important in progressive heart failure.

Apart from early invasive studies on dogs [182], no study has addressed the optimal PR interval for right ventricular output in patients with normal RV function. It cannot be assumed that it will be the same as in the LV, because of the differing Frank-Starling curves and PV loops in the two ventricles. Signs of right, (rather than left) ventricular origin, such as ankle oedema, abdominal discomfort and high JVPs are common in most pacing clinics.

(4) Inappropriate atrioventricular sequencing can result in very large falls in forward flow from RV to PA, as measured by RVSTIs

This finding has not been previously reported.

I find that the optimal resting PR interval, as judged by the longest RVET, AT and AT/RVET ratio, is indeed around 100-150ms, as in the left ventricle at rest. The consequences of inappropriate atrioventricular sequencing, however, with atrial contractions falling 100-150ms after pacing stimulus artefacts, are severe.

RVET, AT and PA velocity fell to 50% or less of their optimal values in many patients, indicating marked reductions in forward flow into the pulmonary artery. In some patients forward flow became difficult to detect at all at this point. The duration of this situation was clearly related to the atrial rate, and was sometimes prolonged to 10-15 seconds when the atrial and ventricular rates became similar. The patients, (supine and relaxed) were asymptomatic, somewhat suprisingly. These changes are considerably greater than those reported under similar conditions in the LV [161], and it is likely that some of the reported reduction in cardiac output with mistimed atrial contraction is due to loss of RV rather than LV output.

It is still not clear whether the RV is "unloaded" into the RA (as the pressure waves in the RA suggest) in the form of tricuspid regurgitation when atrial contractions are mis-timed, or whether sudden falls in filling to the RV alone are responsible for these changes.

(5) This study is further evidence of the haemodynamically unsatisfactory nature of asynchronous single-chamber ventricular pacing.

The debate continues as to whether it is ethical to implant single-chamber asynchronous pacemakers into most patients presenting with complete heart block who are not in atrial fibrillation.
Although most such patients are elderly, and relatively uncomplaining, the proportion of the population at large who are over 75yrs is rapidly rising, and contains many more highly articulate patients who wish to be as active as possible. The rise in such numbers itself suggests a formidable economic burden, not only in cardiology, and arguments based on cost will also have increasing force.

We hope this study will add weight to the view that "VVI" or single-chamber asynchronous ventricular pacing has very significant haemodynamic drawbacks; and that these may become more important as paced patients live so much longer. It also suggests a method for exploring future pacing refinements.

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APPENDIX ONE

RAW DATA

RVSTIs ON NORMAL CONTROL SUBJECTS

PA Flow Values

No.	Sex	Age	Rate	RVPEP	RVET	RVETI	PEP/ET	AT	AT/ET	PEP/AT	AT/PEP
24	1	26	74.62	100	302.9	337.6	33.07	146.5	48.39	.6915	1.465
13	2	21	63.12	127.3	294.6	302.1	43.26	175	59.48	.7302	1.375
19	1	31	65.87	78.95	306.3	320.9	25.82	140.3	45.82	.5654	1.777
22	1	40	56.5	80.23	310.9	301.7	25.86	118.4	38.05	.6876	1.476
24	1	26	58.66	117.5	322.9	319.3	36.47	184.2	56.99	.6432	1.567
24	2	30	57.76	114.4	335.6	329.2	34.11	185.2	55.17	.6231	1.619
20	2	28	74.82	93	298.3	323.0	31.28	157	52.68	.5965	1.688
24	2	64	70.29	97.29	300.8	325.6	32.38	109.2	36.34	.9005	1.122
21	1	52	52	87.86	349.3	325.2	25.23	136.4	39.11	.6518	1.553
24	1	30	74.62	100.2	302.9	337.6	33.14	147.1	48.60	.6904	1.468
21	1	55	69.78	108.6	284.3	306.5	38.23	102.9	36.16	1.098	.9474
20	2	20	76.68	97.25	303	342.2	32.18	131.8	43.54	.7439	1.355
24	2	26	70.68	98.13	301.5	327.2	32.66	143.5	47.67	.6892	1.463
18	2	28	81.67	98.06	290.3	338.5	33.95	136.9	47.17	.7254	1.396
22	1	16	69.91	103.0	304.8	328.5	33.92	138.4	45.48	.7447	1.344
14	2	42	58.45	100.4	314.3	310.2	31.95	153.6	48.88	.6584	1.530
24	1	22	58.73	87.92	333.3	329.7	26.43	105.2	31.58	.85	1.197
17	2	23	75.21	91.76	327.1	365.8	28.22	142.1	43.48	.6523	1.548
22	1	39	73.9	99.32	289.1	320.8	34.43	132.5	45.81	.7582	1.334
18	2	42	90.76	95	273.6	336.5	34.79	148.9	54.40	.6429	1.567
32	1	66	63.18	102.0	302.3	316.4	33.16	131.7	42.78	.7794	1.291
20	2	22	75.34	116	333.3	373.0	34.89	120	36.05	.9717	1.034
24	2	40	62.76	84.37	309.4	316.2	27.34	149.6	48.35	.5667	1.773
24	1	60	71.56	111.5	300.6	328.3	37.17	137.9	45.86	.8175	1.237
20	1	32	82.65	91.5	248	291.0	36.95	120.3	48.57	.7715	1.314
24	2	56	56.82	122.7	317.3	308.8	38.75	154.8	48.76	.8017	1.261
21	2	20	78.95	91.9	287.9	330.2	31.97	152.6	53.06	.6044	1.661
22	1	58	63.42	100.9	322.1	331.1	32.42	116.6	36.19	.8764	1.155
20	1	24	54.16	112.3	330.5	314	34.06	166.8	50.41	.6806	1.486
19	2	26	99.93	91.58	228.7	295.1	40.09	118.7	51.92	.7798	1.296
16	2	16	75.87	91.25	277.5	312.0	32.88	103.8	37.35	.8886	1.137
31	2	23	66.97	94.19	353.7	373.6	26.67	135.5	38.34	.7008	1.438
17	2	44	93.69	113.5	257.4	321.6	44.13	111.5	43.36	1.034	.9819
21	2	60	77.37	100.2	300	340.4	33.49	121.7	40.58	.8291	1.214
40	2	65	86.33	115	268.1	321.6	42.99	103.8	38.67	1.127	.9022
20	1	41	87.35	92.5	275.8	332.4	33.59	133	48.21	.7048	1.438
24	2	24	73.91	88.94	300.4	333.4	29.65	133.8	44.54	.6676	1.504
24	1	19	61.83	116.7	313.3	317.8	37.32	162.7	51.95	.7249	1.395
18	2	22	79.3	95.28	296.7	340.9	32.18	159.4	53.77	.6005	1.673
20	1	53	51.72	98.25	327.8	304.3	30.00	147	44.84	.6747	1.496
21	1	55	66.14	81.67	332.6	349.2	24.6	121.9	36.64	.6794	1.493
24	1	51	60.11	107.7	326.3	326.5	33.10	123.1	37.69	.9189	1.143
15	1	53	68.87	120	294.7	315.7	40.83	148.3	50.45	.8107	1.236
18	2	22	81.33	81.11	296.1	344.7	27.40	134.7	45.50	.6043	1.661
24	1	40	59.46	107.1	297.3	295.3	36.24	99.38	33.63	1.090	.9281
18	1	63	82.04	96.39	296.9	347.2	32.56	110.3	37.16	.8912	1.144
16	1	63	101.0	118.1	229.4	297.7	52.02	91.25	40.00	1.317	.7725
21	1	59	43.8	113.1	369.3	315.3	30.66	167.1	45.26	.6817	1.478
33	2	21	76.15	93.64	305.2	343.5	30.79	134.7	44.16	.7018	1.438
17	2	25	62.27	92.94	299.4	304.9	31.05	147.7	49.29	.633	1.589
14	1	49	72.71	115.7	263.2	289.7	44.23	106.8	40.63	1.096	.9229
21	2	46	57.77	93.33	317.4	311.4	29.46	167.4	52.79	.5597	1.793
24	1	45	51.88	102.7	300.8	279.7	34.17	99.79	33.15	1.058	.9716
24	1	66	55.75	107.3	334.2	322.0	32.13	157.5	47.13	.685	1.468
29	1	27	62	89.69	308.1	313.0	29.16	148.8	48.29	.6067	1.659
16	1	53	55.86	131.6	296.3	285.9	44.49	165.9	55.92	.8091	1.261
38	1	25	82.77	120	259.5	304.2	46.64	107.4	41.38	1.134	.8948
14	1	27	79.36	102.9	302.9	348.2	34.04	132.9	43.91	.7807	1.292

18	1	22	61.69	97.5	308.9	313.0	32.03	147.8	47.88	.674	1.516
23	1	21	80.37	93.26	254.1	293.6	36.81	115	45.24	.8169	1.233
23	2	40	92.58	89.78	285.7	354.6	31.52	153.0	53.57	.5918	1.705
23	1	66	66.78	132.8	283.9	299.5	46.87	114.8	40.41	1.170	.8641
22	1	69	91.65	120.5	227.3	280.9	53.22	91.14	40.10	1.350	.7567
18	1	46	92	83.33	230.8	285.7	36.24	112.2	48.48	.7635	1.347
22	1	65	83.22	108.9	303.2	356.9	36.00	149.1	49.25	.7344	1.370
23	1	51	75.82	92.83	278.5	313	33.40	102.6	36.9	.9129	1.105
17	2	37	78.64	90.29	307.7	352.2	29.41	124.4	40.43	.7404	1.378
21	1	60	57.88	97.62	348.1	341.8	28.07	196.9	56.57	.4989	2.017
19	1	24	62.32	101.1	310.3	316.1	32.67	158.2	50.96	.6496	1.565
24	2	65	78.39	124.6	305.2	348.9	40.86	128.5	42.12	.9744	1.032
23	1	26	42.42	112.4	344.8	289.6	32.64	159.8	46.38	.7068	1.422
24	1	20	58.69	104.8	321.9	318.4	32.61	154.2	47.86	.6857	1.471
10	1	52	77.28	115.5	278.5	316.0	41.57	107.5	38.53	1.094	.9307
19	1	41	67.71	119.7	287.6	305.4	41.71	114.2	39.72	1.057	.9538
21	2	50	79.01	107.4	282.9	324.5	38.09	141.2	49.95	.7717	1.315
21	1	48	61.43	110.7	299.3	302.8	37.04	131.0	43.76	.8525	1.183
22	1	19	86.95	120.7	274.1	329.9	44.05	144.3	52.64	.8429	1.196
21		39.5	70.80	102.7	299.5	321.6	34.75	135.4	45.22	.7908	1.337
40		69	101.0	132.8	369.3	373.6	53.22	196.9	59.48	1.350	2.017
10		16	42.42	78.95	227.3	279.7	24.6	91.14	31.58	.4989	.7614
			70.68	100.2	300.8	320.9	33.4	135.5	45.5	.7404	1.375
			12.72	12.79	28.63	21.04	5.952	23.19	6.246	.1818	.2669
			1.45	1.46	3.26	2.4	.678	2.64	.723	.0207	.0304
			60.77	92.89	285.0	305.9	31.35	115.8	40.05	.6708	1.164
			79.16	113.3	315.8	337.0	37.25	151.1	49.27	.8825	1.521

Heart Rate
Individual means and confidence intervals for subjects

Pt No.		Mean HR	SD	Rt No.	SEM	95%-	95%+
1	24	74.62	4.62	4.898979	.9430536	72.77162	76.46838
2	13	63.12	3.67	3.605551	1.017875	61.12497	65.11503
3	19	65.87	2.93	4.358899	.6721881	64.55251	67.18749
4	22	56.5	1.52	4.690416	.3240651	55.86483	57.13517
5	24	58.66	1.61	4.898979	.3286399	58.01587	59.30413
6	24	57.76	1.66	4.898979	.3388461	57.09586	58.42414
7	20	74.82	2.45	4.472136	.5478367	73.74624	75.89376
8	24	70.29	2.2	4.898979	.4490731	69.40982	71.17018
9	21	52	1.67	4.582576	.3644239	51.28573	52.71427
10	24	74.62	4.62	4.898979	.9430536	72.77162	76.46838
11	21	69.78	2.79	4.582576	.6088279	68.58670	70.97330
12	20	76.68	7.08	4.472136	1.583136	73.57705	79.78295
13	24	70.68	4.03	4.898979	.8226203	69.06766	72.29234
14	18	81.67	4.84	4.242641	1.140799	79.43403	83.90597
15	22	69.91	4.57	4.690416	.9743273	68.00032	71.81968
16	14	58.45	2.58	3.741657	.6895340	57.09851	59.80149
17	24	58.73	2.5	4.898979	.5103104	57.72979	59.73021
18	17	75.21	5.89	4.123106	1.428535	72.41007	78.00993
19	22	73.9	3.01	4.690416	.6417342	72.64220	75.15780
20	18	90.76	1.91	4.242641	.4501913	89.87763	91.64237
21	32	63.18	.55	5.656854	.0972272	62.98943	63.37057
22	20	75.34	6.54	4.472136	1.462388	72.47372	78.20628
23	24	62.76	4.14	4.898979	.8450740	61.10366	64.41634
24	24	71.56	1.86	4.898979	.3796709	70.81585	72.30415
25	20	82.65	1.66	4.472136	.3711873	81.92247	83.37753
26	24	56.82	.98	4.898979	.2000417	56.42792	57.21208
27	21	78.95	2.18	4.582576	.4757150	78.01760	79.88240
28	22	63.42	2.65	4.690416	.5649819	62.31264	64.52736
29	20	54.16	1.39	4.472136	.3108134	53.55081	54.76919
30	19	99.93	3.29	4.358899	.7547778	98.45064	101.4094
31	16	75.87	2.43	4	.6075	74.6793	77.0607
32	31	66.97	4.61	5.567764	.8279804	65.34716	68.59284
33	17	93.69	1.7	4.123106	.4123106	92.88187	94.49813
34	21	77.37	5.15	4.582576	1.123822	75.16731	79.57269
35	40	86.33	1.75	6.324555	.2766993	85.78767	86.87233
36	20	87.35	6.67	4.472136	1.491457	84.42674	90.27326
37	24	73.91	2.52	4.898979	.5143928	72.90179	74.91821
38	24	61.83	5.74	4.898979	1.171673	59.53352	64.12648
39	18	79.3	3.54	4.242641	.8343860	77.66460	80.93540
40	20	51.72	2.62	4.472136	.5858498	50.57173	52.86827
41	21	66.14	1.59	4.582576	.3469664	65.45995	66.82005
42	24	60.11	1.16	4.898979	.2367840	59.64590	60.57410
43	15	68.87	1	3.872983	.2581989	68.36393	69.37607
44	18	81.33	3.27	4.242641	.7707464	79.81934	82.84066
45	24	59.46	4.18	4.898979	.8532389	57.78765	61.13235
46	18	82.04	4.37	4.242641	1.030019	80.02116	84.05884
47	16	101.04	2.1	4	.525	100.011	102.069
48	21	43.8	2.81	4.582576	.6131923	42.59814	45.00186
49	33	76.15	6.94	5.744563	1.208099	73.78213	78.51787
50	17	62.27	3.91	4.123106	.9483143	60.41130	64.12870
51	14	72.71	3	3.741657	.8017837	71.13850	74.28150
52	21	57.77	2.17	4.582576	.4735328	56.84188	58.69812
53	24	51.88	.79	4.898979	.1612581	51.56393	52.19607
54	24	55.75	2.66	4.898979	.5429702	54.68578	56.81422
55	29	62	3.4	5.385165	.6313641	60.76253	63.23747
56	16	55.86	2.7	4	.675	54.537	57.183
57	38	82.77	7.3	6.164414	1.184216	80.44894	85.09106

