SURGERY FOR CONGENITAL HEART DISEASE

EDITORIAL: LEFT VENTRICULAR DYSFUNCTION AFTER OPEN REPAIR OF SIMPLE CONGENITAL HEART DEFECTS IN INFANTS AND CHILDREN

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Progress in the effort to optimize myocardial protection during bypass and ischemic arrest depends on the availability of sensitive and clinically meaningful methods for measuring myocardial injury. Numerous end points have been used by various investigators, including biochemical, mechanical, and structural indices of tissue damage, but the relative clinical relevance of each is not known. Because of its direct, measurable impact on postoperative morbidity and mortality, functional integrity of the myocardium is unquestionably an outcome variable that we need to be able to measure and understand. The dramatic variations in loading conditions that are inherent in the bypass technique have made this goal somewhat elusive. Typical indices of global cardiovascular performance, such as arterial and filling pressures, cardiac output, and ejection fraction, are the mainstays of clinical status assessment but are incapable of distinguishing between altered load and impaired myocardial function. Ultimately, we would like to measure the impact of any intervention on intrinsic myocardial properties such as contractility, compliance, and relaxation to determine important effects, differences between agents, and how to ameliorate adverse consequences. Despite significant work in the animal laboratory, no single approach to this problem has emerged as a clearly superior technique. In addition, numerous technical obstacles, particularly related to the measurement of ventricular volume,

have impeded the transition from animal to human studies. In what must be recognized as a significant technical achievement, Chaturvedi and associates (see page 77) have forged ahead with a feasibility study applying these nascent techniques to the study of myocardial mechanics before and after cardiopulmonary bypass and cardioplegia, for children undergoing repair of congenital heart disease (predominantly atrial septal defects). The authors' purpose was to verify that the method they used was capable of detecting small changes in intrinsic myocardial properties. They did not attempt to prevent variation in clinical management, including the type of cardioplegia (indeed, both St. Thomas' Hospital and modified blood cardioplegia were used), and no conclusions concerning the advantages of a particular approach are claimed. Their primary conclusions are that (1) it is possible to obtain direct measurement of indices derived from pressure-volume relationships with load alteration in this clinical setting and (2) their data indicate a significant fall in contractility without alteration in diastolic properties after bypass and arrest.

Chaturvedi and coworkers used a conductance catheter to measure ventricular volume continuously during the cardiac cycle. Although this technology has been in existence for a number of years, it has been slow to gain widespread use because it is invasive and a number of technical limitations impeded its use. Measurement of absolute ventricular volume depends on an accurate method for obtaining the parallel conductance volume, V_c , and the slope, α , that relates conductance volume to true volume. There are problems with current means to ascertain both of these variables,¹ significantly limiting the accuracy of absolute volume measurements. However, measurement of relative volume, as is needed for the pressure-volume indices used in this study, is not affected. Nevertheless, determination of the absolute position of the pressure-volume relation is affected, limiting the accuracy of the

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method for comparisons between subjects. Moreover, it is now well documented that the conductance catheter volume has a nonlinear relation to true volume over large variations in volume.²⁻⁴ Again, this has a major impact on determination of absolute pressure-volume position, but over the limited range of volume variation typical of studies such as that of Glantz and colleagues,¹ the assessment of relative volume can still be obtained with reasonable accuracy. Because of this, pressure-volume indices derived from conductance catheter studies have been found to accurately measure the direction and magnitude of change in contractile state.³ The study by Applegate, Cheng, and Little³ was performed under conditions in which the range of end-systolic volume for any given experimental animal had broad overlap for all hemodynamic circumstances, so that relative volume for each calculation was determined over a similar volume range. In contrast, as illustrated in Fig. 1 of the article by Chaturvedi and colleagues, the volume ranges during caval occlusion before and after the operation may not overlap. Whether the catheter technique is similarly accurate when end-systolic volume changes in response to the hemodynamic alteration result in no overlap of the pressure-volume data ranges has not been demonstrated. In fact, the nonlinearity of the relationship of conductance volume to true volume over large volume variation would certainly be a significant factor when there is a twofold change in end-systolic volume, as is the case here. Nonlinearities in the relationship between conductance volume and true volume and the failure of the conductance catheter to provide accurate estimates of absolute volume introduces uncertainties in comparisons between subjects, but also limits the range of variation over which within-subject variability can be assumed to be valid.

Although a number of indices derived from the pressure-volume relationship of the left ventricle are known to be relatively load-independent and sensitive to contractile state, three of the most extensively studied are those reported by Chaturvedi and associates: end-systolic elastance (Ees), preload-recruitable stroke work (M_w), and adjusted maximal rate of pressure rise ($dP/dt_{max}/P_{max}$). Each of these indices is known to have individual advantages and limitations. Preload-adjustment of dP/dt_{max} to end-diastolic volume is the more common approach,⁵⁻⁸ but the approach taken by the authors has the potential advantage of making this the only index that does not depend on the volume estimates. In the Chaturvedi study, of the three indices, only Ees was significantly different before and after surgery.

