Evidence for an influence of mechanical restitution on beat-to-beat variations in haemodynamics during chronic atrial fibrillation in patients

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Abstract

Objective: We tested the hypothesis that beat-to-beat changes in haemodynamics during atrial fibrillation include an effect of each preceding R–R interval through the interval–strength relationship (mechanical restitution). Background: The variation in stroke volume and pulse pressure characteristic of atrial fibrillation is usually ascribed to time dependent ventricular filling. Methods: We measured the maximum rate of rise of left ventricular pressure \( \frac{dP}{dt_{\text{max}}} \), and aortic blood velocity and its integral in patients with atrial fibrillation undergoing cardiac catheterisation. The contractile response of isometric human myocardial trabeculae to sequences of atrial fibrillation was also studied, using the recorded ECGs as stimuli. The trabeculae were obtained from the resected right ventricular outflow tracts of patients with Fallot’s tetralogy undergoing operative correction. Results: Beat-to-beat variations in contractile function during atrial fibrillation in the patients were recorded as \( \frac{dP}{dt_{\text{max}}} \) and left ventricular ejection ascending aortic velocity integral. Both these indices correlated well with the response to the same ECG R wave sequences in the isometric model measured as the maximum rate of rise of force, \( \frac{dF}{dt_{\text{max}}} \). Conclusions: Mechanical restitution, which causes beat-to-beat changes in inotropic state, accounts in part for the changes in stroke volume in atrial fibrillation.

Keywords: Mechanical restitution; Postextrasystolic potentiation; Frank–Starling mechanism; Ejection function

1. Introduction

Early studies of atrial fibrillation (AF) attributed beat-to-beat changes in the pulse pressure and stroke volume during atrial fibrillation to variations in ventricular filling, and a modifying influence of aortic diastolic pressure [1–3]. Thus, Einthoven and Korteweg [3], in the first detailed study of this topic, correlated ECG intervals with externally recorded carotid pulse pressure and found that long pauses (greater filling time) were followed by larger pulse pressures and short pauses (lesser filling time) by smaller pulse pressures. However isometric myocardial preparations, in which changes in length are excluded, also show larger force development following long intervals and smaller force following short intervals. This phenomenon is called mechanical restitution [4,5]. The idea that such an inherent inotropic mechanism might explain the irregular amplitude of contractile variables in atrial fibrillation has been proposed [6], but did not gain credence, and interest in the interval–force relationship during atrial fibrillation in humans is relatively recent and largely confined to the role of

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postextrasystolic potentiation, the phenomenon responsible for the strong contractions which follow a normal following a short interval [7–11]. We and others have demonstrated that such postextrasystolic potentiation contributes to pulse variation during atrial fibrillation [9,12,13].

Mechanical restitution is always seen in mammalian cardiac preparations from the isolated myocyte to the intact heart (including that of man), with an increase in the force of contraction as the preceding stimulus interval lengthens until restitution is complete (in man and most mammals at an interval of about 800 to 1000 ms) [4,5,8,14,15]. These changes are independent of muscle length or ventricular filling but instead reflect interval-dependent variations in the concentration of calcium ions released to the contractile proteins upon activation [16,17]. The present study, in the same patients in which we demonstrated postextrasystolic potentiation during atrial fibrillation [9], explores the hypothesis that mechanical restitution also contributes to the beat-by-beat changes of atrial fibrillation. Although the same patients were studied, we examined the results of postextrasystolic potentiation and mechanical restitution separately, and the present paper presents only new results. We recorded beat-by-beat changes in haemodynamics in atrial fibrillation patients during cardiac catheterisation, and then used the ECG recordings to stimulate isolated human myocardial trabeculae contracting at constant muscle length. We then used the interval strength changes observed in the isolated muscle as a measure of its contribution to the in vivo measurements.

The study was subject to local ethical committee approval and all patients had given signed informed consent.