58	14	79.36	2.54	3.741657	.6788436	78.02947	80.69053
59	18	61.69	3.47	4.242641	.8178868	60.08694	63.29306
60	23	80.37	7.18	4.795832	1.497133	77.43562	83.30438
61	23	92.58	4.46	4.795832	.9299743	90.75725	94.40275
62	23	66.78	2.12	4.795832	.4420506	65.91358	67.64642
63	22	91.65	2.11	4.690416	.4498535	90.76829	92.53171
64	18	92	4	4.242641	.9428090	90.15209	93.84791
65	22	83.22	4.25	4.690416	.9061030	81.44404	84.99596
66	23	75.82	3.06	4.795832	.6380541	74.56941	77.07059
67	17	78.64	1.55	4.123106	.3759302	77.90318	79.37682
68	21	57.88	1.53	4.582576	.3338734	57.22561	58.53439
69	19	62.32	2.99	4.358899	.6859530	60.97553	63.66447
70	24	78.39	.66	4.898979	.1347219	78.12595	78.65405
71	23	42.42	3.4	4.795832	.7089490	41.03046	43.80954
72	24	58.69	1.93	4.898979	.3939596	57.91784	59.46216
73	10	77.28	5.14	3.162278	1.625411	74.09419	80.46581
74	19	67.71	4.08	4.358899	.9360162	65.87541	69.54459
75	21	79.01	5.17	4.582576	1.128186	76.79875	81.22125
76	21	61.43	.94	4.582576	.2051248	61.02796	61.83204
77	22	86.95	3.61	4.690416	.7696546	85.44148	88.45852
Av	21.5	70.79584	3.190390	4.603377	.7006259	69.42262	72.16907
Max	40	101.04	7.3	6.324555	1.625411	100.011	102.069
Min	10	42.42	.55	3.162278	.0972272	41.03046	43.80954

RVPEP

P	No.	Mean	SD	RtNo.	SEM	95%-	95%+
1	24	100	6.76	4.898979	1.379879	97.29544	102.7046
2	13	127.31	4.39	3.605551	1.217567	124.9236	129.6964
3	19	78.95	3.15	4.358899	.7226596	77.53359	80.36641
4	22	80.23	6.81	4.690416	1.451897	77.38428	83.07572
5	24	117.5	7.94	4.898979	1.620746	114.3233	120.6767
6	24	114.37	7.56	4.898979	1.543179	111.3454	117.3946
7	20	93	6.16	4.472136	1.377418	90.30026	95.69974
8	24	97.29	6.59	4.898979	1.345178	94.65345	99.92655
9	21	87.86	8.3	4.582576	1.811208	84.31003	91.40997
10	24	100.21	6.51	4.898979	1.328848	97.60546	102.8145
11	21	108.57	6.15	4.582576	1.342040	105.9396	111.2004
12	20	97.25	6.38	4.472136	1.426611	94.45384	100.0462
13	24	98.13	6.73	4.898979	1.373755	95.43744	100.8226
14	18	98.06	9.87	4.242641	2.326381	93.50029	102.6197
15	22	102.95	8.68	4.690416	1.850582	99.32286	106.5771
16	14	100.36	5.36	3.741657	1.432520	97.55226	103.1677
17	24	87.92	6.9	4.898979	1.408457	85.15943	90.68057
18	17	91.76	9.67	4.123106	2.345319	87.16317	96.35683
19	22	99.32	6.6	4.690416	1.407125	96.56204	102.0780
20	18	95	7.28	4.242641	1.715912	91.63681	98.36319
21	32	102.03	7.61	5.656854	1.345271	99.39327	104.6667
22	20	116	5.76	4.472136	1.287975	113.4756	118.5244
23	24	84.37	6.48	4.898979	1.322724	81.77746	86.96254
24	24	111.46	10.48	4.898979	2.139221	107.2671	115.6529
25	20	91.5	6.51	4.472136	1.455680	88.64687	94.35313
26	24	122.71	9.44	4.898979	1.926932	118.9332	126.4868
27	21	91.9	5.36	4.582576	1.169648	89.60749	94.19251
28	22	100.91	8.82	4.690416	1.880430	97.22436	104.5956
29	20	112.25	8.03	4.472136	1.795563	108.7307	115.7693
30	19	91.58	5.79	4.358899	1.328317	88.97650	94.18350
31	16	91.25	9.92	4	2.48	86.3892	96.1108
32	31	94.19	6.84	5.567764	1.228500	91.78214	96.59786
33	17	113.53	8.06	4.123106	1.954837	109.6985	117.3615
34	21	100.24	6.61	4.582576	1.442420	97.41286	103.0671
35	40	115	8.7	6.324555	1.375591	112.3038	117.6962
36	20	92.5	6.98	4.472136	1.560775	89.44088	95.55912
37	24	88.94	4.42	4.898979	.9022287	87.17163	90.70837
38	24	116.67	7.47	4.898979	1.524807	113.6814	119.6586
39	18	95.28	6.52	4.242641	1.536779	92.26791	98.29209
40	20	98.25	5.2	4.472136	1.162755	95.97100	100.5290
41	21	81.67	4.83	4.582576	1.053992	79.60417	83.73583
42	24	107.71	8.34	4.898979	1.702395	104.3733	111.0467
43	15	120	8.45	3.872983	2.181781	115.7237	124.2763
44	18	81.11	6.08	4.242641	1.433070	78.30118	83.91882
45	24	107.08	6.06	4.898979	1.236992	104.6555	109.5045
46	18	96.39	8.37	4.242641	1.972828	92.52326	100.2567
47	16	118.13	6.8	4	1.7	114.798	121.462
48	21	113.1	6.98	4.582576	1.523161	110.1146	116.0854
49	33	93.64	7.73	5.744563	1.345620	91.00258	96.27742
50	17	92.94	5.32	4.123106	1.290290	90.41103	95.46897
51	14	115.71	5.5	3.741657	1.469937	112.8289	118.5911
52	21	93.33	7.13	4.582576	1.555894	90.28045	96.37955
53	24	102.71	5.3	4.898979	1.081858	100.5896	104.8304
54	24	107.29	6.08	4.898979	1.241075	104.8575	109.7225
55	29	89.69	6.35	5.385165	1.179165	87.37884	92.00116
56	16	131.56	9.26	4	2.315	127.0226	136.0974
57	38	120	8.62	6.164414	1.398349	117.2592	122.7408
58	14	102.86	10.32	3.741657	2.758136	97.45405	108.2659

59	18	97.5	9.74	4.242641	2.295740	93.00035	101.9997
60	23	93.26	8.48	4.795832	1.768202	89.79432	96.72568
61	23	89.78	6.12	4.795832	1.276108	87.27883	92.28117
62	23	132.83	9.39	4.795832	1.957950	128.9924	136.6676
63	22	120.45	6.53	4.690416	1.392201	117.7213	123.1787
64	18	83.33	8.22	4.242641	1.937473	79.53255	87.12745
65	22	108.86	8.16	4.690416	1.739718	105.4502	112.2698
66	23	92.83	6.37	4.795832	1.328237	90.22666	95.43334
67	17	90.29	5.99	4.123106	1.452788	87.44253	93.13747
68	21	97.62	5.84	4.582576	1.274392	95.12219	100.1178
69	19	101.05	8.59	4.358899	1.970681	97.18746	104.9125
70	24	124.58	6.41	4.898979	1.308436	122.0155	127.1445
71	23	112.39	7.37	4.795832	1.536751	109.3780	115.4020
72	24	104.79	8.01	4.898979	1.635034	101.5853	107.9947
73	10	115.5	9.26	3.162278	2.928269	109.7606	121.2394
74	19	119.74	8.41	4.358899	1.929386	115.9584	123.5216
75	21	107.38	9.17	4.582576	2.001058	103.4579	111.3021
76	21	110.71	5.76	4.582576	1.256935	108.2464	113.1736
77	22	120.68	9.04	4.690416	1.927334	116.9024	124.4576
Av	21.5	102.6635	7.235974	4.603377	1.592259	99.54268	105.7843
Max	40	132.83	10.48	6.324555	2.928269	128.9924	136.6676
Min	10	78.95	3.15	3.162278	.7226596	77.38428	80.36641

RVET

Individual means and confidence intervals

Pt	No.	Mean	SD	Rt.No	SEM	95%-	95%+
1	24	302.92	10.31	4.898979	2.104520	298.7951	307.0449
2	13	294.62	9.23	3.605551	2.559941	289.6025	299.6375
3	19	306.32	12.57	4.358899	2.883756	300.6678	311.9722
4	22	310.91	9.59	4.690416	2.044595	306.9026	314.9174
5	24	322.92	10.42	4.898979	2.126974	318.7511	327.0889
6	24	335.62	7.56	4.898979	1.543179	332.5954	338.6446
7	20	298.25	11.39	4.472136	2.546881	293.2581	303.2419
8	24	300.83	10.29	4.898979	2.100437	296.7131	304.9469
9	21	349.29	12.38	4.582576	2.701537	343.9950	354.5850
10	24	302.92	10.31	4.898979	2.104520	298.7951	307.0449
11	21	284.29	8.56	4.582576	1.867945	280.6288	287.9512
12	20	303	13.61	4.472136	3.043289	297.0352	308.9648
13	24	301.46	13.23	4.898979	2.700562	296.1669	306.7531
14	18	290.28	14.29	4.242641	3.368185	283.6784	296.8816
15	22	304.77	13.49	4.690416	2.876078	299.1329	310.4071
16	14	314.29	6.75	3.741657	1.804013	310.7541	317.8259
17	24	333.33	11.39	4.898979	2.324974	328.7731	337.8869
18	17	327.06	18.03	4.123106	4.372917	318.4891	335.6309
19	22	289.09	10.08	4.690416	2.149063	284.8778	293.3022
20	18	273.61	7.24	4.242641	1.706484	270.2653	276.9547
21	32	302.28	10.75	5.656854	1.900349	298.5553	306.0047
22	20	333.25	14.53	4.472136	3.249007	326.8819	339.6181
23	24	309.38	9.01	4.898979	1.839159	305.7752	312.9848
24	24	300.63	9.81	4.898979	2.002458	296.7052	304.5548
25	20	248	11.05	4.472136	2.470855	243.1571	252.8429
26	24	317.29	8.59	4.898979	1.753426	313.8533	320.7267
27	21	287.86	9.95	4.582576	2.171268	283.6043	292.1157
28	22	322.05	11.2	4.690416	2.387848	317.3698	326.7302
29	20	330.5	12.24	4.472136	2.736947	325.1356	335.8644
30	19	228.68	6.2	4.358899	1.422378	225.8921	231.4679
31	16	277.5	8.16	4	2.04	273.5016	281.4984
32	31	353.71	13.41	5.567764	2.408507	348.9893	358.4307
33	17	257.35	6.64	4.123106	1.610437	254.1935	260.5065
34	21	300	11.94	4.582576	2.605522	294.8932	305.1068
35	40	268.12	8.96	6.324555	1.416700	265.3433	270.8967
36	20	275.75	11.95	4.472136	2.672101	270.5127	280.9873
37	24	300.42	8.59	4.898979	1.753426	296.9833	303.8567
38	24	313.33	11.29	4.898979	2.304562	308.8131	317.8469
39	18	296.67	10.29	4.242641	2.425376	291.9163	301.4237
40	20	327.75	10.57	4.472136	2.363524	323.1175	332.3825
41	21	332.62	11.47	4.582576	2.502959	327.7142	337.5258
42	24	326.25	11.63	4.898979	2.373964	321.5970	330.9030
43	15	294.67	11.09	3.872983	2.863426	289.0577	300.2823
44	18	296.11	9	4.242641	2.121320	291.9522	300.2678
45	24	297.29	22.26	4.898979	4.543803	288.3841	306.1959
46	18	296.94	12.73	4.242641	3.000490	291.0590	302.8210
47	16	229.37	20.48	4	5.12	219.3348	239.4052
48	21	369.29	7.46	4.582576	1.627905	366.0993	372.4807
49	33	305.15	13.26	5.744563	2.308270	300.6258	309.6742
50	17	299.41	5.83	4.123106	1.413983	296.6386	302.1814
51	14	263.21	17.5	3.741657	4.677072	254.0429	272.3771
52	21	317.38	12.61	4.582576	2.751728	311.9866	322.7734
53	24	300.83	7.61	4.898979	1.553385	297.7854	303.8746
54	24	334.17	6.2	4.898979	1.265570	331.6895	336.6505
55	29	308.1	8.28	5.385165	1.537557	305.0864	311.1136
56	16	296.25	9.4	4	2.35	291.644	300.856

57	38	259.47	18.52	6.164414	3.004341	253.5815	265.3585	
58	14	302.86	9.75	3.741657	2.605797	297.7526	307.9674	
59	18	308.89	29.38	4.242641	6.924932	295.3171	322.4629	
60	23	254.13	8.87	4.795832	1.849523	250.5049	257.7551	
61	23	285.65	11.11	4.795832	2.316595	281.1095	290.1905	
62	23	283.91	9.41	4.795832	1.962121	280.0642	287.7558	
63	22	227.27	12.6	4.690416	2.686329	222.0048	232.5352	
64	18	230.83	8.95	4.242641	2.109535	226.6953	234.9647	
65	22	303.18	11.6	4.690416	2.473128	298.3327	308.0273	
66	23	278.48	12.47	4.795832	2.600175	273.3837	283.5763	
67	17	307.65	9.54	4.123106	2.313790	303.1150	312.1850	
68	21	348.1	11.45	4.582576	2.498595	343.2028	352.9972	
69	19	310.26	10.6	4.358899	2.431807	305.4937	315.0263	
70	24	305.21	6.51	4.898979	1.328848	302.6055	307.8145	
71	23	344.78	8.85	4.795832	1.845353	341.1631	348.3969	
72	24	321.88	9.98	4.898979	2.037159	317.8872	325.8728	
73	10	278.5	10.55	3.162278	3.336203	271.9610	285.0390	
74	19	287.63	11.83	4.358899	2.713988	282.3106	292.9494	
75	21	282.86	11.57	4.582576	2.524781	277.9114	287.8086	
76	21	299.29	8.7	4.582576	1.898496	295.5689	303.0111	
77	22	274.14	7.32	4.690416	1.560629	271.0812	277.1988	
Av	21.	299.4586	11.06779					
Max	40	369.29	29.38					
Min	10	227.27	5.83					

