Left Ventricular Time Varying Elastance Behavior Does Not Reflect a Basic Property of Cardiac Muscle

The article of Hisano and Cooper\(^1\) raises once again the seemingly unresolved question on the myocardial basis for the time varying elastance behavior of the left ventricle, a concept formalized by Suga et al in 1973.\(^2\) From their experiments, Hisano and Cooper conclude that "the correlation of pressure-volume area with oxygen consumption on the ventricular level arises from a basic property of cardiac muscle," but "that the time varying elastance model, on which the concepts of pressure-volume area and force-length area are based, may not provide a complete description of the mechanical basis of cardiac muscle energetics." In order to agree or disagree with this point of view at least one question needs an answer: What is a "basic property" of cardiac muscle?

There can be no disagreement that all aspects of whole heart behavior, including time varying elasticity, must come from basic properties of cardiac tissue. This statement does not require experimental evidence; it stems from logic alone. The conclusion of Hisano and Cooper should therefore have a different meaning. As argued below it pertains to similarities between theories at different levels of understanding.

What is meant is that theories explaining the behavior of a system at a certain level of complexity in many cases cannot be used to describe the behavior of the constituting subsystems and vice versa. For example, theories holding true for molecules cannot reliably predict the properties of the myocyte, nor can adequate theories at the myocyte level be derived from observations on the whole heart. Within this framework, we understand that Hisano and Cooper's conclusion implies that the theory on which the correlation of pressure-volume area and oxygen consumption is based holds true both at the ventricular and papillary muscle level. Two problems arise from such a conclusion.

1. Hisano and Cooper state that the time varying elastance model, which is, according to Suga et al,\(^3\) the theoretical basis of the linear relation between oxygen consumption and pressure-volume area does not hold true for the papillary muscle. Therefore, Hisano and Cooper must assume some other, as yet unknown, theory, which conflicts with the one proposed by Suga et al but explains the findings at both levels of complexity: the whole ventricle and the papillary muscle. The nature of that unformulated theory is, of course, of interest but at least as important is the conclusion that their experiments show that Suga et al's\(^2\) formalism of left ventricular time varying elastance behavior does not follow directly from a basic property of cardiac muscle. Since they do not describe the new theory, disproving the old one is the most important message of their paper. This message should have been brought out much more clearly in the text and also in the title (see title of this letter), since the title should be the shortest abstract of a manuscript.

2. Although we do not know the theory which can explain the relationships between mechanical behavior and energy turnover in papillary muscles and whole ventricles, we do know that a theory which cannot predict a higher energy output during an afterloaded contraction than during an isometric one, both starting at the same length, will not hold true at the level of the contractile proteins. This conclusion should have been presented also by Hisano and Cooper. In contrast to what Hisano and Cooper state in their "Discussion," the most important result of Fenn's findings\(^4\) was not that he found "that load changes after the onset of contraction affected the total energy expenditure" but that the total energy output (heat + work) during loaded shortening was higher than during isometric contraction. Since Fenn's experiments on frog sartorius are highly relevant for Hisano and Cooper's study, two conclusions may be drawn. First, the present experiments support Fenn's results, namely that Suga et al's formalism of left ventricular time varying elasticity does not follow directly from a basic property of cardiac muscle. Second, the yet unknown theory needs to incorporate Fenn's findings and therefore does not necessarily predict a linear relation between pressure-volume (and force-length) area and total energy turnover.

References


**Reply to the Preceding Letter**

Drs. Elzinga, Mast, and Westerhof's major concern is that Dr. Hisano and I should have given greater emphasis in the paper under discussion to the subset of data therein which suggests that the time-varying elastance model does not provide a complete description of the mechanical basis of cardiac muscle energetics. Given this concern with emphasis rather than substance, and my inability to discover any area of genuine disagreement between us, I must say that I am puzzled by the preceding letter. Perhaps it might be useful, in dealing with their concern about emphasis, to place the paper in perspective.

In an earlier series of papers, I showed that the unique relationship between pressure-volume area and energy utilization seen by Dr. Suga and his colleagues in the intact ventricle, and formulated in terms of the time-varying elastance model, would not be expected on the basis of the relation of mechanics to energetics that I found in isolated cardiac muscle. Specifically, I found that energy utilization continued past the time of end-systole. But the recognition of discordances between the mechanics and energetics of isolated linear as opposed to intact ventricular cardiac muscle was not then and is not now unique. Indeed, problems in reconciling the apparently disparate properties of cardiac muscle when studied on these two levels were quite apparent over a decade ago to Dr. Sagawa, the originator of the time-varying elastance model.

The existence of such discordances raises the interesting question of their origin. An efficient experimental or theoretical approach to this question requires a better knowledge of those aspects of isolated muscle energetics that correlate with the physiology of the intact ventricle, as well as a knowledge of those that do not. To this end, Dr. Suga sent his colleague, Dr. Hisano, to my laboratory to carry out the experiments reported in the paper under discussion. The resultant paper was mainly a description of those aspects of cardiac energetics wherein the function of isolated muscle could be correlated with the function of intact ventricular muscle within the framework of the time-varying elastance model. Under a variety of loading conditions there was a close correlation of myocardial oxygen consumption with force-length area in linear cardiac muscle, similar to the correlation between oxygen consumption and pressure-volume area in the ventricle. The similarity of these relationships led us to suggest that the correlation of energetics with mechanics on the ventricular level arises from a basic property of cardiac muscle, at least in the limited sense of being intrinsic to the muscle segments comprising the ventricle.

In the course of these experiments, however, we made two observations in isolated cardiac muscle (Figures 6 and 7) that are clearly inconsistent with the time-varying elastance model: first, time to end-systole is load-dependent; second, energy utilization continues past the time of end-systole, as I have shown before.

I hope that the above precis has clarified the basis for the structure of both the study and its report. A few comments about the two enumerated points in the preceding letter may now be appropriate. With respect to point number 1, it was the intent of this study to better define areas of both concordance and discordance in applying the ventricular time-varying elastance model to linear isolated cardiac muscle. I did not particularly wish to give emphasis to one category or the other, nor is it obvious to me that there is any merit inherent in so doing. What does seem obvious, both from this and from a great many other studies, is that the time-varying elastance model has proven quite successful in correlating energetics with mechanics under a variety of loading conditions. But it is also obvious that the time-varying elastance model does not explain the mechanisms underlying these correlations. Indeed, the paper under discussion provides the two examples noted above which strongly suggest that the time-varying elastance model cannot provide a general solution to the problem of relating cardiac mechanics to energetics. Further work might most usefully focus on attempts to explain both the concordances and the discordances, rather than a single category.

With respect to point number 2 in the preceding letter, I do not know and thus did not state what "the most important result of Fenn's findings" might be. However, it may be worth noting that the Fenn effect as originally described for skeletal muscle in terms of greater energy utilization during afterloaded isotonic contractions than that found in maximum isometric contractions has not been demonstrated in cardiac muscle. Instead, the increased energy liberation seen in isotonic as compared with isometric contractions is only observed in cardiac muscle when the two types of contraction are compared at equivalent loads and at initial lengths less than the optimum length for tension generation.

A treatment both of the Fenn effect as seen in cardiac muscle in particular and of the effects of mechanical variables on cardiac energetics in general will be given elsewhere (G. Cooper, *Annual Review of Physiology*, manuscript in preparation).

However, I do appreciate the fact that the preceding letter provided me with the opportunity to point...
Left ventricular time varying elastance behavior does not reflect a basic property of cardiac muscle.

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