Table 1

<table>
<thead>
<tr>
<th>Patient</th>
<th>Sex</th>
<th>Age</th>
<th>Diagnosis</th>
<th>Drugs</th>
<th>RR interval(s)</th>
<th>C/T ratio</th>
<th>LV</th>
<th>CAD</th>
<th>LVEDP</th>
<th>AVI</th>
<th>LVdP/dtmax</th>
</tr>
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<tr>
<td>1</td>
<td>M</td>
<td>47</td>
<td>AC</td>
<td>D</td>
<td>0.36–0.98</td>
<td>13.5/30</td>
<td>G3</td>
<td>N</td>
<td>2.5–22</td>
<td>0–10.5</td>
<td>150–1750</td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>66</td>
<td>AC</td>
<td>D</td>
<td>0.34–0.98</td>
<td>15.5/32</td>
<td>G1</td>
<td>2</td>
<td>–2.5–30</td>
<td>0–9</td>
<td>450–2350</td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>51</td>
<td>AC</td>
<td>D</td>
<td>0.46–1.15</td>
<td>18/37</td>
<td>G3</td>
<td>N</td>
<td>no data</td>
<td>4.8–15</td>
<td>925–1475</td>
</tr>
<tr>
<td>4</td>
<td>M</td>
<td>69</td>
<td>IHD</td>
<td>D, Ca</td>
<td>0.7–1.95</td>
<td>16/33</td>
<td>G2</td>
<td>1</td>
<td>–2–7</td>
<td>4.5–21</td>
<td>14602150</td>
</tr>
<tr>
<td>5</td>
<td>F</td>
<td>58</td>
<td>ASD</td>
<td>D</td>
<td>0.4–0.78</td>
<td>14.5/27.5</td>
<td>N</td>
<td>N</td>
<td>0.4–6.4</td>
<td>1.5–9</td>
<td>950–1650</td>
</tr>
<tr>
<td>6</td>
<td>F</td>
<td>69</td>
<td>MS</td>
<td>D, A</td>
<td>0.68–1.25</td>
<td>15.2/27.9</td>
<td>N</td>
<td>N</td>
<td>–2–20.5</td>
<td>9.5–20</td>
<td>825–1175</td>
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<td>7</td>
<td>M</td>
<td>64</td>
<td>C</td>
<td>D, Ca</td>
<td>0.4–0.8</td>
<td>16/32</td>
<td>G1</td>
<td>M</td>
<td>4–20</td>
<td>0.9</td>
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<td>8</td>
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<td>DC</td>
<td>D, Ca</td>
<td>0.45–1.14</td>
<td>17/26.5</td>
<td>G2</td>
<td>N</td>
<td>–4–13</td>
<td>2–14</td>
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<td>F</td>
<td>73</td>
<td>DC</td>
<td>D, Ca</td>
<td>0.42–1.09</td>
<td>18/27.5</td>
<td>G2</td>
<td>3</td>
<td>1–26</td>
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<tr>
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<td>M</td>
<td>72</td>
<td>AC</td>
<td>D, A</td>
<td>0.51–1.59</td>
<td>20/34</td>
<td>G2</td>
<td>N</td>
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<td>1050–1575</td>
</tr>
<tr>
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<td>60</td>
<td>DC</td>
<td>D</td>
<td>0.37–0.84</td>
<td>18/34</td>
<td>G2</td>
<td>N</td>
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<td>0–9</td>
<td>350–1500</td>
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<tr>
<td>12</td>
<td>F</td>
<td>53</td>
<td>MS</td>
<td>D</td>
<td>0.4–1.5</td>
<td>15/28</td>
<td>G1</td>
<td>N</td>
<td>–7.5–14.5</td>
<td>no data</td>
<td>1100–1800</td>
</tr>
<tr>
<td>13</td>
<td>M</td>
<td>46</td>
<td>DC</td>
<td>D</td>
<td>0.32–0–77</td>
<td>17.5–29.5</td>
<td>G3</td>
<td>N</td>
<td>0–35</td>
<td>0–9</td>
<td>290–1850</td>
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<tr>
<td>14</td>
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<td>68</td>
<td>AC</td>
<td>Ca</td>
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<td>15.5–32</td>
<td>N</td>
<td>N</td>
<td>–1–9</td>
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<tr>
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<td>M</td>
<td>74</td>
<td>IHD</td>
<td>D</td>
<td>0.37–0.9</td>
<td>14/28</td>
<td>N</td>
<td>3</td>
<td>–4–10</td>
<td>no data</td>
<td>450–1450</td>
</tr>
</tbody>
</table>

AC, alcoholic cardiomyopathy; IHD, ischaemic heart disease; MS, mitral stenosis; DC, dilated cardiomyopathy; C, cardiomyopathy.

A, angiotensin converting enzyme inhibitor; Ca, calcium channel blocker; D, digoxin.