RVETI

Individual means and confidence intervals

Pt.No.		Mean	SD	RtNo.	SEM	95%-	95%+
1	24	337.55	13.27	4.898979	2.708727	332.2409	342.8591
2	13	302.11	14.03	3.605551	3.891222	294.4832	309.7368
3	19	320.9	15.82	4.358899	3.629357	313.7865	328.0135
4	22	301.68	10.14	4.690416	2.161855	297.4428	305.9172
5	24	319.32	12.61	4.898979	2.574005	314.2749	324.3651
6	24	329.23	6.92	4.898979	1.412539	326.4614	331.9986
7	20	322.99	13.4	4.472136	2.996331	317.1172	328.8628
8	24	325.58	12.47	4.898979	2.545428	320.5910	330.5690
9	21	325.17	13.77	4.582576	3.004860	319.2805	331.0595
10	24	337.55	13.27	4.898979	2.708727	332.2409	342.8591
11	21	306.47	9.44	4.582576	2.059977	302.4324	310.5076
12	20	342.19	21.73	4.472136	4.858976	332.6664	351.7136
13	24	327.16	19.02	4.898979	3.882441	319.5504	334.7696
14	18	338.46	18.6	4.242641	4.384062	329.8672	347.0528
15	22	328.54	12.11	4.690416	2.581861	323.4796	333.6004
16	14	310.17	10.45	3.741657	2.792880	304.6960	315.6440
17	24	329.71	12.84	4.898979	2.620954	324.5729	334.8471
18	17	365.8	23.28	4.123106	5.646229	354.7334	376.8666
19	22	320.78	13.26	4.690416	2.827041	315.2390	326.3210
20	18	336.5	9.69	4.242641	2.283955	332.0234	340.9766
21	32	316.36	11.37	5.656854	2.009951	312.4205	320.2995
22	20	373.03	22.28	4.472136	4.981959	363.2654	382.7946
23	24	316.2	12.49	4.898979	2.549511	311.2030	321.1970
24	24	328.3	11.79	4.898979	2.406624	323.5830	333.0170
25	20	291.03	12.68	4.472136	2.835334	285.4727	296.5873
26	24	308.75	8.47	4.898979	1.728932	305.3613	312.1387
27	21	330.15	11.43	4.582576	2.494230	325.2613	335.0387
28	22	331.05	14.19	4.690416	3.025318	325.1204	336.9796
29	20	314	12.8	4.472136	2.862167	308.3902	319.6098
30	19	295.06	8.64	4.358899	1.982152	291.1750	298.9450
31	15	312.04	11.16	3.872983	2.881500	306.3923	317.6877
32	31	373.55	20.9	5.567764	3.753751	366.1926	380.9074
33	17	321.56	7.9	4.123106	1.916031	317.8046	325.3154
34	21	340.36	15.14	4.582576	3.303819	333.8845	346.8355
35	40	321.6	10.95	6.324555	1.731347	318.2066	324.9934
36	20	332.41	18.85	4.472136	4.214988	324.1486	340.6714
37	24	333.37	10.62	4.898979	2.167798	329.1211	337.6189
38	24	317.78	18.71	4.898979	3.819163	310.2944	325.2656
39	18	340.94	13.07	4.242641	3.080629	334.9020	346.9780
40	20	304.29	12.92	4.472136	2.889000	298.6276	309.9524
41	21	349.24	13.64	4.582576	2.976492	343.4061	355.0739
42	24	326.52	11.85	4.898979	2.418871	321.7790	331.2610
43	15	315.67	11.23	3.872983	2.899574	309.9868	321.3532
44	18	344.68	12.6	4.242641	2.969848	338.8591	350.5009
45	24	295.33	17.98	4.898979	3.670152	288.1365	302.5235
46	18	347.16	18.55	4.242641	4.372277	338.5903	355.7297
47	16	297.7	27.31	4	6.8275	284.3181	311.0819
48	21	315.34	11.14	4.582576	2.430947	310.5753	320.1047
49	33	343.49	22.42	5.744563	3.902821	335.8405	351.1395
50	17	304.87	11.01	4.123106	2.670317	299.6362	310.1038
51	14	289.67	19.59	3.741657	5.235648	279.4081	299.9319
52	21	311.41	14.43	4.582576	3.148884	305.2382	317.5818
53	24	279.74	7.26	4.898979	1.481941	276.8354	282.6446
54	24	322.01	9	4.898979	1.837117	318.4093	325.6107
55	29	313.03	10.59	5.385165	1.966514	309.1756	316.8844
56	16	285.91	14.75	4	3.6875	278.6825	293.1375

57	38	304.2	22.05	6.164414	3.576982	297.1891	311.2109
58	14	348.2	10.44	3.741657	2.790207	342.7312	353.6688
59	18	312.98	29.97	4.242641	7.063997	299.1346	326.8254
60	23	293.62	12.08	4.795832	2.518854	288.6830	298.5570
61	23	354.62	13.72	4.795832	2.860818	349.0128	360.2272
62	23	299.52	11.88	4.795832	2.477151	294.6648	304.3752
63	22	280.86	15.61	4.690416	3.328063	274.3370	287.3830
64	18	285.72	11.3	4.242641	2.663436	280.4997	290.9403
65	22	356.93	15.68	4.690416	3.342987	350.3777	363.4823
66	23	313	15.85	4.795832	3.304953	306.5223	319.4777
67	17	352.18	10.76	4.123106	2.609683	347.0650	357.2950
68	21	341.82	11.27	4.582576	2.459316	336.9997	346.6403
69	19	316.06	11.83	4.358899	2.713988	310.7406	321.3794
70	24	348.87	7.61	4.898979	1.553385	345.8254	351.9146
71	23	289.57	11.07	4.795832	2.308255	285.0458	294.0942
72	24	318.35	12.37	4.898979	2.525016	313.4010	323.2990
73	10	316.03	18.31	3.162278	5.790130	304.6813	327.3787
74	19	305.35	14.07	4.358899	3.227879	299.0234	311.6766
75	21	324.46	17.36	4.582576	3.788263	317.0350	331.8850
76	21	302.83	9.14	4.582576	1.994512	298.9208	306.7392
77	22	329.9	9.62	4.690416	2.050991	325.8801	333.9199
Ave	21.	321.6432	13.86779	4.601727	3.060401	315.6449	327.6416
Max	40	373.55	29.97	6.324555	7.063997	366.1926	382.7946
Min	10	279.74	6.92	3.162278	1.412539	274.3370	282.6446

AT (TTP)

Individual means and confidence intervals

Pt	No.	Mean	SD	RtNo.	SEM	95%-	95%+
1	24	146.46	14.1	4.898979	2.878150	140.8188	152.1012
2	13	175	12.25	3.605551	3.397539	168.3408	181.6592
3	19	140.26	9.64	4.358899	2.211568	135.9253	144.5947
4	22	118.41	11.79	4.690416	2.513636	113.4833	123.3367
5	24	184.17	14.72	4.898979	3.004707	178.2808	190.0592
6	24	185.21	15.21	4.898979	3.104728	179.1247	191.2953
7	20	157	10.93	4.472136	2.444022	152.2097	161.7903
8	24	109.17	9.17	4.898979	1.871818	105.5012	112.8388
9	21	136.43	14.59	4.582576	3.183799	130.1898	142.6702
10	24	147.08	14.59	4.898979	2.978171	141.2428	152.9172
11	21	102.86	18.41	4.582576	4.017391	94.98591	110.7341
12	20	131.75	10.17	4.472136	2.274081	127.2928	136.2072
13	24	143.54	12.55	4.898979	2.561758	138.5190	148.5610
14	18	136.94	12.5	4.242641	2.946278	131.1653	142.7147
15	22	138.41	8.51	4.690416	1.814338	134.8539	141.9661
16	14	153.57	12.77	3.741657	3.412926	146.8807	160.2593
17	24	105.21	11.84	4.898979	2.416830	100.4730	109.9470
18	17	142.06	12	4.123106	2.910428	136.3556	147.7644
19	22	132.5	12.79	4.690416	2.726837	127.1554	137.8446
20	18	148.89	10.23	4.242641	2.411234	144.1640	153.6160
21	32	131.72	10.21	5.656854	1.804890	128.1824	135.2576
22	20	120	8.11	4.472136	1.813451	116.4456	123.5544
23	24	149.58	8.33	4.898979	1.700354	146.2473	152.9127
24	24	137.93	12.33	4.898979	2.516851	132.9970	142.8630
25	20	120.25	13.62	4.472136	3.045525	114.2808	126.2192
26	24	154.79	13.55	4.898979	2.765882	149.3689	160.2111
27	21	152.62	7.52	4.582576	1.640999	149.4036	155.8364
28	22	116.59	10.62	4.690416	2.264192	112.1522	121.0278
29	20	166.75	14.98	4.472136	3.349630	160.1847	173.3153
30	19	118.68	10.12	4.358899	2.321687	114.1295	123.2305
31	16	103.75	9.57	4	2.3925	99.0607	108.4393
32	31	135.48	11.57	5.567764	2.078033	131.4071	139.5529
33	17	111.47	11.96	4.123106	2.900726	105.7846	117.1554
34	21	121.67	8.11	4.582576	1.769747	118.2013	125.1387
35	40	103.75	12.18	6.324555	1.925827	99.97538	107.5246
36	20	133	14.55	4.472136	3.253479	126.6232	139.3768
37	24	133.75	8.24	4.898979	1.681983	130.4533	137.0467
38	24	162.71	16.35	4.898979	3.337430	156.1686	169.2514
39	18	159.44	11.49	4.242641	2.708219	154.1319	164.7481
40	20	147	13.51	4.472136	3.020928	141.0790	152.9210
41	21	121.9	14.79	4.582576	3.227443	115.5742	128.2258
42	24	123.12	19.88	4.898979	4.057988	115.1663	131.0737
43	15	148.33	9.57	3.872983	2.470963	143.4869	153.1731
44	18	134.72	10.07	4.242641	2.373522	130.0679	139.3721
45	24	99.38	9.48	4.898979	1.935097	95.58721	103.1728
46	18	110.28	12.77	4.242641	3.009918	104.3806	116.1794
47	16	91.25	12.18	4	3.045	85.2818	97.2182
48	21	167.14	13.28	4.582576	2.897934	161.4601	172.8199
49	33	134.7	11.72	5.744563	2.040190	130.7012	138.6988
50	17	147.65	9.86	4.123106	2.391401	142.9629	152.3371
51	14	106.79	11.2	3.741657	2.993326	100.9231	112.6569
52	21	167.38	9.83	4.582576	2.145082	163.1756	171.5844
53	24	99.79	16.52	4.898979	3.372131	93.18062	106.3994
54	24	157.5	10.22	4.898979	2.086149	153.4111	161.5889
55	29	148.79	10.66	5.385165	1.979512	144.9102	152.6698
56	16	165.94	21.77	4	5.4425	155.2727	176.6073

57	38	107.37	11.01	6.164414	1.786058	103.8693	110.8707
58	14	132.86	9.14	3.741657	2.442768	128.0722	137.6478
59	18	147.78	18.49	4.242641	4.358135	139.2381	156.3219
60	23	115	7.39	4.795832	1.540922	111.9798	118.0202
61	23	153.04	12.41	4.795832	2.587664	147.9682	158.1118
62	23	114.78	12.29	4.795832	2.562642	109.7572	119.8028
63	22	91.14	11.85	4.690416	2.526428	86.18820	96.09180
64	18	112.22	15.55	4.242641	3.665170	105.0363	119.4037
65	22	149.09	9.96	4.690416	2.123479	144.9280	153.2520
66	23	102.61	7.67	4.795832	1.599306	99.47536	105.7446
67	17	124.41	17.67	4.123106	4.285604	116.0102	132.8098
68	21	196.9	15.85	4.582576	3.458754	190.1208	203.6792
69	19	158.16	18.42	4.358899	4.225838	149.8774	166.4426
70	24	128.54	8.78	4.898979	1.792210	125.0273	132.0527
71	23	159.78	10.5	4.795832	2.189401	155.4888	164.0712
72	24	154.17	12.22	4.898979	2.494397	149.2810	159.0590
73	10	107.5	14.19	3.162278	4.487272	98.70495	116.2951
74	19	114.21	10.44	4.358899	2.395100	109.5156	118.9044
75	21	141.19	16.5	4.582576	3.600595	134.1328	148.2472
76	21	130.95	11.14	4.582576	2.430947	126.1853	135.7147
77	22	144.32	11.16	4.690416	2.379320	139.6565	148.9835
Ave	21.5	135.4095	12.23519	4.603377	2.698347	130.1207	140.6982
Max	40	196.9	21.77	6.324555	5.4425	190.1208	203.6792
Min	10	91.14	7.39	3.162278	1.540922	85.2818	96.09180

