The following is the abstract of the article discussed in the subsequent letter:

**Gentles TL and Colan SD.** Wall stress misrepresents afterload in children and young adults with abnormal left ventricular geometry. *J Appl Physiol* 92: 1053–1057, 2002; doi:10.1152/japplphysiol.00750.2001.—Wall stress, although commonly used as an index of afterload, fails to take into account forces generated within the wall of the left ventricle (LV) that oppose systolic fiber shortening. Wall stress may, therefore, misrepresent fiber stress, the force resisting fiber shortening, particularly in the presence of an abnormal LV thickness-to-dimension ratio (h/D). M-mode LV echocardiograms were obtained from 207 patients with a wide range of values for LV mass and/or h/D. Diagnoses were valvar aortic stenosis, coarctation repair, anthracycline treated, and severe aortic and/or mitral regurgitation. End-systolic wall stress (WSes) and fiber stress (FSes) were expressed as age-corrected Z scores relative to a normal population. The difference between WSes and FSes was extreme when h/D was elevated or reduced [WSes Z score − FSes Z score = 0.14 × (h/D)^{-1.47} − 2.13; r = 0.78, P < 0.001], with WSes underestimating FSes when h/D was increased and overestimating FSes when h/D was decreased. Analyses of myocardial mechanics based on wall stress have limited validity in patients with abnormal ventricular geometry.

**Comparing Measures of Afterload: Wall Stress and Fiber Stress**

*To the Editor:* Drs. Gentles and Colan (1) suggest that wall stress (WS) is a poor measure of afterload in patients with abnormal end-diastolic wall thickness-to-dimension (h/D) ratio by comparing meridional end-systolic WS (2) to meridional end-systolic fiber stress (FS) (3) and correctly find that the residual of FS predicted by WS was related to the h/D ratio. Instead of using experimental data, Gentles and Colan could have simply divided their referenced WS and FS formulas to reveal that WS/FS = [ln (1 + 2A)/[2A(1 + A)], where A = h/D. Hence, FS is a simple mathematical transformation of WS that is a function only of h/D. Inspection of the WS/FS function shows that it decreases as h/D increases (see Fig. 1), and FS is always greater than WS. Using echocardiographic data from a recently completed trial (4), WS was used to estimate FS in a linear regression model producing an R² of 0.85 (r = 0.92), which is similar to that reported by Gentles and Colan (1). However, if WS and h/D are both used to estimate FS, the resulting model, not surprisingly, produces an r value that rounds to 1 (R² = 0.993). Hence, all variation reported by Gentles and Colan in their Figs. 2 and 4 was due simply to variation in WS and variation in constructed Z scores. One can exactly calculate the relationship between FS and WS without using the empirically derived equation offered by Gentles and Colan (see Fig. 4 of Ref. 1). The exact relationship between FS and WS is provided above and graphed in Fig. 1. The difference between FS and WS is graphed in Fig. 2 below and can be compared with Gentles and Colan (see Fig. 4 of Ref. 1).

It seems, therefore, somewhat misleading to state that WS “misrepresents” afterload. More precisely, the two formulas represent elements of afterload that are not identical but differ only by a function of h/D. In the clinically relevant range of h/D, say between 0.125 and 0.25, WS/FS = 0.793 and 0.689, respectively, or a doubling of h/D only changes WS/FS by 13.1%. The clinical question is whether afterload is misrepresented by one formula or the other, i.e., whether the correlation between WS and FS so different that rank ordering of patients would change in a clinically important fashion. That will depend on h/D and the value of WS or FS.

Over the past year, I have noted that the Gentles and Colan paper (1) has repeatedly been cited by pediatric cardiologists as justification for not measuring WS (or FS). This seems unfortunate. If WS and h/D are known, then FS can be calculated. In ranges of h/D that are clinically relevant for many cardiac conditions, such as those found in anthracycline cardiotoxicity (as was correctly pointed out in the Gentles and Colan paper), the correlation between WS and FS is quite high, and it remains to be seen whether clinical judgment would change if cardiologists relied on one measure of afterload vs. the other.

**ACKNOWLEDGMENTS**

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**REFERENCES**


![Fig. 1. Relationship between fiber stress (FS) and wall stress (WS). h/D, wall thickness-to-dimension ratio.](image-url)
REPLY

To the Editor: We thank Dr. Silber for his comments on our paper (1). We agree that because wall stress and fiber stress are both functions of wall thickness, chamber dimension, and pressure, and their relationship to pressure is the same, it is clear that their difference will be a function of the relationship between wall thickness and dimension. However, the statement that this is a simple relationship masks the potential implications. When people say a “simple” relationship, they usually mean a linear relationship. Indeed, if the relationship were linear, then the choice of one method of assessing afterload over the other would be unimportant because they would have different but statistically equivalent relationships to midwall function. However, the relationship of wall stress to fiber stress is nonlinear, and predicting their impact on their respective relationships to midwall systolic function is therefore complex.

With regard to our statement that wall stress misrepresents afterload, it is precisely this nonlinear relationship that leads to this conclusion. “Misrepresents” means that the two do not lead to similar conclusions. We would also say that radius misrepresents volume because, although they are related by a straightforward function, an increase in radius does not result in a proportionally similar increase in volume. If one used a change in radius to represent the change in volume, one would completely and nonlinearly misrepresent the magnitude of any change in volume. The same argument holds for wall stress vs. fiber stress. The misrepresentation arises because, as Silber so nicely documents in his letter, these variables are nonlinearly related.

Rather than describe this relationship in mathematical terms, we sought to assess the clinical importance of using one method or the other by demonstrating the impact of the two different formulas on the assessment of afterload in different patient groups with different wall thickness-to-chamber dimension ratios (h/D). In doing so, we demonstrated that estimating afterload without reference to transmural force (i.e., ignoring the impact of h/D) resulted in underestimation of afterload in relatively thick-walled ventricles and overestimation in thin-walled ventricles. Although this could be assumed to be the case at the mathematical level, it would have been very difficult to appreciate whether this impact was or was not clinically important without “real” data that included all three variables. We found that use of fiber stress vs. wall stress is unimportant when h/D was normal or reduced to a relatively minor degree but was important at lower h/D levels. Furthermore, in patients with high h/D values, it explained several long-standing paradoxical issues in patients with hypertrophy.

Silber is of the opinion that the difference between wall stress and fiber stress is only important if it alters “rank ordering.” We disagree that changes in rank order are the sole indicator of clinical relevance. Because of the nonlinear nature between the two variables, the magnitude of misrepresentation of afterload associated with reliance on wall stress is dependent on the degree of relative wall thinning or thickening, even if the rank order within any population is not changed. It seems to us that knowing whether the surrogate variable provides a valid estimate of the relative magnitude of change is at least as important as its impact on rank order. To return to our prior example, use of dimension as an estimate of volume would not alter the rank order but would lead to the misinterpretation that there had been a 100% change in size when indeed the true change had been 800%.

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Fig. 2. Difference between FS and WS. For comparative purposes, Fig. 2 can be compared with Fig. 4 in Ref. 1.
We recommend the use of fiber stress when afterload is assessed in the left ventricle with an abnormal h/D. Calculation of fiber stress is based on exactly the same data as that required for the calculation of wall stress. We are surprised that others have apparently cited our report as a justification not to measure afterload when ventricular mechanics are assessed. The message of this paper is to refine the method of calculating afterload, not to abandon its use.

REFERENCE


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