LV, left ventricular function; N, normal; G1, G2, G3 imply mild, moderate or severe global impairment.

CAD, coronary artery disease; N, normal vessels; M, minor disease; 1,2,3, refer to number of vessels with stenoses > 50%.

LVEDP, left ventricular end diastolic pressure (mmHg).

LVdP/dtmax, mmHg/s. Ranges are given for each patient.

2. Methods

2.1. Patient studies

Patients with chronic atrial fibrillation were studied at cardiac catheterisation following diagnostic angiography (Table 1). The only patients specifically excluded from the study were patients with aortic valve disease where passage of the study catheter across a diseased valve could have been hazardous and patients with mitral regurgitation because this would have precluded measurement of isovolumic LVdP/dtmax. Apart from these exclusions, we studied consecutive patients with atrial fibrillation entering the catheter laboratory; these had a wide range of detailed clinical features (Table 1). All but one of these patients was receiving digoxin, including all the patients whose ECGs were used to stimulate the isolated preparation (below). Other cardioactive drugs were only being taken in isolated cases, precluding the possibility of separated analysis by drug class. A single 8F catheter with a tip micro-manometer (Gaeltec, Skye, Scotland) and an electromagnetic velocity meter [18] mounted on the shaft was positioned to give simultaneous recordings of left ventricular pressure and its rate of change (dP/dt) and ascending aortic velocity. Approximately 15 min was allowed for equilibration of the pressure transducer with body temperature which was normal in all cases. These signals were recorded, together with the ECG, during quiet respiration onto electromagnetic tape over periods of several minutes and subsequently played out onto paper using an ink jet recorder (Mingograf, 800, Siemens Elena, Sweden) at a paper speed of 50 mm/s. The aortic velocity signal of
Fig. 1. (a) Contractile responses to an identical sequence of intervals in an AF patient and an isolated muscle. The contractile response in the patient (LVdP/dt_max) during AF (middle tracing) is correlated with the contractile response (dF/dt_max) in an isolated ventricular muscle strip (upper tracing) when stimulated to contract isometrically in response to the same ECG sequence (lower tracing). (b) Original recordings from patient 1 during AF.
each contraction was integrated using a Gould integrating circuit to yield ‘stroke distance’ (aortic velocity integral, AVI), which is proportional to stroke volume for each beat.

2.2. Isolated cardiac muscle studies

We obtained right ventricular tissues resected from four consecutive patients undergoing cardiopulmonary bypass surgery for Fallot’s tetralogy. These were transported to the laboratory in sodium bicarbonate buffered Tyrode solution aerated with a mixture of 95% oxygen and 5% carbon dioxide to give a pH of approximately 7.4. Single trabeculae were dissected in Tyrode solution and mounted in an organ bath between a stationary hook and a tension transducer (AE 801 silicon beam strain gauge, AME Horten, Norway). The composition of the Tyrode solution was: NaCl, 0.118 M; glucose, 0.0065 M; Na pyruvate, 0.005 M; NaHCO₃, 0.024 M; NaH₂PO₄·2H₂O, 0.0004 M; KCl, 0.004 M; CaCl₂, 0.0018 M; MgCl₂·6H₂O, 0.001 M. The muscles were continuously perfused with fresh Tyrode solution (50 ml/min) at room temperature (for justification, see Section 4).

2.3. Stimulation

The muscles were stimulated via a programmable signal generator (Digitimer, Devices using 2 ms square wave pulses at a voltage of 1.5 times threshold, with the muscle length held constant at 95% of that length which gave maximum developed tension. Each muscle was initially paced continuously at 1 Hz until a steady state was established. When this was reached the muscle was stimulated with the sequences derived from the ECGs of one or more of the AF patients, each sequence being repeated three or four times. The time course of mechanical restitution was then examined using a range of single interval variations introduced into a background of fixed interval pacing, with a return to steady state after each interval variation.

Recordings of force, and the rate of change of force derived using a differential amplifier (Gould 13-461571), together with the original driving ECG or stimulus sequence were recorded onto paper and electromagnetic tape. $LVD_P/\text{d}t_{\text{max}}$ for each beat was recorded in the patients and was correlated on the same beats with the maximum rate of change of force ($dF/\text{d}t_{\text{max}}$) recorded, for the corresponding sequence of intervals, in the isolated muscles. $dF/\text{d}t_{\text{max}}$ correlates closely with the amount of intracellular calcium released to the contractile proteins [17,19]. Under the circumstances of the study (isometric at all times with constant milieu) this measure is an index purely of the inotropic effect of changing interval.