RVPEP/RVET%

Individual means and confidence intervals

Pt	No.	Mean	SD	RtNo.	SEM	95%-	95%+
1	24	33.065	2.755	4.898979	.5623620	31.96277	34.16723
2	13	43.261	2.239	3.605551	.6209869	42.04387	44.47813
3	19	25.821	1.564	4.358899	.3588062	25.11774	26.52426
4	22	25.859	2.705	4.690416	.5767079	24.72865	26.98935
5	24	36.466	3.273	4.898979	.6680983	35.15653	37.77547
6	24	34.114	2.665	4.898979	.5439908	33.04778	35.18022
7	20	31.277	3.039	4.472136	.6795411	29.94510	32.60890
8	24	32.378	2.498	4.898979	.5099021	31.37859	33.37741
9	21	25.233	3.014	4.582576	.6577087	23.94389	26.52211
10	24	33.137	2.722	4.898979	.5556259	32.04797	34.22603
11	21	38.23	2.599	4.582576	.5671483	37.11839	39.34161
12	20	32.18	2.817	4.472136	.6299003	30.94540	33.41460
13	24	32.66	3.263	4.898979	.6660571	31.35453	33.96547
14	18	33.954	4.626	4.242641	1.090359	31.81690	36.09110
15	22	33.915	3.907	4.690416	.8329752	32.28237	35.54763
16	14	31.951	1.898	3.741657	.5072618	30.95677	32.94523
17	24	26.429	2.527	4.898979	.5158217	25.41799	27.44001
18	17	28.221	3.982	4.123106	.9657769	26.32808	30.11392
19	22	34.429	3.007	4.690416	.6410946	33.17245	35.68555
20	18	34.791	3.339	4.242641	.7870098	33.24846	36.33354
21	32	33.158	3.022	5.656854	.5342192	32.11093	34.20507
22	20	34.89	2.586	4.472136	.5782472	33.75664	36.02336
23	24	27.337	2.74	4.898979	.5593002	26.24077	28.43323
24	24	37.172	4.251	4.898979	.8677317	35.47125	38.87275
25	20	36.954	2.974	4.472136	.6650066	35.65059	38.25741
26	24	38.746	3.711	4.898979	.7575047	37.26129	40.23071
27	21	31.971	2.294	4.582576	.5005918	30.98984	32.95216
28	22	32.419	3.499	4.690416	.7459893	30.95686	33.88114
29	20	34.057	3.318	4.472136	.7419274	32.60282	35.51118
30	19	40.087	2.957	4.358899	.6783823	38.75737	41.41663
31	16	32.879	3.33	4	.8325	31.2473	34.5107
32	31	26.667	2.195	5.567764	.3942336	25.89430	27.43970
33	17	44.126	3.091	4.123106	.7496776	42.65663	45.59537
34	21	33.491	2.903	4.582576	.6334865	32.24937	34.73263
35	40	42.994	4.198	6.324555	.6637621	41.69303	44.29497
36	20	33.59	2.724	4.472136	.6091049	32.39615	34.78385
37	24	29.653	2.022	4.898979	.4127390	28.84403	30.46197
38	24	37.323	3.304	4.898979	.6744262	36.00112	38.64488
39	18	32.181	2.842	4.242641	.6698658	30.86806	33.49394
40	20	30.002	1.789	4.472136	.4000326	29.21794	30.78606
41	21	24.6	1.927	4.582576	.4205059	23.77581	25.42419
42	24	33.102	3.391	4.898979	.6921850	31.74532	34.45868
43	15	40.829	3.85	3.872983	.9940657	38.88063	42.77737
44	18	27.403	2.008	4.242641	.4732901	26.47535	28.33065
45	24	36.238	3.693	4.898979	.7538305	34.76049	37.71551
46	18	32.557	3.6	4.242641	.8485281	30.89388	34.22012
47	16	52.024	6.848	4	1.712	48.66848	55.37952
48	21	30.658	2.298	4.582576	.5014647	29.67513	31.64087
49	33	30.79	3.313	5.744563	.5767193	29.65963	31.92037
50	17	31.054	1.907	4.123106	.4625154	30.14747	31.96053
51	14	44.228	4.601	3.741657	1.229669	41.81785	46.63815
52	21	29.457	2.582	4.582576	.5634386	28.35266	30.56134
53	24	34.173	2.142	4.898979	.4372339	33.31602	35.02998
54	24	32.132	2.202	4.898979	.4494814	31.25102	33.01298
55	29	29.157	2.538	5.385165	.4712948	28.23326	30.08074
56	16	44.494	4.037	4	1.00925	42.51587	46.47213

57	38	46.644	6.234	6.164414	1.011288	44.66187	48.62613
58	14	34.042	3.995	3.741657	1.067709	31.94929	36.13471
59	18	32.029	5.774	4.242641	1.360945	29.36155	34.69645
60	23	36.813	4.192	4.795832	.8740924	35.09978	38.52622
61	23	31.517	3.01	4.795832	.6276284	30.28685	32.74715
62	23	46.868	4.152	4.795832	.8657518	45.17113	48.56487
63	22	53.219	4.837	4.690416	1.031252	51.19775	55.24025
64	18	36.24	4.723	4.242641	1.113222	34.05809	38.42191
65	22	36.004	3.581	4.690416	.7634718	34.50760	37.50040
66	23	33.404	2.771	4.795832	.5777934	32.27152	34.53648
67	17	29.406	2.544	4.123106	.6170106	28.19666	30.61534
68	21	28.07	1.884	4.582576	.4111225	27.26420	28.87580
69	19	32.667	3.582	4.358899	.8217672	31.05634	34.27766
70	24	40.859	2.682	4.898979	.5474610	39.78598	41.93202
71	23	32.635	2.546	4.795832	.5308777	31.59448	33.67552
72	24	32.609	2.956	4.898979	.6033910	31.42635	33.79165
73	10	41.57	4.131	3.162278	1.306337	39.00958	44.13042
74	19	41.707	3.54	4.358899	.8121317	40.11522	43.29878
75	21	38.085	4.207	4.582576	.9180427	36.28564	39.88436
76	21	37.043	2.514	4.582576	.5485998	35.96774	38.11826
77	22	44.052	3.489	4.690416	.7438573	42.59404	45.50996
Ave	21.	34.74606	3.200909	4.603377	.7059102	33.36248	36.12965
Max	40	53.219	6.848	6.324555	1.712	51.19775	55.37952
Min	10	24.6	1.564	3.162278	.3588062	23.77581	25.42419

AT/RVET x 100

Individual means and confidence intervals

Pt.No.		Mean	SD	Rt No.	SEM	95%-	95%+
1	24	48.387	4.786	4.898979	.9769382	46.47220	50.30180
2	13	59.475	4.872	3.605551	1.351250	56.82655	62.12345
3	19	45.816	3.019	4.358899	.6926061	44.45849	47.17351
4	22	38.05	3.246	4.690416	.6920495	36.69358	39.40642
5	24	56.99	3.481	4.898979	.7105561	55.59731	58.38269
6	24	55.173	4.204	4.898979	.8581379	53.49105	56.85495
7	20	52.681	3.778	4.472136	.8447865	51.02522	54.33678
8	24	36.343	3.481	4.898979	.7105561	34.95031	37.73569
9	21	39.11	4.343	4.582576	.9477203	37.25247	40.96753
10	24	48.603	5.052	4.898979	1.031235	46.58178	50.62422
11	21	36.163	6.436	4.582576	1.404450	33.41028	38.91572
12	20	43.538	3.473	4.472136	.7765864	42.01589	45.06011
13	24	47.666	4.251	4.898979	.8677317	45.96525	49.36675
14	18	47.173	3.631	4.242641	.8558349	45.49556	48.85044
15	22	45.479	3.14	4.690416	.6694502	44.16688	46.79112
16	14	48.876	4.071	3.741657	1.088021	46.74348	51.00852
17	24	31.584	3.571	4.898979	.7289273	30.15530	33.01270
18	17	43.481	3.519	4.123106	.8534829	41.80817	45.15383
19	22	45.805	3.757	4.690416	.8009951	44.23505	47.37495
20	18	54.397	3.014	4.242641	.7104066	53.00460	55.78940
21	32	42.784	3.71	5.656854	.6558415	41.49855	44.06945
22	20	36.052	2.608	4.472136	.5831665	34.90899	37.19501
23	24	48.347	2.211	4.898979	.4513185	47.46242	49.23158
24	24	45.863	3.676	4.898979	.7503604	44.39229	47.33371
25	20	48.569	5.83	4.472136	1.303628	46.01389	51.12411
26	24	48.764	3.732	4.898979	.7617913	47.27089	50.25711
27	21	53.064	2.893	4.582576	.6313044	51.82664	54.30136
28	22	36.187	2.822	4.690416	.6016524	35.00776	37.36624
29	20	50.409	3.449	4.472136	.7712198	48.89741	51.92059
30	19	51.924	4.52	4.358899	1.036959	49.89156	53.95644
31	16	37.354	2.969	4	.74225	35.89919	38.80881
32	31	38.338	3.345	5.567764	.6007797	37.16047	39.51553
33	17	43.362	4.957	4.123106	1.202249	41.00559	45.71841
34	21	40.583	2.588	4.582576	.5647479	39.47609	41.68991
35	40	38.674	4.144	6.324555	.6552239	37.38976	39.95824
36	20	48.214	4.779	4.472136	1.068617	46.11951	50.30849
37	24	44.542	2.787	4.898979	.5688940	43.42697	45.65703
38	24	51.947	5.081	4.898979	1.037155	49.91418	53.97982
39	18	53.773	3.84	4.242641	.9050967	51.99901	55.54699
40	20	44.838	3.703	4.472136	.8280160	43.21509	46.46091
41	21	36.638	4.173	4.582576	.9106233	34.85318	38.42282
42	24	37.692	5.943	4.898979	1.213110	35.31430	40.06970
43	15	50.446	4.287	3.872983	1.106899	48.27648	52.61552
44	18	45.502	3.22	4.242641	.7589613	44.01444	46.98956
45	24	33.633	4.324	4.898979	.8826328	31.90304	35.36296
46	18	37.157	4.143	4.242641	.9765145	35.24303	39.07097
47	16	39.999	5.743	4	1.43575	37.18493	42.81307
48	21	45.256	4.418	4.582576	.9640866	43.36639	47.14561
49	33	44.164	3.556	5.744563	.6190201	42.95072	45.37728
50	17	49.294	2.78	4.123106	.6742490	47.97247	50.61553
51	14	40.626	3.879	3.741657	1.036706	38.59406	42.65794
52	21	52.794	3.322	4.582576	.7249198	51.37316	54.21484
53	24	33.151	5.333	4.898979	1.088594	31.01736	35.28464
54	24	47.132	2.917	4.898979	.5954301	45.96496	48.29904
55	29	48.287	3.078	5.385165	.5715703	47.16672	49.40728
56	16	55.918	6.271	4	1.56775	52.84521	58.99079

57	38	41.377	2.881	6.164414	.4673599	40.46097	42.29303
58	14	43.91	3.396	3.741657	.9076192	42.13107	45.68893
59	18	47.879	4.193	4.242641	.9882996	45.94193	49.81607
60	23	45.243	2.228	4.795832	.4645701	44.33244	46.15356
61	23	53.571	3.738	4.795832	.7794269	52.04332	55.09868
62	23	40.413	3.879	4.795832	.8088274	38.82770	41.99830
63	22	40.096	4.758	4.690416	1.014409	38.10776	42.08424
64	18	48.479	5.355	4.242641	1.262186	46.00512	50.95288
65	22	49.252	3.929	4.690416	.8376656	47.61018	50.89382
66	23	36.9	3.033	4.795832	.6324242	35.66045	38.13955
67	17	40.431	5.458	4.123106	1.323759	37.83643	43.02557
68	21	56.57	4.207	4.582576	.9180427	54.77064	58.36936
69	19	50.957	5.379	4.358899	1.234027	48.53831	53.37569
70	24	42.117	2.773	4.898979	.5660363	41.00757	43.22643
71	23	46.379	3.34	4.795832	.6964381	45.01398	47.74402
72	24	47.864	2.989	4.898979	.6101271	46.66815	49.05985
73	10	38.531	4.066	3.162278	1.285782	36.01087	41.05113
74	19	39.724	3.457	4.358899	.7930902	38.16954	41.27846
75	21	49.948	5.868	4.582576	1.280503	47.43821	52.45779
76	21	43.759	3.584	4.582576	.7820929	42.22610	45.29190
77	22	52.643	3.794	4.690416	.8088835	51.05759	54.22841
Ave	21.	45.22221	3.928065	4.603377	.8685763	43.51980	46.92462
Max	40	59.475	6.436	6.324555	1.56775	56.82655	62.12345
Min	10	31.584	2.211	3.162278	.4513185	30.15530	33.01270

RVPEP/AT

Individual means and confidence intervals

Pt	No	Mean	SD	Rt.No.	SEM	95%-	95%+
1	24	.6915	.1014	4.898979	.0206982	.6509316	.7320684
2	13	.7302	.0494	3.605551	.0137011	.7033459	.7570541
3	19	.5654	.0458	4.358899	.0105072	.5448058	.5859942
4	22	.6876	.1172	4.690416	.0249871	.6386252	.7365748
5	24	.6432	.0785	4.898979	.0160237	.6117935	.6746065
6	24	.6231	.078	4.898979	.0159217	.5918935	.6543065
7	20	.5965	.071	4.472136	.0158761	.5653829	.6276171
8	24	.9005	.125	4.898979	.0255155	.8504896	.9505104
9	21	.6518	.0965	4.582576	.0210580	.6105263	.6930737
10	24	.6904	.1025	4.898979	.0209227	.6493915	.7314085
11	21	1.0976	.2557	4.582576	.0557983	.9882353	1.206965
12	20	.7439	.0913	4.472136	.0204153	.7038860	.7839140
13	24	.6892	.0823	4.898979	.0167994	.6562731	.7221269
14	18	.7254	.1256	4.242641	.0296042	.6673758	.7834242
15	22	.7447	.0881	4.690416	.0187830	.7078854	.7815146
16	14	.6584	.0724	3.741657	.0193497	.6204746	.6963254
17	24	.85	.1468	4.898979	.0299654	.7912678	.9087322
18	17	.6523	.1005	4.123106	.0243748	.6045253	.7000747
19	22	.7582	.1037	4.690416	.0221089	.7148665	.8015335
20	18	.6429	.0815	4.242641	.0192097	.6052489	.6805511
21	32	.7794	.086	5.656854	.0152028	.7496025	.8091975
22	20	.9717	.0906	4.472136	.0202588	.9319928	1.011407
23	24	.5667	.0633	4.898979	.0129211	.5413747	.5920253
24	24	.8175	.1308	4.898979	.0266994	.7651691	.8698309
25	20	.7715	.1148	4.472136	.0256701	.7211867	.8218133
26	24	.8017	.1178	4.898979	.0240458	.7545702	.8488298
27	21	.6044	.056	4.582576	.0122202	.5804484	.6283516
28	22	.8764	.1427	4.690416	.0304237	.8167695	.9360305
29	20	.6806	.0961	4.472136	.0214886	.6384823	.7227177
30	19	.7798	.1104	4.358899	.0253275	.7301581	.8294419
31	16	.8886	.1431	4	.035775	.818481	.958719
32	31	.7008	.0835	5.567764	.0149970	.6714058	.7301942
33	17	1.0336	.1654	4.123106	.0401154	.9549738	1.112226
34	21	.8291	.0945	4.582576	.0206216	.7886817	.8695183
35	40	1.1265	.1755	6.324555	.0277490	1.072112	1.180888
36	20	.7048	.1037	4.472136	.0231880	.6593515	.7502485
37	24	.6676	.0531	4.898979	.0108390	.6463556	.6888444
38	24	.7249	.0925	4.898979	.0188815	.6878923	.7619077
39	18	.6005	.0616	4.242641	.0145193	.5720423	.6289577
40	20	.6747	.0813	4.472136	.0181792	.6390687	.7103313
41	21	.6794	.0912	4.582576	.0199015	.6403931	.7184069
42	24	.9189	.3067	4.898979	.0626049	.7961944	1.041606
43	15	.8107	.0582	3.872983	.0150272	.7812467	.8401533
44	18	.6043	.053	4.242641	.0124922	.5798152	.6287848
45	24	1.0904	.1492	4.898979	.0304553	1.030708	1.150092
46	18	.8912	.1712	4.242641	.0403522	.8121096	.9702904
47	16	1.3166	.1926	4	.04815	1.222226	1.410974
48	21	.6817	.0792	4.582576	.0172829	.6478256	.7155744
49	33	.7018	.096	5.744563	.0167115	.6690455	.7345545
50	17	.633	.0663	4.123106	.0160801	.6014830	.6645170
51	14	1.0964	.1406	3.741657	.0375769	1.022749	1.170051
52	21	.5597	.056	4.582576	.0122202	.5357484	.5836516
53	24	1.058	.1958	4.898979	.0399675	.9796637	1.136336
54	24	.685	.071	4.898979	.0144928	.6565941	.7134059
55	29	.6067	.0699	5.385165	.0129801	.5812590	.6321410
56	16	.8091	.1449	4	.036225	.738099	.880101

