

Difficulties in the Assessment of Cardiac Function in Patients After Cardiomyoplasty

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Abstract

Though echocardiography and radionuclide scanning (MUGA) are well validated for most clinical situations, little information is available on their accuracy in a patient with an actively contracting cardiomyoplasty wrap. The limitations placed on these modalities by cardiomyoplasty in light of recent investigation into three-dimensional motions, by tagged magnetic resonance imaging, of the wrapped heart are discussed. Marked translation of the heart along its long axis as well as gross lateral translation leads to exaggeration of left ventricular ejection fraction when evaluated by echocardiography and MUGA. Imaging modalities that are capable of 3-dimensional analysis are necessary in order to accurately evaluate the mechanical systolic effects of cardiomyoplasty.

Key words: Cardiomyoplasty, three-dimensional analysis, echocardiography (Echo), radionuclide imaging (MUGA)

BAM 3 (4): 313-316, 1993

An estimated 2.3 million Americans suffer from chronic heart failure and the numbers are increasing by 400,000 new patients per year [9]. It is estimated that between 35,000 and 165,000 patients per year could benefit from cardiac replacement or an assist device. Though cardiac transplantation is an effective treatment for some patients, the short supply of donors and the complications of immunosuppressive therapy limit its widespread use. Despite vigorous research, an effective long-term mechanical cardiac assist device is not yet available [1]. Recently, there has been a renewed interest in the use of cardiomyoplasty, the placement of an autologous skeletal muscle graft wrapped around the heart, to assist failing cardiac function.

Cardiomyoplasty has been performed clinically for eight years with the majority of patients reporting significant functional improvement. In 1985, Carpentier performed the first CMP and reported a 23% increase in the patient's LVEF by echocardiogram with graft pacing on versus off [2]. Magovern reported an increase in ejection fraction from 28% pre- to 52% post-cardiomyoplasty in one patient [8]. Despite encouraging hemodynamic results such as these, consistent objective improvement in left ventricular function, as measured by echocardiography, radionuclide scintigraphy (MUGA scans), and cardiac catheterization, has not correlated well with the substantial subjective

improvement noted in symptoms. The inconsistency in the effects of the skeletal muscle graft on cardiac function could be attributed to differences in the intrinsic preload characteristics of cardiac versus skeletal muscle "conditioned" to become a slower contracting, less fatiguable muscle; to alterations in loading conditions; to intrinsic changes in the mechanics of the skeletal muscle secondary to the trauma of the surgery to create the graft; and/or to metabolic changes from the "conditioning" process [7]. Others have attributed this absence of consistent objective evidence to the heterogeneity of the patient population and the variability of imaging techniques between centers.

Another potential reason for the reported variability in hemodynamic changes is the very reliability of the measurements used to assess ventricular function following cardiomyoplasty. Most often echocardiography and radionuclide scanning have been used to measure ventricular function in this patient group. Though these methods are well validated for most clinical situations, little information is available on their performance in the patient with an actively contracting cardiomyoplasty wrap. It is the purpose of this paper, therefore, to examine these commonly used clinical methods, reviewing their underlying geometric assumptions, and to discuss the limitations placed on these modalities by cardiomyoplasty in light of

recent investigations into the three-dimensional motions of the wrapped heart.

Echocardiography is the most common clinical method of assessing ventricular function. The detection of ultrasound waves generated by a probe and reflected from anatomic structures allows the generation of visual images in a variety of modes. From calibrated images the changing dimensions of the cardiac chambers can be measured throughout the cardiac cycle. When used for evaluation of ventricular function post-cardiomyoplasty, echocardiography may produce encouraging but erroneous results. The ejection fraction is generally calculated from the change in diameter of the heart from end-diastole to end-systole. There is an implicit assumption that this measurement is made at the same transverse, or short-axis, section of the heart at both points in time. It has been shown that the heart moves differently in space during the stimulation of the muscle (assisted beat) in comparison to the non-stimulated (unassisted beat). Specifically, there is marked translation of the heart along its long axis toward its base as well as lateral translation orthogonal to the long axis [4, 5]. Since the roughly cone-shaped left ventricle (LV) moves substantially along its long axis with wrap stimulation, measurement of the LV cavity diameter is made at a more apical portion of the heart during the assisted beat compared to the unassisted beat (Fig 1). This error would tend to increase the calculated ejection fraction.