### Table 2

Residual variances after linear regression of $LVD_P/\text{d}t_{\text{max}}$ upon $dF/\text{d}t_{\text{max}}$ during spontaneous atrial fibrillation with pre-preceding intervals in excess of 500 ms (see text)

<table>
<thead>
<tr>
<th>Patient</th>
<th>Muscle</th>
<th>Degrees of freedom</th>
<th>Correlation coefficient</th>
<th>$r^2$</th>
<th>Regression variance</th>
<th>Residual variance</th>
<th>% F variance ratio</th>
<th>Null probability</th>
</tr>
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<tbody>
<tr>
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<td>1</td>
<td>68</td>
<td>0.79</td>
<td>0.63</td>
<td>1859330</td>
<td>16430</td>
<td>0.84</td>
<td>113.2</td>
</tr>
<tr>
<td>1</td>
<td>2</td>
<td>75</td>
<td>0.80</td>
<td>0.64</td>
<td>3006285</td>
<td>22856</td>
<td>0.76</td>
<td>131.5</td>
</tr>
<tr>
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<td>4</td>
<td>76</td>
<td>0.80</td>
<td>0.64</td>
<td>3082581</td>
<td>22927</td>
<td>0.74</td>
<td>134.5</td>
</tr>
<tr>
<td>2</td>
<td>4</td>
<td>120</td>
<td>0.77</td>
<td>0.59</td>
<td>5460097</td>
<td>31644</td>
<td>0.58</td>
<td>172.5</td>
</tr>
<tr>
<td>5</td>
<td>3</td>
<td>53</td>
<td>0.76</td>
<td>0.58</td>
<td>319020</td>
<td>4485</td>
<td>1.41</td>
<td>71.1</td>
</tr>
<tr>
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<td>0.75</td>
<td>607105</td>
<td>2998</td>
<td>0.49</td>
<td>202.5</td>
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<tr>
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<td>4</td>
<td>51</td>
<td>0.85</td>
<td>0.72</td>
<td>2162691</td>
<td>16843</td>
<td>0.79</td>
<td>124.4</td>
</tr>
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<td>0.77</td>
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<td>0.77</td>
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<td>2162691</td>
<td>16843</td>
<td>0.78</td>
<td>128.4</td>
</tr>
</tbody>
</table>

The residual variance is also expressed as % of variance due to regression to emphasise the very dominant role of $dF/\text{d}t_{\text{max}}$ as the determinant of $LVD_P/\text{d}t_{\text{max}}$. The null probability is calculated from the F variance ratios; these very low probabilities also emphasise the same conclusion.
2.4. Measurement and analysis

Continuous sequences of 100 or more beats during atrial fibrillation, free of beats showing aberrant conduction, were selected for analysis. These were also the sequences used to drive the isolated muscles. Measurements of all recorded and derived variables were made using a digitising pad and desk top computer. Measurements were not made on any beats which followed preceding intervals of more than 1300 ms where an influence of aortic pressure on $L V d P / d t_{\text{max}}$ could not be excluded (see Section 4).

Data were tested by linear or Spearman rank (non-parametric) correlation analyses as appropriate. The value of $n$ exceeded 100 in each case. No intergroup comparisons were made. The number of patients studied during catheterisation was 15. The number of experiments with the isolated preparation was 12.

2.5. Gating to reduce the confounding effect of PESP on mechanical restitution

The force of a beat is dependent not only on the preceding interval, which determines the extent of restitution, but also on the duration of the pre-preceding interval, which determines the degree of potentiation [9,10]. In atrial fibrillation, this pre-preceding interval varies and can confound attempts to study mechanical restitution. In order to reduce this confounding influence, the relationship between the force of a beat and its preceding interval was examined only on those beats where the pre-preceding interval was more than 500 ms (an interval beyond which postextrasystolic potentiation is usually less pronounced [20]). This manoeuvre was a compromise between eliminating the influence of postextrasystolic potentiation completely and losing excessive data points. Data obtained in

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Fig. 3. Mechanical restitution in isolated human ventricular muscle contracting at constant length (a) when muscle was stimulated with an AF sequence from a patient; all beats with pre-preceding intervals > 0.5 s plotted (see Section 2). (c) during a pacing protocol in which all intervals are held constant except for a single test pulse interval (the preceding interval). (b) Dependence of $L V d P / d t_{\text{max}}$ on preceding interval during AF (gated data, see Section 2).