57	38	1.1342	.1772	6.164414	.0287456	1.077859	1.190541
58	14	.7807	.1186	3.741657	.0316972	.7185735	.8428265
59	18	.674	.1334	4.242641	.0314427	.6123723	.7356277
60	23	.8169	.1113	4.795832	.0232077	.7714130	.8623870
61	23	.5918	.0743	4.795832	.0154926	.5614345	.6221655
62	23	1.1704	.1567	4.795832	.0326742	1.106359	1.234441
63	22	1.3498	.2363	4.690416	.0503793	1.251057	1.448543
64	18	.7635	.173	4.242641	.0407765	.6835781	.8434219
65	22	.7344	.0847	4.690416	.0180581	.6990061	.7697939
66	23	.9129	.1267	4.795832	.0264188	.8611192	.9646808
67	17	.7404	.1209	4.123106	.0293226	.6829278	.7978722
68	21	.4989	.0512	4.582576	.0111728	.4770014	.5207986
69	19	.6496	.1089	4.358899	.0249834	.6006326	.6985674
70	24	.9744	.095	4.898979	.0193918	.9363921	1.012408
71	23	.7068	.0702	4.795832	.0146377	.6781101	.7354899
72	24	.6857	.0914	4.898979	.0186569	.6491324	.7222676
73	10	1.0935	.1781	3.162278	.0563202	.9831125	1.203888
74	19	1.0572	.1247	4.358899	.0286081	1.001128	1.113272
75	21	.7717	.1172	4.582576	.0255751	.7215727	.8218273
76	21	.8525	.0957	4.582576	.0208835	.8115684	.8934316
77	22	.8429	.1092	4.690416	.0232815	.7972682	.8885318
Ave	21.	.7907623	.1113299	4.603377	.0244804	.7427808	.8387439
Max	40	1.3498	.3067	6.324555	.0626049	1.251057	1.448543
Min	10	.4989	.0458	3.162278	.0105072	.4770014	.5207986

PAVmax (cm/sec)

Individual means and confidence intervals

Pt.	No.	Mean	SD	Rt No.	SEM	95%-	95%+
1	24	135.83	4.34	4.898979	.8858988	134.0936	137.5664
2	13	52.31	3.88	3.605551	1.076118	50.20081	54.41919
3	19	48.95	2.09	4.358899	.4794789	48.01022	49.88978
4	22	68.86	3.06	4.690416	.6523942	67.58131	70.13869
5	24	50.21	2.75	4.898979	.5613414	49.10977	51.31023
6	24	48.96	2.07	4.898979	.4225370	48.13183	49.78817
7	20	46.25	2.75	4.472136	.6149187	45.04476	47.45524
8	24	50.42	2.52	4.898979	.5143928	49.41179	51.42821
9	21	42.14	3.38	4.582576	.7375765	40.69435	43.58565
10	24	135.83	4.34	4.898979	.8858988	134.0936	137.5664
11	21	40.95	2.56	4.582576	.5586378	39.85507	42.04493
12	20	40.95	2.56	4.472136	.5724334	39.82803	42.07197
13	24	59.17	2.41	4.898979	.4919392	58.20580	60.13420
14	18	51.67	2.43	4.242641	.5727565	50.54740	52.79260
15	22	57.73	3.69	4.690416	.7867106	56.18805	59.27195
16	14	46.07	3.5	3.741657	.9354143	44.23659	47.90341
17	24	40.21	1.02	4.898979	.2082066	39.80192	40.61808
18	17	74.41	3.91	4.123106	.9483143	72.55130	76.26870
19	22	42.05	2.52	4.690416	.5372658	40.99696	43.10304
20	18	70.28	3.2	4.242641	.7542472	68.80168	71.75832
21	32	54.96	3.35	5.656854	.5922019	53.79928	56.12072
22	20	49.5	1.54	4.472136	.3443545	48.82507	50.17493
23	24	54.17	3.19	4.898979	.6511560	52.89373	55.44627
24	24	48.54	3.12	4.898979	.6368673	47.29174	49.78826
25	20	62.25	5.25	4.472136	1.173936	59.94909	64.55091
26	24	40.83	1.9	4.898979	.3878359	40.06984	41.59016
27	21	49.76	1.09	4.582576	.2378575	49.29380	50.22620
28	22	50.45	2.13	4.690416	.4541175	49.55993	51.34007
29	20	44.75	1.97	4.472136	.4405054	43.88661	45.61339
30	19	65.53	3.69	4.358899	.8465441	63.87077	67.18923
31	16	85	6.83	4	1.7075	81.6533	88.3467
32	31	107.42	5.9	5.567764	1.059671	105.3430	109.4970
33	17	40.29	1.21	4.123106	.2934681	39.71480	40.86520
34	21	40.95	2.01	4.582576	.4386180	40.09031	41.80969
35	40	113.13	7.48	6.324555	1.182692	110.8119	115.4481
36	20	52.75	3.02	4.472136	.6752925	51.42643	54.07357
37	24	68.96	2.54	4.898979	.5184753	67.94379	69.97621
38	24	57.5	2.55	4.898979	.5205166	56.47979	58.52021
39	18	73.33	2.97	4.242641	.7000357	71.95793	74.70207
40	20	67.75	4.44	4.472136	.9928142	65.80408	69.69592
41	21	51.43	3.22	4.582576	.7026616	50.05278	52.80722
42	24	58.75	3.97	4.898979	.8103729	57.16167	60.33833
43	15	57.67	4.17	3.872983	1.076689	55.55969	59.78031
44	18	62.22	5.21	4.242641	1.228009	59.81310	64.62690
45	24	100.42	4.15	4.898979	.8471152	98.75965	102.0803
46	18	46.11	3.66	4.242641	.8626703	44.41917	47.80083
47	16	103.44	9.08	4	2.27	98.9908	107.8892
48	21	60.71	2.87	4.582576	.6262853	59.48248	61.93752
49	33	85	4.84	5.744563	.8425359	83.34863	86.65137
50	17	59.12	1.96	4.123106	.4753698	58.18828	60.05172
51	14	58.57	3.06	3.741657	.8178194	56.96707	60.17293
52	21	54.29	3.27	4.582576	.7135725	52.89140	55.68860
53	24	57.92	4.15	4.898979	.8471152	56.25965	59.58035
54	24	46.67	3.51	4.898979	.7164757	45.26571	48.07429
55	29	90	5.35	5.385165	.9934701	88.05280	91.94720
56	16	63.75	5	4	1.25	61.3	66.2

57	38	96.71	6.81	6.164414	1.104728	94.54473	98.87527
58	14	92.5	3.8	3.741657	1.015593	90.50944	94.49056
59	18	144.72	6.29	4.242641	1.482567	141.8142	147.6258
60	23	59.35	1.72	4.795832	.3586448	58.64706	60.05294
61	23	70.22	3.84	4.795832	.8006953	68.65064	71.78936
62	23	61.74	3.57	4.795832	.7443965	60.28098	63.19902
63	22	55.45	3.42	4.690416	.7291464	54.02087	56.87913
64	18	56.39	4.47	4.242641	1.053589	54.32497	58.45503
65	22	68.18	4.24	4.690416	.9039710	66.40822	69.95178
66	23	52.83	3.31	4.795832	.6901827	51.47724	54.18276
67	17	68.82	3.32	4.123106	.8052183	67.24177	70.39823
68	21	41.19	4.45	4.582576	.9710696	39.28670	43.09330
69	19	57.11	3.46	4.358899	.7937784	55.55419	58.66581
70	24	58.12	4.38	4.898979	.8940638	56.36764	59.87236
71	23	56.09	3.68	4.795832	.7673330	54.58603	57.59397
72	24	73.96	3.9	4.898979	.7960842	72.39968	75.52032
73	10	44.5	3.69	3.162278	1.166880	42.21291	46.78709
74	19	53.95	3.94	4.358899	.9038980	52.17836	55.72164
75	21	42.86	2.54	4.582576	.5542734	41.77362	43.94638
76	21	63.33	3.29	4.582576	.7179369	61.92284	64.73716
77	22	53.41	3.58	4.690416	.7632586	51.91401	54.90599
Ave	21.5	63.09831	3.562727	4.603377	.7811482	61.56726	64.62936
Max	40	144.72	9.08	6.324555	2.27	141.8142	147.6258
Min	10	40.21	1.02	3.162278	.2082066	39.28670	40.61808

APPENDIX TWO

ANOVA ON SCATTER WITHIN AND BETWEEN SUBJECTS FOR EACH RVSTI

One-way analysis of variance   RVPEP

Individual 95% confidence intervals based on pooled s.d.

```
Sub No. Mean    SD

 1   24  100.00 6.76                   <*>
 2   13  127.31 4.39                                         < * >
 3   19   78.95 3.15  <*->
 4   22   80.23 6.81   <*->
 5   24  117.50 7.94                                 <-*>
 6   24  114.37 7.56                                <*->
 7   20   93.00 6.16           <-*>
 8   24   97.29 6.59             <-*>
 9   21   87.86 8.30        <-*->
10   24  100.21 6.51                   <*->
11   21  108.57 6.15                       <*->
12   20   97.25 6.38                 <-*>
13   24   98.13 6.73                  <*->
14   18   98.06 9.87                 <-*->
15   22  102.95 8.68                    <*->
16   14  100.36 5.36                  <-*->
17   24   87.92 6.90         <-*>
18   17   91.76 9.67           <-*->
19   22   99.32 6.60               <-*>
20   18   95.00 7.28             <-*>
21   32  102.01 7.61                   <*>
22   20  116.00 5.76                               <-*->
23   24   84.37 6.48      <*->
24   24  111.4610.48                           <-*>
25   20   91.50 6.51          <-*>
26   24  122.71 9.44                                    <*->
27   21   91.90 5.36           <-*->
28   22  100.91 8.82                   <*->
29   20  112.25 8.03                           <*->
30   19   91.58 5.79           <-*>
31   16   91.25 9.92           <-*>
32   31   94.19 6.84             <*>
33   17  113.53 8.06                             <-*->
34   21  100.24 6.61                   <*->
35   40  115.00 8.70                             <-*>
36   20   92.50 6.98             <*->
37   24   88.96 4.42          <*->
38   24  116.67 7.47                               <*->
39   18   95.28 6.52              <-*>
40   20   98.25 5.70                <*->
41   21   81.67 4.83    <-*>
42   24  107.71 8.34                      <-*>
43   15  120.00 8.45                                 <-*->
                     ---/--------/--------/--------/--------/------/------/-
                       80      90      100     110      120   130    140
                                                           (ms)
```

```
  44   18   81.11 6.08   <-*>
  45   24  107.08 6.06                       <-*>
  46   18   96.39 8.37               <-*->
  47   16  118.13 6.80                                <-*->
  48   21  113.10 6.98                             <-*>
  49   33   93.64 7.73              <*>
  50   17   92.94 5.32             <*->
  51   14  115.71 5.50                      <-*->
  52   21   93.33 7.13              <-*>
  53   24  102.71 5.31                     (*->
  54   24  107.99 6.08                       <-*>
  55   29   89.69 6.35        <-*>
  56   16  131.56 9.26                                          <-*->
  57   38  120.00 8.62                                  <*>
  58   14  102.8610.32                   <-*->
  59   18   97.50 9.74               <-*>
  60   23   93.26 8.48              <-*>
  61   23   89.78 6.12            <-*>
  62   23  132.83 9.39                                             <*->
  63   22  120.45 6.53                            <*->
  64   18   83.33 8.22     <-*>
  65   22  108.86 8.16                        <*->
  66   23   92.83 6.37             <*->
  67   17   90.29 5.99           <-*->
  68   21   97.62 5.84               <-*>
  69   19  101.05 8.59                  <-*>
  70   24  124.58 6.41                                       <*->
  71   23  112.39 7.36                             <*->
  72   24  104.79 8.01                      <*->
  73   10  115.50 9.26                      <--*->
  74   19  119.74 8.41                          <-*->
  75   21  106.38 9.17                         <-*>
  76   21  110.71 5.76                           <*->
  77   22  120.68 9.04                                   <*->

                  ---/-------/-------/-------/-------/-------/-------/------
                    80     90     100    110    120    130    140 (ms)
```

Analysis of variance on RVPEP

Source	Degrees freedom	Sum squares	Mean squares	F
Subjects	76	259847.2	3419.0	62.53
Error	1575	86113.4	54.7	
Total	1651	345960.6		

