Editorial

Time intervals and global cardiac function. Use and limitations

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This editorial refers to "Myocardial performance index, a Doppler-derived index of global left ventricular function, predicts congestive heart failure in elderly man" by J. Arnlöv et al. on page 2220 and "The effects of changes in loading conditions and modulation of inotropic state on the myocardial performance index: comparison with conductance catheter measurements" by M.M.H. Cheung et al. on page 2238.

Clinicians are familiar with the diagnostic and prognostic implications of some of the cardiac intervals that are audible at the bedside. They usually result from myocardial or valvular events that are affected by function, haemodynamics, and electrical activity of the heart. Correctly auscultating an S4 or S3 gallop sound enables clinicians to diagnose abnormal myocardial relaxation, compliance, or both with elevated filling pressures. Because myocardial relaxation and contraction are orchestrated by intracellular recycling of calcium ions, the timing of these cardiac events is in fact related to the health of myocardial cells. The left ventricle is a pump with two interrelated functions: systolic ejection and diastolic filling. Systolic ejection is preceded by isovolumic contraction and occurs at elevated pressures. Elevated pressures are a prerequisite for fast, efficient autoregulation of blood flow as a function of the metabolic needs of the organs under different working conditions. Diastolic filling is preceded by isovolumic relaxation and occurs at low pressures. These low pressures are necessary for the intimate contact between circulation and air in the pulmonary alveoli. The theoretically optimal pressure domain curve of the left ventricle is rectangular with instantaneous pressure rise, elevated systolic pressures, instantaneous fall and low diastolic pressures. This theoretically optimal situation is approached by cyclic interaction of myofilaments and supposes competent mitral and aortic valves.

Systolic function may be described by velocity of pressure rise (dP/dt max), the velocity of ejection, the extent of ejection or the ejection fraction. Diastolic function may be described by the velocity of pressure decline (time constant τ), the filling velocity or by the diastolic pressure-volume relation. When looking at diastolic function it is essential to make the distinction between active myocardial relaxation and passive stiffness of the ventricle.

An alternative non-invasive approach of global cardiac function is the use of time intervals. This approach is unrelated to the use of timing measurements in the evaluation of regional asynchrony. Most of the available knowledge on time intervals with regard to global function was derived from the electrocardiogram, the phonocardiogram and the carotid pulse tracing. The pre-ejection period (PEP, measured as the time interval between Q and carotid rise) includes excitation-contraction coupling and isovolumic contraction. The ejection period (LVET) is measured as the interval between the steep ascent and the dicrotic notch on the carotid pulse tracing. A healthy ventricle has a short pre-ejection period (PEP) and a long ejection time. A diseased ventricle has a long pre-ejection period and a short ejection time. The ratio of PEP/LVET therefore was proposed as an index of myocardial contractility. Normal values are (mean SD) 0.34 ± 0.04. These values increase in diseased ventricles.

The myocardial performance index (MPI) is an attempt to expand the use of such time intervals in order to characterise both systolic and diastolic function and to describe performance with a single value, which would have a quantitative and prognostic significance. It is defined as the sum of isovolumic contraction time and isovolumic relaxation time divided by ejection time.

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Two papers in this issue of the *Journal* use this index and illustrate what such an index can and cannot provide. Arnlöv et al.\(^7\) showed that the index was elevated in elderly men and that the subjects in the higher quartiles had an increased risk of subsequently developing congestive heart failure. This suggests that the index may detect subclinical myocardial dysfunction. It can distinguish between hearts that are prone to develop congestive heart failure and hearts that are not.

The MPI does not provide information on mechanisms of dysfunction and does not allow making inferences about impaired myocardial contraction, impaired and incomplete myocardial relaxation, systolic load alterations or diastolic filling pressures. Cheung et al.\(^8\) demonstrated, in a well controlled experimental setting in this issue of the *Journal*, how insensitive the MPI could be to marked changes in myocardial contractility as induced by dobutamine. This can easily be understood by the fact that unlike calcium, dobutamine shortens both isovolumic and ejection times so that the effect on the ratio may be unpredictable.

A matter of concern is that the right and left heart MPI index are both load-dependent. This issue was initially raised by Gutgesell\(^9\) who criticized the use of the MPI index in pulmonary hypertension by stressing the fact that pulmonary pressures as well as right ventricular function affect right heart time intervals and that the right heart MPI index could be considered as no more than a kind of “sedimentation rate” of right heart circulation. The MPI is elevated as a consequence of right ventricular dysfunction, increased pulmonary pressures or a combination of both, so that its predictive value in pulmonary hypertension is questionable. In the left ventricle, time intervals are similarly affected by changes in blood pressure and changes in filling pressures.\(^2\)

Another noticeable issue is the duration of isovolumic relaxation in different phases of cardiac disease. In initial phases of left ventricular overload, hypertrophy or ischaemia the time interval between aortic valve closure and mitral valve opening increases. This may be due to myocardial overload, slowed myocardial relaxation or a combination of both. When cardiac disease evolves to a more advanced stage, we will observe systolic myocardial dysfunction on top and filling pressures will further increase.\(^10\) The consequence is a longer isovolumic contraction time and a shorter ejection time, both contributing to an increased MPI index and an impaired functional status and prognosis. The isovolumic relaxation time however will markedly shorten acting in opposite direction on the MPI index, masking the increasing severity of disease. Dandel et al.\(^11\) recently stressed this issue and concluded that, because of the complex interrelationship between systolic and diastolic function in heart diseases and the bidirectional changes of isovolumic relaxation time, the apparently simple MPI index must be used with great caution.

If we would use time intervals derived from echocardiographical measurements, which still appears to be advisable, I would suggest for systole to measure time from onset of the QRS complex to aortic valve opening (pre-ejection time PEP) and left ventricular ejection time (LVET). Weissler derived an index (PEP/LVET) that was less heart rate-dependent than the individual components and proposed this ratio as a measure of LV systolic function. The variability of this index as a measure of LV systolic dysfunction is significant and it is influenced by haemodynamics and conduction disturbances, although it remains clinically useful. With regards to diastole, we simply need the isovolumic relaxation time, to be interpreted in view of the other measurements of diastolic function, and the total filling time.\(^2,10\)

In the course of the last 20 years, we gradually learned how to separately assess myocardial contraction, myocardial relaxation, end-diastolic elastic LV properties and filling pressures. We have used 2D information, time intervals, flow signals and tissue Doppler in order to develop a comprehensive view on each patient’s physiology. In contrast, the MPI, although a simple and attractive tool, will never reveal the detailed picture in an individual patient.

### References