Fig. 4. Relation between beat-by-beat ejection volume (AVI) in the intact heart and the contractile response ($d F / d t_{\text{max}}$) of isolated human ventricular muscle to an identical sequence of intervals.
the isolated muscles were dealt with in the same way as the patient data.

3. Results

When the right ventricular muscle trabeculae were stimulated to contract at constant length in response to AF sequences derived from the patients’ ECG’s, dF/dtmax varied widely from beat to beat. These variations closely followed the variations in DVL/dtmax in the corresponding patients in response to the identical sequence of intervals (Fig. 1a). A typical sequence of beats, showing the great variability of flow and pressure with R–R interval change from beat to beat in vivo is shown in Fig. 1b.

This very similar behaviour between the muscle trabeculae at constant length and the patients’ hearts, in response to identical sequences of stimulation, was confirmed by significant linear correlations between dF/dtmax and LVD/dtmax (Fig. 2, Table 2). The magnitude of the dependence of LVD/dtmax upon inotropic state as indicated by dF/dtmax, and the smaller dependence on anything else, is indicated by the very small residual variances following these linear regressions and the high values for coefficient of determination (all above 0.5, Table 2).

The variation in dF/dtmax and LVD/dtmax showed a curvilinear relation with preceding interval, with the onset of recovery between 400 and 500 ms followed by a sharply rising phase which subsequently levels off at long intervals (Fig. 3a,b). In order to confirm that these changes are typical of mechanical restitution, we compared them to the results when the same muscles were stimulated with the standard protocol for examining restitution (a series of single interval variations during a sequence of steady pacing); typical restitution behaviour was seen (Fig. 3c).

Good quality aortic velocity signals, which could be reliably integrated, were obtained in 11 of the 15 patients. In all these patients the aortic velocity integral (proportional to stroke volume) varied on a beat-by-beat basis (Table 1). We examined the relationships between AVI and both the isovolumic index of contractile function, LVD/dtmax, and the isometric index of the interval–strength relationship, dF/dtmax. AVI was correlated with dF/dtmax for all pulse sequences where both were studied (Fig. 4), indicating an influence of contractility.

The presence of positive relationships between LVD/dtmax or AVI and preceding R–R interval were shown by significant positive correlations by Spearman rank analysis (Table 3).

4. Discussion

The results of this study are consistent with the hypothesis that beat-to-beat changes in haemodynamics during atrial fibrillation include an effect of each preceding R–R interval through the interval–strength relationship (mechanical restitution). Mechanical restitution is a significant determinant of the beat-to-beat variation of contractile, or inotropic state, of the left ventricle during atrial fibrillation and stroke volume is also influenced by mechanical restitution. Together with previous studies [9,13,21], these findings show that the amplitude of haemodynamic variables in atrial fibrillation is modified by the cumulative influ-
ences of interval–force relationships, comprising mechanical restitution and postextrasystolic potentiation (including its decay). These changes in contractile function are a critical determinant on a beat-by-beat basis.

In order to establish unequivocally what role is played by interval-dependent contractility changes in atrial fibrillation, we used an ex vivo isolated cardiac muscle. This was obtained during surgical excisions of hypertrophied muscle during the treatment of right ventricular outflow obstruction associated with Tetralogy of Fallot. The use of right ventricular tissue as opposed to the left ventricle from which LVdP/dtmax was obtained is justified by the fact that the form and time constants of mechanical restitution are the same in the two ventricles and in isolated tissue from the two ventricles [15,22,23].

The striking similarity in contractile response between the in vivo and in vitro studies in response to the same atrial fibrillation sequences was confirmed using linear regression analyses, which showed that most of the variations in LVdP/dtmax (as judged by residual variance) were dependent on interval–strength determined changes in contractile state (Table 2). Our argument here is (a) that the beat-to-beat variation of dF/dtmax in the isolated muscle gives unequivocal evidence that the sequence of varying intervals causes variation in inotropic state (interval–force relationship), and (b) the beat-to-beat variation in LVdP/dtmax and AVI in the patients is well correlated with dF/dtmax, and (c) therefore the beat-to-beat variation in stroke volume (proportional to AVI) is influenced by inotropic state in addition to the well known influence of filling. The variation in inotropic state is determined in turn by variation of R–R interval.