One-Way Analysis of Variance on RVET

Individual 95% confidence intervals based on pooled s.d.

```
Pt N   Mean   SD

 1 24  302.9 10.31            <*>
 2 13  294.6  9.23          <*>
 3 19  306.3 12.57            <*>
 4 22  310.9  9.59             <*>
 5 24  322.9 10.42                <*>
 6 24  335.6  7.56                  <*>
 7 20  298.3 11.39           <*>
 8 24  300.8 10.29           <*>
 9 21  349.3 12.38                     <*>
10 24  302.9 10.31            <*>
11 21  284.3  8.56        <*>
12 20  303.0 13.61            <*>
13 24  301.5 13.23           <*>
14 18  290.3 14.29         <*>
15 22  304.8 13.49            <*>
16 14  314.3  6.75               <*>
17 24  333.3 11.39                   <*>
18 17  327.1 18.03                <*->
19 22  289.1 10.08          <*>
20 18  273.6  7.24      <*>
21 32  308.3 10.75              <*>
22 20  333.3 14.53                   <*>
23 24  309.4  9.01              <*>
24 24  300.6  9.81           <*>
25 20  248.0 11.05 <*>
26 24  317.3  8.58              <*>
27 21  287.9  9.95          <*>
28 22  322.1 11.20                    <*>
29 20  330.5 12.24                       <*>
30 19  228.7  6.20<*>
31 16  277.5  8.16       <*->
32 31  353.7 13.41                           <*>
33 17  257.4  6.64  <*->
34 21  300.0 11.94           <*>
35 40  268.1  8.96     <*>
36 20  275.8 11.95      <*>
37 24  300.4  8.59           <*>
38 24  313.3 11.29               <*>
39 18  296.7 10.29          <*>
40 20  327.8 10.57                  <*>
41 21  332.6 11.47                   <*>
42 24  326.3 11.63                  <*>
43 15  294.7 11.09          <*>
                ----/----/----/----/----/----/----/---
                   250       300       350       400    (ms)
```

```
44 18  296.1  9.00          <*>
45 24  297.3 22.26          <*>
46 18  296.9 12.73          <*>
47 16  229.4 20.48>
48 21  369.3  7.46                              <*>
49 33  305.2 13.26             <*>
50 17  299.4  5.83          <*>
51 14  263.2 17.50   <-*>
52 21  317.4 12.61               <*>
53 24  300.8  7.61           <*>
54 24  334.2  6.20                   <*>
55 29  308.1  8.28              <*>
56 16  296.3  9.40          <*>
57 38  259.5 18.52    <*>
58 14  302.9  9.75          <-*>
59 18  308.9 29.38              <*>
60 23  254.1  8.87  <*>
61 23  285.7 11.11         <*>
62 23  283.9  9.41         <*>
63 22  227.3 12.60>
64 18  230.8  8.95>
65 22  303.2 11.60            <*>
66 23  278.5 12.47       <*>
67 17  307.7  9.54            <-*>
68 21  348.1 11.45                     <*>
69 19  310.3 10.60              <*>
70 24  305.2  6.51            <*>
71 23  344.8  8.85                    <*>
72 24  321.9  9.98               <*>
73 10  278.5 10.55      <-*>
74 19  287.6 11.83        <-*>
75 21  282.9 11.57        <*>
76 21  299.3  8.70           <*>
77 22  274.1  7.32      <*>
                 ---/----/----/----/----/----/----/----/----
                   250       300       350       400   (ms)
```

Source	Deg. Freedom	Sum Sq	Mean Sq	F
Subjects	76	1331763	17523	129.06
Error	1575	213844	136	
Total	1651	1545608		

One-way analysis of variance - AT (Acceleration Time)

Mean and 95% confidence intervals based on pooled s.d.

Sub.	No.	Mean	S.d.	
1	24	146.46	14.10	<-*>
2	13	175.00	12.25	<-*->
3	19	140.26	9.64	<-*->
4	22	118.41	11.79	<-*>
5	24	184.17	14.72	<-*>
6	24	185.21	15.21	<-*>
7	20	157.00	10.93	<-*>
8	24	109.17	9.17	<*->
9	21	136.43	14.59	<-*->
10	24	147.08	14.59	<*>
11	21	102.86	18.41	<*->
12	20	131.75	10.17	<-*>
13	24	143.64	12.55	<*>
14	18	136.94	12.50	<-*->
15	22	138.41	8.51	<-*>
16	14	153.57	12.77	<-*->
17	24	105.21	11.86	<*>
18	17	142.06	12.00	<-*>
19	22	132.50	12.79	<-*>
20	18	148.89	10.23	<-*>
21	32	131.72	10.21	<-*>
22	20	120.00	8.11	<*->
23	24	149.58	8.33	<-*>
24	24	137.92	12.33	<*->
25	20	120.85	13.62	<*->
26	24	154.79	13.55	<*->
27	21	152.62	7.52	<-*>
28	22	116.59	10.62	<*->
29	20	166.75	14.98	<*->
30	19	118.68	10.12	<-*->
31	16	103.75	9.57	<-*>
32	31	135.48	11.57	<-*>
33	17	111.47	11.96	<-*->
34	21	121.67	8.11	<-*>
35	40	103.75	12.18	<*>
36	20	133.00	14.55	<-*->
37	24	133.75	8.24	<*->
38	24	162.71	16.35	<*->
39	18	159.44	11.49	<-*>
40	20	147.00	13.51	<-*->
41	21	121.90	14.79	<-*>
42	24	123.12	19.88	<*->
43	15	148.33	9.57	<*->
44	18	134.72	10.07	<*->
45	24	99.38	9.48	<*->

--/-------/-------/-------/-------/-------/-------/

87 105 123 140 158 175 19

(ms)

```
45   24  36.238 3.693                 <*->
46   18  32.557 3.600          <-*>
47   16  52.024 6.848                                           <-*->
48   21  30.658 2.298         <-*>
49   33  30.790 3.313          <*>
50   17  31.054 1.907          <-*->
51   14  44.228 4.601                              <-*->
52   21  29.457 2.582        <*->
53   24  34.173 2.142               <*->
54   24  32.132 2.202            <*>
55   29  29.157 2.538       <*>
56   16  44.494 4.037                               <*->
57   38  46.444 6.234                                    <*>
58   14  34.042 3.995              <-*->
59   18  32.029 5.774           <-*->
60   23  36.813 4.193                   <-*>
61   23  31.517 3.010           <-*>
62   23  46.868 4.152                                   <-*>
63   22  53.219 4.837                                              <*->
64   18  36.240 4.723                   <*->
65   22  36.004 3.581                   <*>
66   23  33.404 2.771             <*->
67   17  29.406 2.544        <*->
68   21  28.070 1.884      <*->
69   19  32.667 3.582            <-*>
70   24  40.859 2.682                          <*>
71   23  32.635 2.546            <-*>
72   24  32.609 2.956            <-*>
73   10  41.570 4.131                         <--*->
74   19  41.707 3.540                          <-*>
75   21  38.085 4.207                     <*->
76   21  37.043 2.514                    <*>
77   22  44.052 3.489
                     --/-------/-------/-------/-------/-------/-------/
                      25      30      35      40      45      50      55
```

Analysis of variance on RVPEP/RVET

Source	Deg. freedom	Sum squares	Mean squares	F
Subjects	76	57684.6	759.0	67.52
Error	1575	17704.8	11.2	
Total	1651	75389.4		

One-way analysis of variance on PA max velocity

Mean and 95% confidence intervals based on pooled s.d.

```
Sub No. Mean   S.d.

1   24 135.83 4.34                                        <*>
2   13  52.31 3.88        <*>
3   19  48.95 2.09      <*>
4   22  68.86 3.06              <*>
5   24  50.21 2.75       <*>
6   24  48.96 2.07      <*>
7   20  46.25 2.75     <*>
8   24  50.42 2.52       <*>
9   21  42.14 3.38   <*>
10  24 135.83 4.34                                         <*>
11  21  40.95 2.56  <*>
12  20  40.25 1.12  <*>
13  24  59.17 2.41          <*>
14  18  51.67 2.43        <*>
15  22  57.73 3.69          <*>
16  14  46.07 3.50     <*>
17  24  40.21 1.02   <*>
18  17  74.41 3.91                 <*>
19  22  42.05 2.52    <*>
20  18  70.28 3.20               <*>
21  32  54.69 3.35         <*>
22  20  49.50 1.54      <*>
23  24  54.17 3.19         <*>
24  24  48.54 3.12      <*>
25  20  62.25 5.25            <*>
26  24  40.83 1.90   <*>
27  21  49.76 1.09       <*>
28  22  50.45 2.13       <*>
29  20  44.75 1.97     <*>
30  19  65.53 3.69             <*>
31  16  85.00 6.83                     <*>
32  31 107.42 5.90                              <*>
33  17  40.29 1.21    <*>
34  21  40.95 2.01    <*>
35  40 113.13 7.48                                 <*>
36  20  52.75 3.02        <*>
37  24  69.96 2.54               <*>
38  24  57.50 2.55          <*>
39  18  73.33 2.97                <*>
40  20  67.75 4.44              <*>
41  21  51.43 3.22        <*>
42  24  58.75 3.97          <*>
43  15  57.67 4.17          <*>
44  18  62.22 5.21            <*>
45  24 100.42 4.15                           <*>
                     --/-------/-------/-------/-------/-------/-------/
                      50      70      90      110     130     150     17
                                                           (cm/sec)
```

```
46   18  110.28  12.77          <-*>
47   16   91.25  12.18 <-*->
48   21  167.14  13.28                                    <-*>
49   33  134.70  11.72                    <*->
50   17  147.65   9.86                           <-*->
51   14  106.79  11.20        <-*>
52   21  167.38   9.03                                    <-*>
53   24   99.79  16.52    <-*>
54   24  157.50  10.22                                 <*>
55   29  148.79  10.66                            <-*>
56   16  165.94  21.77                                     <*->
57   38  107.37  11.01         <*>
58   14  132.86   9.14                   <-*->
59   18  147.78  18.49                            <*->
60   23  115.00   7.39             <-*>
61   23  153.04  12.41                              <-*>
62   23  114.78  12.29            <-*>
63   22   91.14  11.85   <*->
64   18  112.22  15.55          <-*->
65   22  149.09   9.96                            <-*>
66   23  102.61   7.67        <*->
67   17  124.41  17.67                 <-*>
68   21  196.90  15.85                                                 <*
->
69   19  158.16  18.42                                 <*->
70   24  128.54   8.78                  <-*>
71   23  159.78  10.50                                 <-*>
72   24  154.17  12.22                                <*>
73   10  107.50  14.19        <--*->
74   19  114.21  10.44           <-*>
75   21  141.19  16.50                          <*->
76   21  130.95  11.14                    <*->
77   22  144.32  11.16                           <*->
                      --/-------/-------/-------/-------/-------/-------/
                       87      105     123     140     158     175    193
                                                             (ms)
```

Analysis of variance on AT

Source	Deg. Freedom	Sum squares	Mean squares	F
Subjects	76	871653	11469	73.22
Error	1525	246544	157	
Total	1651	1118197		

```
          One-way analysis of variance on AT/RVET

          Mean and 95% confidence intervals based on pooled s.d.

Subj No. Mean   S.d.
1    24  48.387 4.786                               <*->
2    13  59.475 4.872                                                <-*-
->
3    19  45.816 3.019                         <-*->
4    22  38.050 3.246              <-*->
5    24  56.990 3.481                                            <-*->
6    24  55.173 4.204                                          <*->
7    20  52.681 3.778                                      <-*>
8    24  36.343 3.481            <*->
9    21  39.110 4.343               <-*->
10   24  48.603 5.052                               <-*>
11   21  36.163 6.436           <-*->
12   20  43.538 3.473                      <-*>
13   24  47.666 4.251                             <-*>
14   18  47.173 3.631                            <-*->
15   22  45.479 3.140                           <*->
16   14  48.876 4.071                                <-*->
17   24  31.584 3.571   <-*>
18   17  43.481 3.519                      <*->
19   22  45.805 3.757                           <-*>
20   18  54.397 3.014                                          <*->
21   32  42.784 3.710                     <-*>
22   20  36.052 2.608           <-*->
23   24  48.347 2.211                                <*->
24   24  45.863 3.676                           <-*>
25   20  48.569 5.830                                <-*>
26   24  48.764 3.732                                <-*>
27   21  53.064 2.893                                       <-*->
28   22  36.187 2.822            <*->
29   20  50.409 3.449                                    <*->
30   19  51.924 4.520                                    <-*->
31   16  37.364 2.969             <-*->
32   31  38.338 3.345               <*->
33   17  43.362 4.957                      <-*->
34   21  40.583 2.588                  <-*>
35   40  38.674 4.144               <-*>
36   20  48.214 4.779                              <-*->
37   24  44.542 2.787                        <-*>
38   24  51.947 5.081                                    <-*->
39   18  53.773 3.840                                       <-*->
40   20  44.838 3.703                        <-*->
41   21  36.638 4.173            <-*>
42   24  37.692 5.943              <-*>
43   15  50.446 4.287                                  <-*->

                     ---/-------/-------/-------/-------/-------/-------/
---
                       30      35      40      45      50      55      60
```

```
44   18  45.502 3.220                         <-*>
45   24  33.633 4.324      <-*>
46   18  37.157 4.143             <-*->
47   16  39.999 5.743                 <-*->
48   21  45.256 3.418                          <*->
49   33  44.164 3.556                        <*->
50   17  49.294 2.780                               <-*->
51   14  40.626 3.879                  <-*->
52   21  52.794 3.322                                     <-*>
53   24  33.151 5.333      <*->
54   24  47.132 2.917                             <*->
55   29  48.287 3.078                               <*->
56   16  55.918 6.271                                           <-*->
57   38  41.377 2.881                    <*->
58   14  43.910 3.396                       <-*->
59   18  47.879 4.193                               <-*->
60   23  45.243 2.228                          <*->
61   23  53.571 3.738                                       <-*>
62   23  40.413 3.879                   <*->
63   22  40.096 4.758                 <-*->
64   18  48.479 5.355                                <*->
65   22  49.252 3.939                                 <*->
66   23  36.900 3.033    <-*->
67   17  40.431 5.458                   <*->
68   21  56.570 4.207                                            <-*>
69   19  50.957 5.379                                   <-*->
70   24  42.117 2.773                    <-*->
71   23  46.379 3.340                            <*->
72   24  47.864 2.989                             <-*>
73   10  38.531 4.066              <--*->
74   19  39.724 3.457                 <-*->
75   21  49.948 5.868                                 <-*->
76   21  43.759 3.584                       <-*>
77   22  52.643 3.794                                    <-*>
                     ---/--------/--------/--------/--------/--------/--------/
                       30      35      40      45      50      55      60
```