Radionuclide scintigraphy, or MUGA scanning, has been also been widely used to evaluate ventricular function following cardiomyoplasty. MUGA scans rely on the selective visualization of a pool of radiolabeled blood cells in the LV using a "region of interest" window oriented in the left-anterior-oblique projection, which excludes radiation signals from other parts of the heart, such as the right ventricle. A gated image is obtained by acquiring repetitive

images of the heart at specified times in the cardiac cycle referenced to the QRS complex. The cycle is usually broken down into 16-32 segments, or time slices. The number of tracer counts occurring during each time slice are summed for many beats to create a final image. Thus, the final image is a "movie" of the 16 time slices played repetitively in sequence representing the chamber volumes over time from systole to diastole. The ejection fraction is calculated by the ratio of the number of counts in the LV at end-systole and end-diastole. This method correlates well with ejection fraction measured by contrast ventriculography in most patient populations. However, the proper use of this modality is based on a number of assumptions which likely do not apply to the patient who has undergone cardiomyoplasty.

The calculation of end-diastolic and end-systolic counts depends on summing the counts within the pre-defined "region of interest". Since the data are acquired over many cardiac cycles, there is a geometric assumption that the heart, and hence the LV, will be centered at the same position in space at each time slice for each of the beats acquired. However, stimulation of the muscle wrap causes substantial translation of the heart along the short-axis plane [4, 5]. This virtually ensures that the LV will move out of the region of interest during the assisted beats (Fig 2). In canine studies of cardiomyoplasty three-dimensional MRI reconstructions reveal magnitudes of displacement with wrap stimulation that would cause an artifactual component of ejection fraction heart of up to 26% attributable solely to "disappearance" of the LV outside the region of interest [4].

Another type of error potentially associated with MUGA scanning arises from considerations of gating and triggering. As currently performed, MUGA scans acquire data with every heart beat in a given time interval. Many

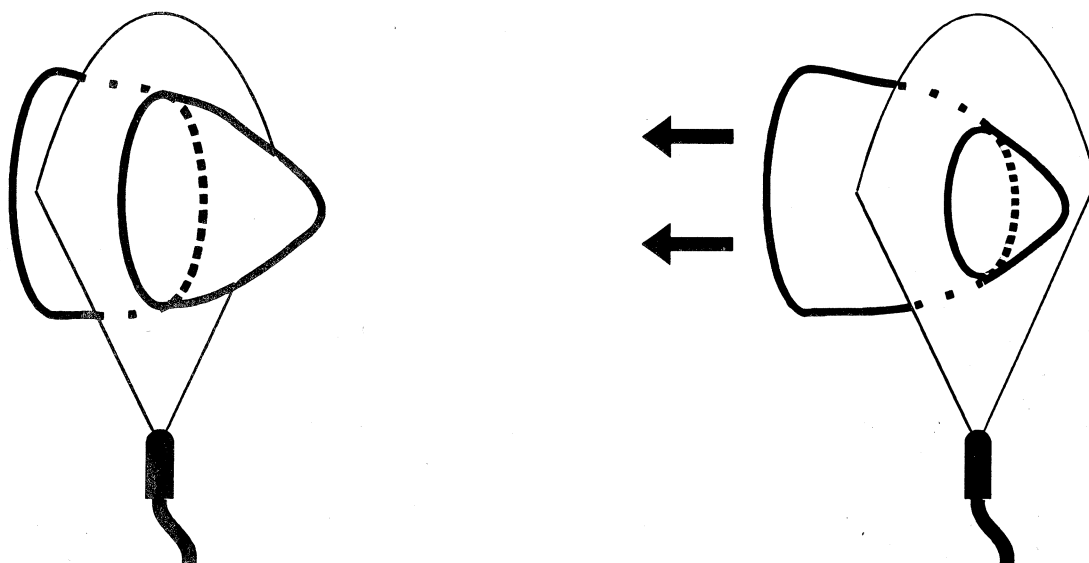


Figure 1. Long axis shortening produced by cardiomyoplasty results in artifactual decrease in left ventricular chamber when evaluated by two dimensional echocardiography.

