LETTERS TO THE EDITOR

Beat to beat left ventricular performance in spontaneous atrial fibrillation does not depend on afterload

EDITOR,—The recent article by Muntinga and colleagues[1] confirms, using non-invasive techniques, the findings obtained more directly by Brookes and colleagues[2] that beat to beat left ventricular performance in spontaneous atrial fibrillation depends on beat to beat variation in cycle length, left ventricular end diastolic volume (EDV), and contractility. Their contention that afterload is another independent determinant rests on their fig 5 in which ejection fraction is plotted against end systolic pressure/stroke volume (ESP/SV). However, ejection fraction is SV/EDV, so they have SV on both axes, which is invalid. A plot of a variable, in this case SV, against its reciprocal 1/SV will lead inevitably to an inverse hyperbolic relation as a mathematical necessity. In this case it is accompanied by a small amount of scatter caused by the other variables, but the main relation shown is a mathematical artefact and not an actual dependence of ejection fraction on afterload.

Figure 3 is also incorrect because SV/EDV is plotted against EDV (EDV appearing on both axes), but in this case a plot of SV against EDV would have resulted in a positive relation and the same conclusion.

In the study by Brookes and colleagues,[2] the left ventricular systolic pressure (directly measured with catheter tip manometer) varied rather little during atrial fibrillation, which the authors attributed to clamping of the arterial systolic pressure by peripheral mechanisms. This finding and the invalidity of using ESP/SV raised the question, "What is the afterload in the intact mammal?". I prefer not to use the term because there are so many different indices that purport to be "afterload"; I prefer to use the measured variable. Many workers in the field would accept using left ventricular systolic pressure. However, the term was invented to describe the constant force or stress in an isolated strip of muscle caused during shortening during contraction in a particular experimental set up. The only corresponding variable in the intact human is systolic wall stress, but this declines during ejection so that there is no single value. However, inspection of directly measured left ventricular pressure–volume loops during spontaneous atrial fibrillation[2] shows that, most of the time, contraction takes place over similar mid-systolic values implying the same wall stress.

Of course, left ventricular performance will depend on "afterload" (if that can be defined) if "afterload" changes, but my conclusion is that in spontaneous atrial fibrillation, there are no important changes.

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1 Muntinga HJ, Gosselink ATM Blanksma PK, *et al*. Left ventricular beat to beat performance in atrial fibrillation: dependence on contractility, preload, and afterload. *Heart* 1999;**82**:575–80.
2 Brookes CIO, White PA, Staples M, *et al*. Myocardial contractility is not constant during spontaneous atrial fibrillation in patients. *Circulation* 1998;**98**:1762–8.

This letter was shown to the authors who reply as follows:

Based on a recent study by Brookes and colleagues,[1] Professor Noble concludes that in chronic atrial fibrillation there are no important beat to beat changes of left ventricular afterload measured by left ventricular systolic pressure. Based on fig 5 of our article he concludes that the relation between afterload as calculated by the ratio of end systolic pressure (ESP) and stroke volume (SV), and ejection fraction is a mathematical artefact, instead of a physiological relation.[2] He rejects left ventricular afterload as an important measure of left ventricular performance. The conclusion that afterload, preload, and contractility are independent determinants of left ventricular ejection fraction, however, rests on a multivariate model of left ventricular ejection fraction.

In our study we measured non-invasively peripheral blood pressure, which we assumed to change, parallel with aortic pressure.[2] We calculated left ventricular volumes in millilitres from results of measurements with a "nuclear stethoscope" and a Swan Ganz catheter. Left ventricular afterload was then calculated as the fraction of ESP and SV. The validity of the ESP to SV relation as a measure of effective arterial elastance was tested by Sunagawa and colleagues.[3] The arterial system properties consist of three elements: peripheral resistance, arterial compliance, and characteristic impedance of the arterial system. In table 1 of our article we demonstrate that this measure of afterload varies significantly from beat to beat in each investigated patient. The argument that a limited variation of end systolic *pressure* in patients with atrial fibrillation (in our patient group the average ESP was 126 mm Hg and the average standard deviation of ESP was 13 mm Hg) is measured because arterial pressure is damped by baroreceptor and other reflex mechanisms, confirms in our opinion the observation that *afterload*, which unites the above mentioned properties of the arterial system, changes from beat to beat.

In experimental models of the intact cardiovascular system a unique relation exists in the left ventricle between SV and ESP when preload and contractility remain constant.[4 5] In this situation, afterload determines the exact value for SV and ESP. SV is therefore inevitably both a measure of left ventricular performance and a measure of left ventricular afterload. Indeed, this results in a mathematical relation between ejection fraction and afterload. The other measured factors—end diastolic volume and ESP—also influence the measure of interdependence between ejection fraction and afterload, and can determine the value of this relation. The conclusion in our article that ejection fraction in patients with atrial fibrillation is dependent on afterload (apart from the dependency on preload and contractility) is based on the multivariate analysis. Figure 5 is added to illustrate the univariate relation between ejection fraction and afterload. It further illustrates that SV importantly determines the direction and nature of the relation between ejection fraction and afterload. The multivariate analysis is also the basis for the conclusion that ejection fraction is dependent on preload. The univariate relation between ejection fraction and preload is illustrated with figure 3. If this relation had only a mathematical nature, a negative hyperbolic relation would have been found (1/EDV versus EDV) instead of a linear positive relation. SV apparently determines the direction of this relation. This finding can be explained physiologically by the Frank-Starling mechanism.[6] The differences between figures 3 and 5 contribute in our opinion largely to their importance to the present article.

We agree with Professor Noble that a mathematical relation exists between ejection fraction and the described measures of afterload and preload, but we do not share his opinion that we may not use these measures in a model to describe left ventricular beat to beat performance.

1 Brookes CIO, White PA, Staples M, *et al*. Myocardial contractility is not constant during spontaneous atrial fibrillation in patients. *Circulation* 1998;**98**:1762–1768.
2 Muntinga HJ, Gosselink ATM, Blanksma PK, *et al*. Left ventricular beat to beat performance in atrial fibrillation: dependence on contractility, preload, and afterload. *Heart* 1999;**82**:575–80.
3 Sunagawa K, Maughan WL, Burkhoff D, *et al*. Left ventricular interaction with arterial load studied in isolated canine ventricle. *Am J Physiol* 1983;**245**:H773–80.
4 Suga H, Sagawa K, Shoukas AA. Load independence of the instantaneous pressure-volume ratio of the canine left ventricle and effects of epinephrine and heart rate on the ratio. *Circ Res* 1973;**32**:314–22.
5 Suga H, Sagawa K. Instantaneous pressure-volume relationships and their ratio in the excised, supported canine left ventricle. *Circ Res* 1974;**35**:117–26.
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