Analysis of variance on AT/RVET

Source	Deg. freedom	Sum squares	Mean squares	F
Subjects	76	64413.8	847.6	53.41
Error	1575	24992.8	15.9	
Total	1651	89406.7		

```
         One-way analysis of variance on RVPEP/RVET x 100%

         Means and 95% confidence intervals based on pooled s.d.

Subj No. Mean   S.d.
1    24  33.065 2.755              <*>
2    13  43.261 2.239                             <-*->
3    19  25.821 1.564  <-*>
4    22  25.859 2.705  <-*>
5    24  36.466 3.273                   <*->
6    24  34.114 2.665               <*>
7    20  31.277 3.039           <*->
8    24  32.378 2.490             <*->
9    21  25.233 3.014  <*->
10   24  33.137 2.722             <*>
11   21  38.230 2.599                      <*->
12   20  32.180 2.817            <*->
13   24  32.660 3.263            <-*>
14   18  33.954 4.626              <-*->
15   22  33.915 3.907               <*>
16   14  31.951 1.898          <-*->
17   24  26.429 2.527    <*->
18   17  28.221 3.982      <*->
19   22  34.429 3.007               <*->
20   18  34.791 3.339               <-*>
21   32  33.158 3.022              <*>
22   20  34.890 2.586               <-*>
23   24  27.337 2.740     <*->
24   24  37.172 4.251                    <*->
25   20  36.954 2.974                   <-*>
26   24  38.746 3.711                      <-*>
27   21  31.971 2.294            <*>
28   22  31.419 3.499           <*->
29   20  34.057 3.318               <*->
30   19  40.087 2.957                         <*->
31   16  32.879 3.330           <-*->
32   31  26.667 2.195   <-*>
33   17  44.126 3.091                               <*->
34   21  33.491 2.903              <*->
35   40  42.994 4.198                              <*>
36   20  33.590 2.724             <-*>
37   24  29.653 2.022       <-*>
38   24  37.325 3.304                    <*->
39   18  32.181 2.842            <*->
40   20  30.002 1.789         <*>
41   21  24.600 1.927*>
42   24  33.102 3.391            <*>
43   15  40.829 3.850                        <-*->
44   18  27.403 2.008   <*->

                     --/-------/-------/-------/-------/-------/-------/
                      25      30      35      40      45      50      55
```

```
46  18  46.11  3.66     <*>
47  16 103.44  9.08                            <*>
48  21  60.71  2.87           <*>
49  33  85.00  4.84                     <*>
50  17  59.17  1.96           <*>
51  14  58.57  3.06           <*>
52  21  54.29  3.27         <*>
53  24  57.92  4.15          <*>
54  24  46.67  3.51     <*>
55  29  90.00  5.35                       <*>
56  16  63.75  5.00            <*>
57  38  96.71  6.81                          <*>
58  14  92.50  3.80                        <*>
59  18 144.72  6.29                                             <*>
60  23  59.35  1.72           <*>
61  23  70.22  3.84               <*>
62  23  61.74  3.57            <*>
63  22  55.45  3.42         <*>
64  18  56.39  4.47          <*>
65  22  68.18  4.24              <*>
66  23  52.83  3.31        <*>
67  17  68.82  3.32              <*)
68  21  41.19  4.45     <*>
69  19  57.11  3.46          <*>
70  24  58.12  4.38          <*>
71  23  56.09  3.68         <*>
72  24  73.96  3.90                 <*>
73  10  44.50  3.69     <*>
74  19  53.95  3.94         <*>
75  21  42.86  2.54    <*>
76  21  63.33  3.29            <*>
77  22  53.41  3.58         <*>
                    ------/-------/-------/-------/-------/-------/-----

                         50      70      90      110     130     150
                                                       (cm/sec)
```

Analysis of variance on PA Vmax

Source	Deg. Freedom	Sum squares	Mean squares	F
Subjects	76	898478.4	11822.1	773.11
Error	1575	24084.2	15.3	
Total	1651	922562.6		

APPENDIX THREE

CUMULATIVE FREQUENCY DATA FOR PACED PATIENTS FOR EACH RVSTI WITH RESPECT TO THE PR INTERVAL

Results on paced patients

Cumulative frequency nadirs/all/peaks RVPEP

PR interval	Nadirs	All	Peaks	
-520	0	.000463	0	
-490	0	.001664	0	
-480	0	.002772	0	
-470	0	.003698	0	
-460	0	.004936	0	
-450	0	.00784	0	
-445	0	.00852	0	
-440	0	.009711	0	
-435	0	.011934	0	
-420	0	.012447	0	
-405	0	.01493	.008333	-400
-395	0	.015953	.008333	
-390	0	.017143	.008333	
-380	0	.019707	.019444	
-375	0	.020994	.019444	
-370	0	.022659	.019444	
-360	.011111	.027003	.019444	
-355	.011111	.027837	.019444	
-350	.011111	.034368	.052778	
-340	.011111	.037731	.052778	
-335	.011111	.038757	.052778	
-330	.011111	.041762	.052778	
-325	.011111	.044912	.052778	
-320	.011111	.050261	.052778	
-315	.011111	.050724	.052778	
-310	.034444	.057056	.052778	
-305	.034444	.059687	.052778	
-300	.034444	.067745	.052778	-300
-295	.034444	.068579	.052778	
-290	.034444	.074738	.052778	
-285	.034444	.07592	.052778	
-275	.034444	.085754	.052778	
-270	.034444	.099952	.052778	
-265	.034444	.102971	.061111	
-260	.034444	.107626	.061111	
-255	.034444	.109645	.061111	
-250	.034444	.118071	.069444	
-245	.034444	.121907	.069444	
-240	.034444	.130217	.069444	
-235	.034444	.133674	.069444	
-230	.034444	.144375	.077778	
-225	.034444	.149428	.077778	
-220	.067778	.164112	.111111	
-215	.076111	.169154	.111111	
-210	.076111	.174659	.111111	
-205	.076111	.177311	.144444	
-200	.076111	.191959	.152778	-200
-195	.076111	.196112	.152778	
-190	.076111	.206392	.152778	
-185	.109444	.210319	.152778	
-180	.109444	.22253	.152778	
-175	.12254	.227392	.152778	
-170	.135635	.24726	.159444	
-165	.135635	.255366	.192778	
-160	.135635	.273516	.232778	

-155	.135635	.278594	.239444	
-150	.146746	.301896	.287778	
-145	.146746	.308698	.304444	
-140	.146746	.321716	.346111	
-135	.151508	.325759	.379444	
-130	.172937	.341827	.379444	
-125	.172937	.346391	.379444	
-120	.172937	.359032	.379444	
-115	.20627	.369755	.398889	
-110	.20627	.37802	.398889	
-105	.20627	.379731	.398889	
-100	.20627	.393307	.407222	-100
-95	.20627	.398538	.407222	
-90	.20627	.409637	.407222	
-85	.20627	.415615	.407222	
-80	.239603	.424731	.435	
-75	.250714	.429753	.435	
-70	.250714	.439468	.479444	
-65	.250714	.443885	.512778	
-60	.300714	.459777	.512778	
-50	.300714	.473575	.512778	
-45	.300714	.477096	.512778	
-40	.300714	.481461	.512778	
-35	.300714	.485614	.523889	
-30	.300714	.495962	.573889	
-25	.317381	.504897	.607222	
-20	.317381	.517476	.607222	
-15	.317381	.519766	.607222	
-10	.317381	.524096	.607222	
0	.342381	.548122	.607222	0
10	.342381	.550448	.607222	
15	.359048	.555723	.607222	
20	.359048	.560637	.607222	
25	.359048	.562477	.607222	
30	.425714	.568805	.66	
35	.430476	.574833	.66	
40	.451905	.583648	.693333	
45	.451905	.588498	.693333	
50	.458571	.592701	.693333	
55	.458571	.597647	.726667	
60	.458571	.603646	.726667	
65	.458571	.605905	.726667	
70	.491905	.617468	.726667	
75	.508571	.623355	.733333	
80	.546667	.633062	.733333	
85	.546667	.637684	.733333	
90	.586667	.651326	.733333	
95	.586667	.654428	.733333	
100	.586667	.665552	.733333	100
105	.586667	.67104	.733333	
110	.586667	.680849	.788889	
115	.586667	.685461	.788889	
120	.586667	.701679	.788889	
125	.586667	.708071	.788889	
130	.586667	.722775	.788889	
135	.586667	.725957	.8	
140	.62	.733711	.8	
145	.62	.741148	.8	
150	.626667	.752762	.811111	
155	.626667	.758154	.827778	
160	.626667	.766386	.861111	
165	.626667	.769247	.861111	

170	.626667	.77726	.869444	
175	.633333	.782359	.869444	
180	.666667	.791193	.869444	
185	.7	.797033	.886111	
190	.711111	.804111	.886111	
195	.711111	.805369	.886111	
200	.711111	.812549	.902778	200
205	.711111	.814369	.902778	
210	.711111	.822538	.902778	
215	.711111	.827307	.911111	
220	.711111	.836256	.944444	
225	.761111	.842505	.944444	
230	.761111	.846574	.944444	
235	.761111	.847798	.944444	
240	.769444	.853921	.977778	
245	.769444	.858176	.977778	
250	.811111	.868674	.977778	
255	.811111	.869269	.977778	
260	.811111	.875782	.977778	
265	.811111	.882973	.977778	
270	.844444	.890078	.977778	
275	.844444	.892037	.977778	
280	.844444	.899047	.988889	
285	.844444	.90056	.988889	
290	.855556	.90869	.988889	
295	.888889	.911272	.988889	
300	.897222	.91646	.988889	300
305	.897222	.919688	.988889	
310	.897222	.931219	.988889	
315	.897222	.933927	.988889	
320	.897222	.940411	.988889	
325	.897222	.942718	.988889	
330	.897222	.946005	.988889	
335	.897222	.94724	.988889	
340	.897222	.956257	.988889	
345	.897222	.956822	.988889	
350	.947222	.962504	.988889	
355	.947222	.963954	.988889	
360	.947222	.968693	.988889	
365	.947222	.970481	.988889	
370	.955556	.974061	.988889	
375	.955556	.97469	.988889	
380	.955556	.976512	.988889	
385	.966667	.977902	.988889	
390	.966667	.983607	.988889	
395	.966667	.984462	.988889	
400	.966667	.985663	.988889	400
405	.966667	.986176	.988889	
410	.977778	.988486	.988889	
420	.988889	.990186	.988889	
425	.988889	.990815	.988889	
430	.988889	.991328	.988889	
435	.988889	.991923	.988889	
440	.988889	.993254	.988889	
445	.988889	.993849	.988889	
465	.988889	.994312	.988889	
470	.988889	.994908	.988889	
475	.988889	.995514	.988889	
480	.988889	.995977	.988889	
485	.988889	.997167	.988889	
490	1	.99768	.988889	
500	1	.998881	1	

510	1	1	1

Kolmogorov-Smirnov max d for nadirs .209345 at PR interval -8

Kolmogorov-Smirnov max d for peaks .129020 at PR interval 50

Results on paced patients

Cumulative frequency RVET

PR interval	Nadirs	All	Peaks	
-520	0	.000463	0	
-490	0	.001664	0	
-480	0	.002772	0	
-470	0	.003698	0	
-460	0	.004936	0	
-450	0	.00784	0	
-445	0	.00852	0	
-440	0	.009711	0	
-435	0	.011934	0	
-430	0	.012447	0	
-420	0	.014205	0	
-405	0	.01493	0	
-400	0	.015525	0	-400
-395	0	.015953	0	
-390	0	.017143	0	
-380	0	.019707	0	
-375	0	.020994	0	
-370	0	.022659	0	
-360	0	.027003	0	
-355	0	.027837	0	
-350	0	.034368	0	
-340	0	.037731	0	
-335	0	.038757	0	
-330	0	.041762	0	
-325	0	.044912	0	
-320	0	.050261	0	
-315	0	.050724	0	
-310	0	.057056	0	
-305	0	.059687	0	
-300	0	.067745	0	-300
-295	0	.068579	0	
-290	0	.074738	0	
-285	0	.07592	0	
-280	0	.082776	.033333	
-275	0	.085754	.033333	
-270	0	.099952	.033333	
-265	0	.102971	.033333	
-260	0	.107626	.033333	
-255	0	.109645	.033333	
-250	0	.118071	.033333	
-245	0	.121907	.033333	
-240	0	.130217	.033333	
-235	0	.133674	.033333	
-230	0	.144375	.033333	
-225	0	.149426	.033333	
-220	0	.164112	.033333	
-215	0	.169154	.033333	
-210	.016667	.174659	.033333	
-205	.016667	.177311	.033333	
-200	.016667	.191959	.033333	-200
-195	.05	.196112	.033333	
-190	.05	.206392	.033333	
-185	.05	.210319	.033333	
-180	.06667	.22253	.033333	
-175	.072222	.227392	.033333	

-170	.155556	.24726	.033333	
-165	.205556	.255366	.033333	
-160	.205556	.273516	.033333	
-155	.261111	.278594	.033333	
-150	.288889	.301896	.033333	
-145	.288889	.308698	.033333	
-140	.305556	.321716	.033333	
-135	.305556	.325759	.033333	
-130	.372222	.341827	.033333	
-125	.372222	.346391	.033333	
-120	.405556	.359032	.033333	
-115	.405556	.369755	.033333	
-110	.438889	.37802	.033333	
-105	.438889	.379731	.033333	
-100	.544444	.393307	.033333	-100
-95	.55	.398538	.033333	
-90	.55	.409637	.033333	
-85	.6	.415615	.033333	
-80	.733333	.424731	.033333	
-75	.733333	.429753	.033333	
-70	.783333	.439468	.033333	
-65	.816667	.443885	.033333	
-60	.9	.459777	.033333	
-50	.916667	.472575	.033333	
-45	.95	.477096	.033333	
-40	.95	.481461	.033333	
-35	.966667	.485614	.033333	
-30	.966667	.495962	.033333	
-25	.966667	.504897	.033333	
-20	1	.517476	.033333	
-15	1	.519766	.033333	
-10	1	.524094	.033333	
0	1	.548122	.033333	0
10	1	.550448	.05	
15	1	.555723	.083333	
20	1	.560637	.083333	
25	1	.562447	.083333	
30	1	.568805	.083333	
35	1	.574833	.083333	
40	1	.583648	.1	
45	1	.588498	.116667	
50	1	.592701	.116667	
55	1	.597647	.133333	
60	1	.603646	.2	
65	1	.605905	.216667	
70	1	.617468	.233333	
75	1	.623355	.266667	
80	1	.633062	.283333	
85	1	.637684	.3	
90	1	.651326	.316667	
95	1	.654428	.361111	
100	1	.665552	.377778	100
105	1	.67104	.37778	
110	1	.680849	.377778	
115	1	.685461	.388889	
120	1	.701679	.455556	
125	1	.708071	.455556	
130	1	.722775	.472222	
135	1	.725957	.488889	
140	1	.733711	.522222	
145	1	.741148	.566667	
150	1	.752762	.594444	