Taken on their own, our observations in the catheter studies inevitably raise the question of whether LVdP/dtmax was sufficiently independent of the degree of left ventricular filling (left ventricular filling pressure or volume) in our study. The relationship of LVdP/dtmax to left ventricular volume is curvilinear, with an ascending limb, a plateau, and a descending limb ([24], based on [25]). Thus the influence of a change of left ventricular volume on LVdP/dtmax can vary in different circumstances [26–29] in the dog. The studies pertinent to our own work are those which have been carried out in conscious patients during catheterisation [15,24,30,31].

These studies have consistently shown LVdP/dtmax to have a weak or negligible dependence on left ventricular volume (or end-diastolic pressure) over the range studied. However, the possible volume dependence of LVdP/dtmax was the reason for relying on the responses of the isolated muscle preparation which was unequivocally isometric.

In the present study, the small residual variances of LVdP/dtmax after linear regression upon dF/dtmax during atrial fibrillation (Table 2), and the high values for the coefficient of determination (r²) confirm the slight influence of other determinants of LVdP/dtmax, such as filling; in only two patients did residual variance exceed 1% of the total. Any significant influence of aortic end-diastolic pressure on LVdP/dtmax is also excluded by this analysis, and would be unlikely as long as LVdP/dtmax is reached before aortic valve opening [32,33]. This requirement is likely to be met when the aortic pressure remains above 50 mmHg [34] and in man changes in arterial pressure have been shown to have a negligible effect on LVdP/dtmax [30].

There are a number of other factors which could affect the relationship between LVdP/dtmax of the patients and dF/dtmax of the isolated preparation: differences in the time course of mechanical restitution between the isolated muscles and the patients with which each is compared, shifts in the mechanical restitution curves between isolated tissue versus the intact heart [23,35], measurement errors of LVdP/dtmax and dF/dtmax which are inherent in such experiments, differences due to temperature [22,36], slowing of the initial speed of restitution caused by hypertrophy [37] in the Fallot’s patients, differences caused by the difference in age between the catheter patients (older) and the patients from whom the isolated preparations were obtained (2–16 years), differences caused by different drug therapies (e.g. calcium channel blockers slow the upstroke of mechanical restitution), the influence of decay of post-extrasystolic potentiation following short interval. All of these sources of variation are subject to the same consideration, namely that the residual variances of LVdP/dtmax after linear regression upon dF/dtmax during atrial fibrillation (Table 2), and the high values for the coefficient of determination (r²) confirm the slight influence of determinants of LVdP/dtmax other than contractility, as expressed by the dF/dtmax of the isolated preparation.

We used room temperature to make sure that there was no hypoxic core to the muscle which can occur at 37°C. Lower temperatures are known to increase contractility and to slow the dynamics of mechanical restitution [22,35,36]. The former response would not affect our results, but the latter might be a potential source of variation to be considered in the manner described in the previous paragraph. The use of a lower temperature for this muscle is justified because the mechanical restitution curves are, in fact, sufficiently similar for the two temperatures (Fig. 2) that no large spurious variance appears in the analysis.

We conclude that the very large changes in LVdP/dtmax from beat-to-beat which were observed in these patients (Table 1) are reflecting predominantly an inotropic response to interval variation rather than a response to changes in filling or aortic pressure.

The findings of this study which confirms the importance of interval force relationships and of mechanical restitution in particular during atrial fibrillation, are entirely consistent with earlier animal models of atrial fibrillation where the effects of interval and volume could be more easily separated, and preceding as well as pre-preceding interval was shown to be an important determinant of...
varying contractile function [11,38,39]. Edmands and colleagues [40], induced experimental atrial fibrillation in dogs and related the rate of change of tension (from strain gauges stitched into the left ventricular free wall) to pulse pressure. They found that the inotropic variation correlated better with pulse pressure than did either end-diastolic pressure or filling time. More recently, using a computerised nuclear probe to assess relative change in ventricular volume during atrial fibrillation [13], Gosselink concluded that “the interval force relation explains the varying left ventricular performance during atrial fibrillation over the entire range of R–R intervals”, and that “the contribution of the Frank-Starling mechanism to varying left ventricular performance during atrial fibrillation remains a matter of doubt and debate”. We concur.

References

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