Evolution of the Study of Left Ventricular Function
Everything Old Is New Again

Blase A. Carabello, MD

The science of cardiology has evolved parallel to most medical sciences, first emphasizing anatomy, then physiology, and now molecular biology. In the 1960s, when it had become obvious that effective medical and surgical therapies were available for cardiac diseases, there developed a heightened interest in measuring cardiac function as a way of evaluating the heart’s response to those therapies. Because the heart is a muscle, it was logical that measurements of muscle function would be prognostic indicators of the success or failure of a given therapy.

The cardiac muscle translates force into motion, generating cardiac output that is the product of heart rate and stroke volume. Stroke volume is dependent upon mechanical and myocardial muscle (the innate ability of the muscle to generate force), preload, and afterload. Because contractility is the fundamental ability of the heart muscle to do its job, this property generated the greatest focus for measurement. The ideal measure of contractility would have the characteristics listed in Table 1. Unfortunately, despite literally hundreds of investigations, this ideal measure was never developed. Each index of function went through a typical evolution of discovery, enthusiasm, concern for imperfections, and eventual abandonment. The strengths and weaknesses of many of the indexes are listed in Table 2.1–20 The result has been that ejection fraction was chosen by the cardiology community at large and remains the index overwhelmingly used to assess cardiac function in both clinical and experimental studies. The success and persistence of ejection fraction as the premiere indicator of function stems in part from its ease of application and ability to be understood. One of the key aspects of the heart that has attracted attention is the fact that it is one of the few internal organs that moves under its own force. This movement is easy to observe and quantify; there is the general assumption that the more the heart empties, the stronger it is, and ejection fraction quantitates this extent of emptying. Further, application of ejection fraction has usually led to correct interpretation of the pathophysiology present. Although ejection fraction is highly dependent upon preload and afterload1–4 in addition to contractility, in the most common causes of cardiac dysfunction (coronary disease and dilated cardiomyopathy), loading conditions are usually “normal,” and ejection fraction reliably reports at least gross abnormalities in contractility. In some specific instances, however, ejection fraction causes a significant misinterpretation of the actual pathophysiology. In aortic stenosis, excess afterload may cause the ejection fraction to be reduced in the face of relatively normal contractility.21 In such cases, the ejection fraction would mislead the clinician into thinking that severe muscle dysfunction was present when it was not. In mitral regurgitation, augmented preload increases ejection fraction and may cause an overestimation of contractility, falsely leading the clinician to believe that because ejection fraction is “normal,” contractility is also normal, which would ultimately lead to an untimely delay in correction of the lesion.22,23 Perhaps the most common misuse and misunderstanding of ejection fraction, however, occurs in the case of concentric left ventricular hypertrophy. Here, a normal ejection fraction may be maintained by the subnormal function of sarcomeres laid down in parallel.5 Subnormal shortening of extra parallel sarcomeres leads to the same thickening and to the same displacement of blood as would normal shortening of fewer sarcomeres. Thus, in the many cases of concentric left ventricular hypertrophy, an ejection fraction of 0.55 indicates substantial muscle dysfunction.24 This dysfunction can be detected by the use of afterload-corrected midwall-mechanics, but unfortunately difficulty of application has led only a few investigators to use this concept productively.

In a previous issue of Circulation, Derumeaux and colleagues25 report use of tissue Doppler imaging (tDi) to differentiate physiological from pathological pressure overload hypertrophy in rats. Tissue Doppler imaging is able to quantitate the velocity of the myocardium as it moves. In addition, a velocity gradient between the endocardium and epicardium may help to account for changes in performance due to concentric hypertrophy and helps to remove apparent changes due to motion artifact. In the study by Derumeaux et al.,25 tDi was normal in exercising rats that were expected to have physiological hypertrophy and normal contractility. Contractility, however, was abnormal in pressure overload hypertrophy created by banding when “conventional” parameters of left ventricular function “failed” to detect functional abnormalities. It seems logical that tDi would be sensitive in

TABLE 1. Properties of an Ideal Index of Contractility

| (1) Sensitive to changes in inotrophy |
| (2) Independent of load |
| (3) Independent of heart size and mass |
| (4) Easy and safe to apply |
| (5) Proven to be useful in the clinical setting |
detecting abnormalities in cardiac function similar to mid-wall mean velocity of contractile shortening (VcF). One could predict from previous studies that tDi would be relatively insensitive to changes in preload but would be sensitive to changes in afterload, as is suggested by the current study. When afterload was reduced by debanding it for 2 months, tDi returned to normal, suggesting that it had been primarily an afterload mismatch that reduced tDi.

Although I agree with the authors that their tDi techniques were sensitive in detecting both systolic and diastolic abnormalities in function, I do not agree with their statement that “conventional techniques” failed to detect these abnormalities. Rather, it was the interpretation of the data that failed to detect contractile abnormalities. Concentric hypertrophy increases dP/dt. In the exercising versus sedentary rats, the radius to thickness (r/h) ratio fell from approximately 1.7 to 1.5, indicating an increase in concentricity of 12%. Concomitantly, dP/dt rose by 12%, as was expected. Conversely, in the 2-month banded rats, the r/h ratio fell to 1.2, or a 30% increase in concentricity. Although dP/dt should have increased in similar fashion, there was virtually no increase in dP/dt. In fact, this lack of dP/dt increase in the 2-month banded rats despite the presence of concentric hypertrophy indicates that there was substantial left ventricular dysfunction indicated by this “conventional” parameter. If the authors had employed d-stress/dt, they almost certainly would have observed a decrease in contractility. Likewise, the presence of concentric hypertrophy should have increased its shortening fraction, but this parameter was unchanged at 2 months, indicating a functional defect. Had mid-wall mechanics been employed, they too almost certainly would have demonstrated decreased function for 2 months. Nonetheless, tDi provides a more straightforward indicator of function without having to go through the mental gymnastics exercised above. As such, it is likely to be a useful tool. Future studies using tDi to compare the effects of changes in tDi with changes in preload, afterload, contractility, left ventricular thickness, and left ventricular dimension to define the effects of each on myocardial velocities will be necessary to place tDi in the proper perspective of its uses and limitations in examining cardiac function. I would predict that tDi will be a successful advance once it is used within the context of its known limitations. It has the advantages of being easily employed and understandable, provides some advances over ejection fraction, and should help to advance our studies of cardiac physiology. However, tDi cannot fulfill the criteria listed in Table 1 because it almost certainly will be afterload-dependent.

References


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