155	1	.758154	.594444	
160	1	.766386	.616667	
165	1	.769247	.616667	
170	1	.77726	.627778	
175	1	.782359	.661111	
180	1	.791193	.705556	
185	1	.797033	.738889	
190	1	.804111	.738889	
195	1	.805369	.738889	
200	1	.812549	.75	200
205	1	.814369	.783333	
210	1	.822523	.816667	
215	1	.827307	.816667	
220	1	.836256	.816667	
225	1	.842505	.861111	
230	1	.846574	.861111	
235	1	.847798	.861111	
240	1	.853291	.872222	
245	1	.858176	.872222	
250	1	.858176	.872222	
255	1	.869269	.872222	
260	1	.875782	.872222	
265	1	.882973	.883333	
270	1	.890078	.883333	
275	1	.892037	.905556	
280	1	.899047	.905556	
285	1	.90056	.905556	
290	1	.90869	.938889	
295	1	.911272	.972222	
300	1	.91646	.972222	300
305	1	.919688	.972222	
310	1	.931219	.972222	
315	1	.933927	.972222	
320	1	.940411	.972222	
325	1	.942718	.972222	
330	1	.946005	.972222	
335	1	.94724	.972222	
340	1	.956257	.988889	
345	1	.956822	.988889	
350	1	.962506	.988889	
355	1	.963954	.988889	
360	1	.968693	.988889	
365	1	.970481	.988889	
370	1	.974061	.988889	
375	1	.97469	.988889	
380	1	.976512	.988889	
385	1	.977902	.988889	
390	1	.983607	1	
395	1	.984462	1	
400	1	.985663	1	400
405	1	.986176	1	
410	1	.988486	1	
420	1	.990186	1	
425	1	.990815	1	
430	1	.991328	1	
435	1	.991923	1	
440	1	.993254	1	
445	1	.993849	1	
465	1	.994312	1	
470	1	.994908	1	
475	1	.995514	1	
480	1	.995977	1	

485	1	.997167	1
490	1	.99768	1
500	1	.998881	1
510	1	1	1

Kolmogorov-Smirnof max d for nadirs 0.482524 at PR interval -20

Kolmogorov-Smirnov max d for peaks 0.514789 at PR interval 0

Cumulative frequency: AT

PR interval	Nadirs	All	Peaks	
-520	0	.000496	0	
-490	0	.001785	0	
-480	0	.00297	0	
-470	.017857	.003962	0	
-460	.017857	.005288	0	
-450	.017857	.0084	0	
-445	.017857	.009129	0	
-440	.017857	.010404	0	
-435	.017857	.012787	0	
-430	.017857	.013336	0	
-420	.017857	.01522	0	
-405	.017857	.015996	0	
-400	.017857	.016634	0	-400
-395	.017857	.017092	0	
-390	.017857	.018368	0	
-380	.017857	.021115	0	
-375	.017857	.022493	0	
-370	.017857	.024277	0	
-360	.017857	.028932	0	
-355	.017857	.029825	0	
-350	.017857	.036823	0	
-340	.017857	.040426	0	
-335	.017857	.041525	0	
-330	.017857	.044645	0	
-325	.017857	.04727	0	
-320	.035714	.053001	0	
-315	.035714	.053497	0	
-310	.035714	.060281	0	
-305	.035714	.0631	0	
-300	.071429	.070033	.035714	-300
-295	.071429	.070926	.035714	
-290	.071429	.076676	.035714	
-285	.071429	.077941	.071429	
-280	.071429	.084437	.107143	
-275	.071429	.087628	.107143	
-270	.071429	.101074	.107143	
-265	.071429	.104308	.107143	
-260	.071429	.109296	.107143	
-255	.071429	.111459	.107143	
-250	.071429	.119636	.107143	
-245	.071429	.123746	.107143	
-240	.071429	.13265	.107143	
-235	.071429	.136355	.107143	
-230	.071429	.147819	.142857	
-225	.071429	.153231	.142857	
-220	.107143	.164583	.142857	
-215	.107143	.168219	.142857	
-210	.107143	.174118	.142857	
-205	.107143	.176959	.142857	
-200	.142857	.192654	.178571	-200
-195	.142857	.197104	.178571	
-190	.142857	.208118	.178571	
-185	.154762	.212325	.178571	
-180	.190476	.223642	.196429	
-175	.190476	.228851	.196429	
-170	.220238	.248372	.196429	
-165	.291667	.257057	.196429	

-160	.291667	.276504	.214286	
-155	.291667	.281944	.214286	
-150	.327381	.306911	.232143	
-145	.363095	.314198	.232143	
-140	.363095	.328147	.232143	
-135	.380952	.332479	.232143	
-130	.434524	.347928	.232143	
-125	.470238	.352818	.232143	
-120	.470238	.361914	.232143	
-115	.506952	.371637	.232143	
-110	.505952	.380492	.232143	
-105	.505952	.382325	.232143	
-100	.52381	.395956	.232143	-100
-95	.571429	.40156	.232143	
-90	.571429	.411686	.232143	
-85	.571429	.41809	.232143	
-80	.571429	.424326	.232143	
-75	.571429	.429706	.232143	
-70	.60119	.440115	.232143	
-65	.60119	.444848	.232143	
-60	.630952	.461875	.232143	
-50	.684524	.475587	.232143	
-45	.696429	.480431	.232143	
-40	.696429	.485108	.267857	
-35	.714286	.489558	.267857	
-30	.714286	.498879	.267857	
-25	.714286	.508452	.267857	
-20	.75	.516631	.267857	
-15	.785714	.519085	.267857	
-10	.785714	.523721	.303571	
0	.821429	.5477	.303571	0
10	.821429	.550193	.321429	
15	.821429	.555844	.339286	
20	.821429	.561109	.339286	
25	.821429	.563081	.375	
30	.857143	.568095	.375	
35	.857143	.574553	.375	
40	.857143	.583997	.375	
45	.857143	.589194	.392857	
50	.857143	.593698	.464286	
55	.857143	.598996	.5	
60	.857143	.605424	.571429	
65	.857143	.607844	.571429	
70	.857143	.620233	.571429	
75	.892857	.62654	.571429	
80	.892857	.636941	.607143	
85	.892857	.641894	.642857	
90	.892857	.652978	.642857	
95	.892857	.656302	.642857	
100	.892857	.66822	.660714	100
105	.892857	.674099	.696429	
110	.928571	.68461	.803571	
115	.928571	.68955	.803571	
120	.940476	.703395	.803571	
125	.940476	.710243	.821429	
130	.940476	.724232	.857143	
135	.940476	.727641	.857143	
140	.940476	.735949	.857143	
145	.940476	.742151	.857143	
150	.940476	.752829	.857143	
155	.940476	.758606	.857143	
160	.940476	.767425	.857143	

165	.940476	.770491	.857143	
170	.940476	.77731	.857143	
175	.940476	.782774	.857143	
180	.940476	.792238	.892857	
185	.940476	.79673	.892857	
190	.940476	.804313	.892857	
195	.940476	.805661	.928571	
200	.940476	.811587	.928571	200
205	.940476	.813538	.928571	
210	.940476	.82229	.928571	
215	.940476	.8274	.928571	
220	.952381	.836988	.946429	
225	.952381	.844684	.982143	
230	.952381	.848043	.982143	
235	.952381	.849355	.982143	
240	.952381	.855915	.982143	
245	.952381	.860474	.982143	
250	.952381	.869956	.982143	
255	.952381	.870593	.982143	
260	.952381	.877572	.982143	
265	.952381	.885276	.982143	
270	.952381	.890272	.982143	
275	.952381	.892371	.982143	
280	.952381	.899881	.982143	
285	.964286	.901503	.982143	
290	.964286	.910214	.982143	
295	.964286	.91298	.982143	
300	.964286	.918538	.982143	300
305	.964286	.921997	.982143	
310	.964286	.932586	.982143	
315	.964286	.935487	.982143	
320	.964286	.940668	.982143	
325	.964286	.94314	.982143	
330	.964286	.945745	.982143	
335	.964286	.947069	.982143	
340	1	.954964	.982143	
345	1	.955569	.982143	
350	1	.961659	.982143	
355	1	.963211	.982143	
360	1	.967372	.982143	
365	1	.969289	1	
370	1	.973124	1	
375	1	.973798	1	
380	1	.97575	1	
385	1	.97724	1	
390	1	.983352	1	
400	1	.984639	1	400
405	1	.985189	1	
410	1	.987664	1	
420	1	.989485	1	
425	1	.990159	1	
430	1	.990709	1	
435	1	.991346	1	
440	1	.992772	1	
445	1	.99341	1	
465	1	.993906	1	
470	1	.994544	1	
475	1	.995193	1	
480	1	.995689	1	
485	1	.996965	1	
490	1	.997514	1	
500	1	.998801	1	

510	1	1	1

Komogorov-Smirnof max d for nadirs .289048 at PR +30

Kolmogorov-Smirnof max d for peaks .251228 at PR -15

Results on paced patients

Cumulative frequency for PA Vmax

PR interval	Nadirs	All	Peaks	
-520	0	.000542	0	
-490	0	.001241	0	
-480	0	.00252	0	
-470	0	.003603	0	
-460	0	.005031	0	
-450	0	.007855	.009615	
-445	0	.00864	.009615	
-440	0	.009327	.009615	
-435	0	.011206	.009615	
-430	0	.011798	.009615	
-420	0	.013826	.009615	
-405	0	.014662	.009615	-400
-395	0	.015155	.009615	
-390	0	.015842	.009615	
-380	0	.018809	.009615	
-375	0	.020293	.009615	
-370	0	.022214	.009615	
-360	0	.02654	.009615	
-355	0	.027512	.009615	
-350	0	.034351	.009615	
-340	.003497	.038247	.009615	
-335	.003497	.03943	.009615	
-330	.003497	.042898	.022436	
-325	.003497	.045617	.022436	
-320	.003497	.050384	.022436	
-315	.003497	.050926	.022436	
-310	.003497	.056827	.022436	
-305	.003297	.059862	.022436	
-300	.003497	.066618	.022436	-300
-295	.003497	.06758	.022436	
-290	.003497	.073046	.024359	
-285	.011189	.074409	.024359	
-280	.011189	.080679	.024359	
-275	.011189	.083428	.024359	
-270	.040035	.097916	.041026	
-265	.040035	.101406	.044872	
-260	.040035	.106053	.044872	
-255	.043531	.107656	.044872	
-250	.043531	.116462	.044872	
-245	.047028	.120889	.044872	
-240	.047028	.129805	.083333	
-235	.047028	.133802	.083333	
-230	.06014	.146164	.084872	
-225	.06014	.151999	.08641	
-220	.063098	.163522	.08641	
-215	.063098	.166751	.087949	
-210	.063098	.171659	.087949	
-205	.063098	.174727	.087949	
-200	.066057	.191628	.089872	-200
-195	.066057	.195734	.089872	
-190	.066057	.20687	.095366	
-185	.07305	.211401	.095366	
-180	.117429	.223588	.100861	
-175	.117429	.228472	.102784	
-170	.178618	.249495	.104707	
-165	.178618	.258863	.110476	

-160	.222996	.278415	.128791	
-155	.245186	.284297	.128791	
-150	.256374	.309046	.138022	
-145	.256374	.315482	.138022	
-140	.264067	.328341	.147363	
-135	.283297	.333006	.149286	
-130	.286794	.348193	.19478	
-125	.325256	.352733	.19478	
-120	.328214	.361078	.19478	
-115	.337829	.370823	.202473	
-110	.35706	.378946	.204011	
-105	.35706	.38092	.204011	
-100	.379788	.394148	.205549	-100
-95	.379788	.400183	.205549	
-90	.379788	.408957	.205549	
-85	.389403	.415862	.205549	
-80	.416326	.421851	.205549	
-75	.474018	.42692	.205549	
-70	.539481	.437443	.207088	
-65	.549096	.441853	.207088	
-60	.56674	.458778	.216319	
-50	.60816	.472132	.216319	-50
-45	.617775	.477348	.216319	
-40	.621272	.480934	.216319	
-35	.640503	.485047	.216319	
-30	.640503	.495084	.216319	
-25	.678964	.503217	.230678	
-20	.724419	.512033	.230678	
-15	.734034	.514675	.230678	
-10	.734034	.519668	.230678	
0	.750882	.544773	.239634	0
10	.789343	.547458	.239634	
15	.792302	.553543	.239634	
20	.809609	.558495	.239634	
25	.812568	.559932	.239634	
30	.812568	.565332	.239634	
35	.816841	.5716	.241172	
40	.836072	.581053	.244634	
45	.836072	.586649	.244634	
50	.855303	.591499	.244634	50
55	.862995	.597205	.244634	
60	.867269	.603402	.246172	
65	.867269	.606008	.246172	
70	.879235	.61729	.246172	
75	.879235	.624082	.246172	
80	.879235	.635283	.251557	
85	.879235	.640616	.293095	
90	.879235	.651874	.296941	
95	.879235	.654735	.304634	
100	.887782	.667578	.3213	100
105	.887782	.673223	.3213	
110	.887782	.684549	.366795	
115	.887782	.689152	.370641	
120	.899747	.703382	.409103	
125	.899747	.710039	.409103	
130	.909363	.724425	.424487	
135	.909363	.728096	.424487	
140	.909363	.735638	.428333	
145	.909363	.742325	.457179	
150	.909363	.753823	.554872	
155	.909363	.760045	.608077	
160	.909363	.769558	.619231	

165	.909363	.772859	.619231	
170	.909363	.779477	.625	
175	.909363	.784675	.625	
180	.913636	.792775	.63141	
185	.913636	.79762	.641026	
190	.913636	.805099	.660513	
195	.913636	.806551	.660513	
200	.917133	.812941	.668846	200
205	.917133	.814355	.670385	
210	.917133	.823781	.684487	
215	.917133	.829283	.692179	
220	.917133	.838922	.692179	
225	.936364	.846133	.692179	
230	.936364	.850835	.696026	
235	.936364	.852561	.696026	
240	.936364	.858626	.696026	
245	.936364	.863535	.734487	
250	.936364	.871662	.790513	
255	.936364	.872349	.790513	
260	.93986	.879864	.790513	
265	.93986	.887474	.790513	
270	.947552	.892854	.790513	
275	.947552	.895122	.790513	
280	.947552	.903218	.790513	
285	.947552	.904964	.792051	
290	.954545	.91294	.797821	
295	.954545	.915919	.836282	
300	.958042	.921912	.840128	300
305	.958042	.925638	.87859	
310	.958042	.936354	.882436	
315	.961538	.939478	.882436	
320	.961538	.944378	.884359	
325	.961538	.947041	.884359	
330	.961538	.949849	.88782	
335	.961538	.951271	.88782	
340	.961538	.957674	.88782	
345	.961538	.958326	.88782	
350	.961538	.964892	.910256	
355	.961538	.966563	.929487	
360	.961538	.971053	.942308	
365	1	.973116	.942308	
370	1	.977255	.942308	
375	1	.97798	.942308	
380	1	.980083	.942308	
385	1	.981686	.942308	
390	1	.987582	.942308	
400	1	.988282	.942308	400
405	1	.988873	.942308	
410	1	.991539	.951923	
420	1	.993508	.951923	
430	1	.9941	.951923	
440	1	.995635	.951923	
465	1	.996177	.951923	
475	1	.998876	.990385	
480	1	.997418	.990385	
490	1	.99801	1	
500	1	.998709	1	
510	1	1	1	

Kolmogorov-Smirnof max d for nadirs .265790 at PR +55

Kolmogorov-Smirnof max d for peaks .383726 at PR +80