Cardiomyoplasty: assessment of cardiac function

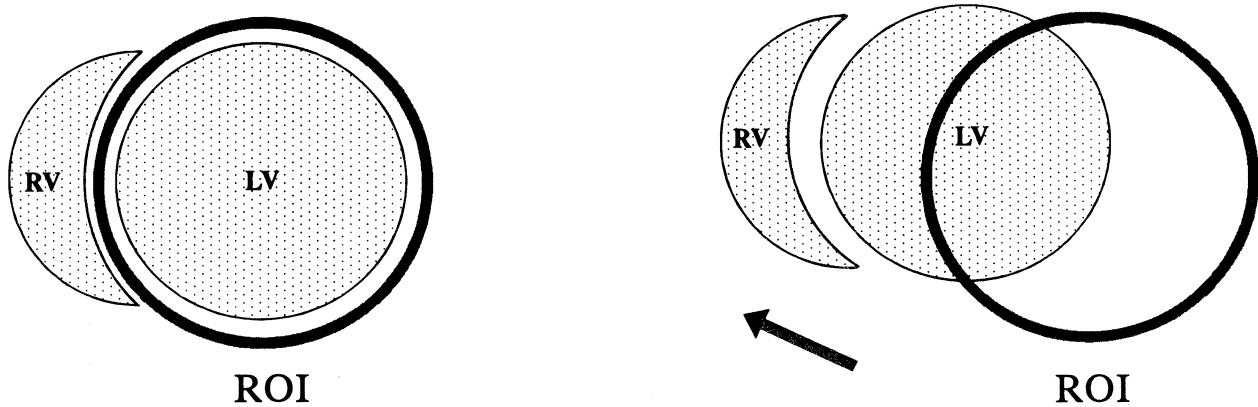


Figure 2. Translational motion orthogonal to the long axis produced by cardiomyoplasty results in an artifactual increase in LV ejection fraction when evaluated by MUGA. (LV = left ventricle, RV = right ventricle, ROI = region of interest.).

cardiomyoplasty patients have their cardiomyostimulators programmed to stimulate the muscle wrap with every other heart beat. If both the assisted and unassisted beats are acquired during the imaging interval, each time slice will have aggregated data from multiple assisted and unassisted beats. Because of the differential motion of each family of beats in space, the image will appear more blurred due to the non-superimposition of the tracer counts. This error will lead to the prescription of an inaccurate region of interest. Such an error would tend toward an overestimation of ejection fraction. Moreover, any comparison of the ejection fractions of the assisted beat versus the unassisted would be impossible without segregation of data from the

two different types of beats, as we have demonstrated using pressure-volume analysis [3].

The MUGA scanner is triggered by the QRS complex of the electrocardiogram to recognize a new cardiac cycle. The cardiomyostimulator produces a burst of electrical pulses to create a tetanic contraction of the skeletal muscle wrap. Any of these pulses may be misinterpreted by the MUGA scanner as a QRS complex, and result in mistriggering. Figure 3 shows the effect of mistriggering on the radionuclide scan. Similar to the effect of a premature beat, if the radionuclide scanner interprets the pulses used for skeletal muscle burst stimulation during the assisted beat as additional QRS complexes, the time activity curve of