The authors note that other investigators⁷ have found M_w to be less sensitive to changes in contractility than Ees, leading them to reject the negative results from the other two indices and to conclude that they are able to detect mild impairment of contractility. They argue that the magnitude of the change of both indices was similar to the study by Little and colleagues.⁷ However, in that study the change in both M_w and Ees in response to altered contractility was significant, whereas the *p* value of 0.75 for the change in M_w reported by Chaturvedi's group in fact contradicts their conclusions. Interestingly, Chaturvedi and associates found that $dP/dt_{max}/P_{max}$ actually rose after bypass, and Little and coworkers⁷ found preload-adjusted dP/dt_{max} to be the most contractility-sensitive of the indices. It seems therefore that at the least these represent conflicting results. In other studies in which these three indices have been directly compared, Ees has been found to be equally⁵ or less⁸ sensitive to changes in contractility than M_w . These discrepancies can perhaps be explained by an observation about which all three studies agreed: that M_w is more stable and reproducible⁶⁻⁸ than Ees, primarily because of the wider range of stroke work changes that can be achieved during load manipulation. The impact of this can be readily appreciated from the extremely limited data range that is used to estimate Ees (Fig. 1 in the Chaturvedi article). The narrow pressure range that can be achieved with caval occlusion results in a reproducibility for M_w that is twice that of Ees.⁶ In animal studies the correlation coefficient for the regression of end-systolic pressure versus end-systolic volume is routinely 0.95 or higher,⁷ in striking contrast to the weak average *r* value of 0.78 found by Chaturvedi and associates. It is worth noting that Feneley and colleagues,⁶ in a study on caval occlusion-generated pressure volume indices in human beings, also found Ees *n*-values of 0.79 on average, compared with an M_w *n*-value of 0.95 generated from the same data. Thus, in the only study comparing these indices using data obtained in a fashion similar to that used by Chaturvedi and colleagues, preload-recruitable stroke work (M_w) was found to be the most reliable index of contractility.⁶ It is clear that, contrary to conclusions reached by Chaturvedi and associates, an equally good argument can be mounted in favor of rejecting the results of the Ees as technically inadequate and accepting the results of the M_w indicating that no change in contractility occurred after bypass in the children studied.

Congenital heart disease introduces additional confounding factors to the analysis of ventricular mechanics. Ventricular shape often changes dramatically before and after repair of congenital heart disease in association with alteration of the instantaneous transeptal pressure difference. Even some of the simpler and most common lesions, such as atrial septal defects, ventricular septal defects, and right ventricular outflow obstruction, are included in this category. With regard to the conductance catheter, the impact of acute shape change on α and V_c is not known. This is of particular importance when α is assumed and not measured, as in the study by Chaturvedi and coworkers. The variation in α with ventricular size⁹ implies that at least it cannot be assumed to be invariant in situations characterized by large changes in size and shape. Similarly, the E_s and M_w relationships have been verified in right ventricles,⁸ suggesting that complex shape in and of itself does not invalidate these relationships. However, this does not address the issue of whether acute change in shape alters either of these slope values, preventing valid comparison of preoperative and postoperative measurements. There is certainly a theoretic basis for expecting a change in the slope and/or position of these relationships, because the relationship between myocardial fiber shortening and volume change is highly dependent on the three-dimensional chamber configuration.

In summary, despite the technical feat that the method used by Chaturvedi's group represents, and the care with which this study was conducted, large areas of uncertainty remain as to the validity of the measurements, analysis, and conclusions. This work is an example of the hazards one faces when moving new methods from the animal laboratory to the clinical arena. The practical problems encountered in the clinical setting, such as the difficulties in measuring necessary parameters (such as α for the impedance catheter) and the problems of analyses based on narrow data ranges become major rather than minor obstacles. The areas in which the experimental basis for the analyses are inadequate, such as the effect of ventricular shape change on indices of contractility, can render a result uninterpretable. Furthermore, the ability to reach conclusions is severely limited when indices that are normally close and nearly equivalent yield contradictory results. Much work remains to be done before these methods will fulfill their promise of providing a valid measure of the myocardial effects of cardiopulmonary bypass and cardioplegia.

Finally, a word of caution must be stated when evaluating techniques to measure contractile function in a clinical setting. In addition to evaluation of the reliability and reproducibility of the results, careful consideration must be given to the potential risks, both short term and long term, imposed when invasive techniques are used. The added risk of blindly inserting two stiff catheters into the left ventricular apex, and the resultant transmural scar that may have long-term effects on arrhythmia risk, is not known but is likely to be higher than the risk of a child undergoing repair of atrial septal defect alone. Chaturvedi and colleagues point out that "...at present, combined use of conductance catheters and micromanometers in the perioperative setting remain research rather than clinical tools." We would also add that even as a research tool, careful consideration should be given to the potential risks incurred by a more widespread application of these techniques. The quality and importance of the information obtained must be weighed against these potentially increased risks.

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