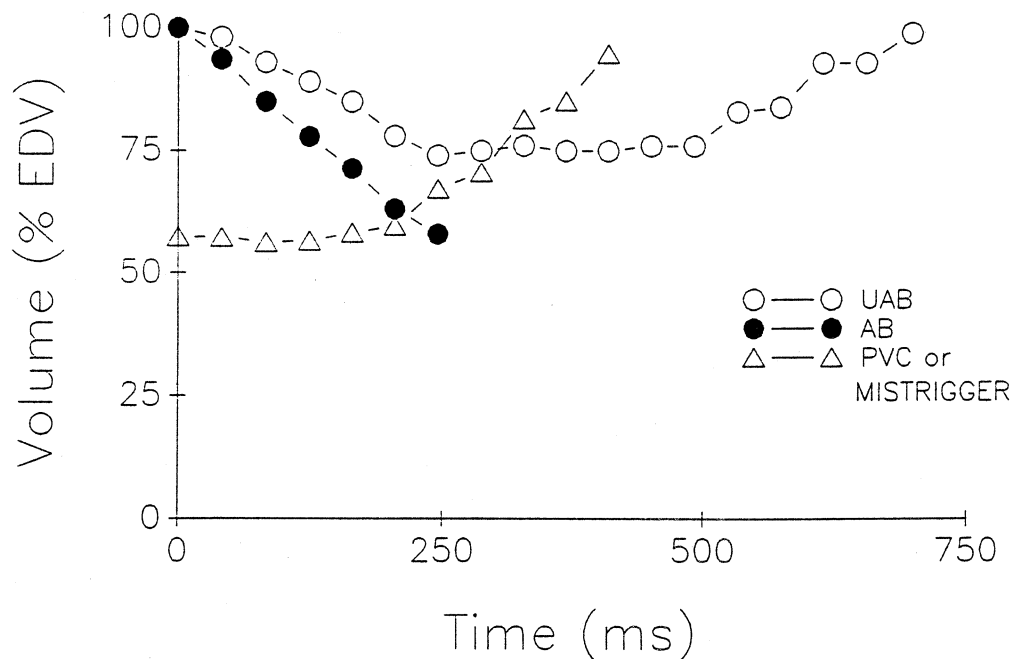


Figure 3. The effect on mistriggering or premature ventricular contractions on the radionuclide time activity curve (UAB = unassisted beat, AB = assisted beat).

the assisted beat will be altered as shown. The result of this mistriggering is that the first few time slices (systole) have counts that would normally have been added to time slices at the end of the beat (diastole). Since the ejection fraction is calculated from the numbers of end-diastolic and end-systolic counts, the erroneous addition of counts to systole and relative reduction of diastolic counts will result in the incorrect estimation of the ejection fraction. As with motion error, this mistriggering would result in an overestimation of ejection fraction.

Theoretically, measures could be taken to compensate for some of the motion artifact, but they would be impracticable. The complexity of the motions, which include not only translation, but also rotation of the cardiac axes, and their rapidity during one cardiac cycle preclude effective manipulation of the echocardiographic probe or the MUGA region of interest using current technology. The shortcoming of both of these modalities in this setting is their limitation to two-dimensional imaging. The ideal technique for the regional evaluation of cardiomyoplasty mechanics would provide detailed information in three dimensions with fine temporal resolution.

Radio-frequency-tagged magnetic resonance (MR) imaging is an innovation which allows non-invasive marking of areas of interest within tissues and the tracking of these tags through time [4]. With this technique we have successfully characterized the regional mechanical effects of dynamic cardiomyoplasty in the healthy and myopathic canine heart [4, 5].

Finally, our recent work using pressure-volume analysis suggests that the primary benefit of CMP may be to improve chronic diastolic function rather than to improve acute systolic function [6]. Using two dimensional echo and MUGA to compare acute changes in systolic function as a result of cardiomyoplasty is not the best method of demonstrating chronic improvement in diastolic function.

In summary, the most widely used imaging modalities for determining cardiac function, echocardiography and radionuclide scintigraphy, are prone to many errors if used in patients who have undergone cardiomyoplasty. These difficulties stem largely from the exaggerated motion of the heart with stimulation of its encircling muscle wrap, but shortcomings of data acquisition may also introduce error. Magnetic resonance imaging has shown promise in the study of the regional interactions between cardiac and skeletal muscle and of the beat-to-beat variation in cardiac function in dynamic cardiomyoplasty. Detailed, accurate information regarding the mechanical and hemodynamic effects of this new surgical procedure are crucial for optimizing post-operative cardiac function through the rational design of wrap orientation and conditioning protocols.

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