in the population studied, the authors concluded that GCS contributed more than twice as much to EF compared with GLS. However, as recognized by the authors, this conclusion seems to be inconsistent with a previous cardiac magnetic resonance study by Carlsson et al. (2), which reported that long-axis LV contraction accounts for approximately 60% of the LV stroke volume. Understanding the reason for the apparent divergence between the findings and conclusions of Stokke et al. (1) and Carlsson et al. (2) is therefore of considerable importance.

A fundamental principle underlying the cardiac magnetic resonance study of Carlsson et al. (2) was that apically directed motion of the mitral annulus resulting from contraction of LV long-axis fibers, and therefore shortening of the left ventricle in its long axis, must also lead to short-axis (radial) thickening. This principle is based on conservation of LV mass, which still applies even if a small percentage of myocardial compressibility is assumed, as it was in the study of Stokke et al. (1). The only way that long-axis contraction-mediated short-axis thickening would not be contributing to a lower LV end-systolic volume, and thus larger stroke volume and absolute value of GCS, is if the epicardial border expanded at the same time. However, it is the opposite which occurs (3,4). Hence, an explanation for the apparent discrepancy in the findings of the 2 studies is an intrinsic limitation of the equation used for modeling the effects of changes in GLS on EF, as independence of GLS and GCS is assumed in the equation and a dependent change in GCS as a result of a change in GLS is not possible.

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REPLY: Interaction Between Longitudinal, Circumferential, and Radial Deformations and Their Contributions to Ejection Fraction

We read with interest the comments from Dr. Matthews and colleagues who propose "myocardial contraction fraction" (MCF) as an alternative systolic function parameter. We believe it is difficult to evaluate this parameter due to the limited number of studies applying MCF. However, MCF can easily be extracted in our mathematical model, and we encourage such a theoretical investigation, which we believe would provide valuable insights regarding the relation between MCF versus strains, ejection fraction (EF), wall thickness, and cavity volume.

We also appreciate the comments by Dr. Carlsson and colleagues, as the different assumptions we use in our respective models (1,2) and the consequently diverging conclusions should be made clear. The main difference in our assumptions is with respect to epicardial motion, as also pointed out by Dr. Peverill in his letter. We agree that there is no outward epicardial motion; rather, it moves slightly inward. As the longitudinally oriented fibers contract, they generate stretching forces in both the radial direction, giving rise to 1 component of wall thickening, and also in the circumferential direction. However, there is no circumferential stretch because there are actively contracting circumferentially oriented fibers. Active circumferential fiber shortening directly reduces the cavity diameter and indirectly reduces it further by generating another component of radial stretching forces that contribute to the wall thickening.

Hypothetically, a left ventricle with only longitudinal fibers would only have passive intercellular and intracellular tissue structures resisting the increased pressure during systole in the circumferential direction. Hence, these would stretch (due to increased pressure + Poisson's ratio effect), resulting in an outward motion of the epicardium. Similarly, in a hypothetical ventricle with only circumferential fibers, it would stretch in the longitudinal direction during systole. We have already performed a finite element simulation study that showed this effect (3).

It is noteworthy that despite outward motion in 1 direction, the space occupied within the pericardium would still be reduced by the stroke volume (outer left ventricular volume = cavity volume + incompressible myocardial volume).

Carlsson et al. (2) extracted the longitudinal component to stroke volume by using a cylinder approach: a constant outer epicardial area multiplied by the longitudinal decent. Effectively, this approach incorporates circumferential shortening of every layer inside the epicardium, as well as wall thickening caused by both the longitudinal and circumferential shortening. We therefore argue that this theoretical volume exaggerates the pure longitudinal contribution. To perform what we believe is a fair investigation of their individual contribution to EF, circumferential shortening was fixed to a prescribed value, and the longitudinal shortening was varied, and vice versa. This perspective shows that circumferential shortening contributes more to EF, which is consistent with the following: 1) numerous studies showing loss of longitudinal shortening and still preserved EF; 2) circumferential shortening's quadratic impact on EF as opposed to only linear for longitudinal shortening; and 3) the good agreement of our model with measurements.

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Arterial Thromboembolism in Non-Hodgkin Lymphoma

In a recent paper, Navi et al. (1) showed that patients with cancer have an increased risk of myocardial infarction and ischemic stroke in the months after the cancer diagnosis. The study included almost 280,000 pairs of cancer (8 types, including non-Hodgkin lymphoma [NHL]) and matched noncancer patients. Due to the size and the methodologic rigor, this study settles a question that, as the authors point out, had received little attention.

NHL is a heterogeneous group, ranging from aggressive lymphomas that can threaten the patient's life in weeks to indolent lymphomas that require no treatment for years. In line with solid tumors, where the risk of venous thromboembolism is generally greater in clinically more aggressive cancers (2), the risk of venous thromboembolism is higher in high-grade lymphomas (3,4). Indeed, the effect of NHL subtype might be greater than that of tumor stage, also well-documented (4), and which Navi et al. (1) found to be relevant for the risk of arterial thromboembolism. Importantly, however, stage and NHL histology are not unrelated. Aggressive lymphomas are often symptomatic, leading the patient to seek medical help earlier, whereas indolent lymphomas are more often diagnosed in asymptomatic patients, already in stage IV. Therefore, the risk of arterial thromboembolism in aggressive NHL could be underestimated when not taking the histological subtype into account. Because the clinical approach to patients with aggressive and indolent lymphomas

TABLE 1 Classification of Aggressive Versus Indolent Non-Hodgkin Lymphoma According to the International Classification of Diseases for Oncology, 3rd Edition Histology Classification

Aggressive	Indolent
9590*,9591*,9596* 9597,9673,9675,9678-9680,9684,9687,9688,9700-9702,9705,9708,9709,9712,9714-9719,9724-9729,9735,9737,9738,9811-9818,9827,9837	9670,9671,9689,9690, 9691,9695,9698, 9699,9823

*Ideally, a sensitivity analysis would be performed excluding 9590, 9591, and 9596, given that those categories are unspecific, even though they are probably most likely to be used for aggressive non-Hodgkin lymphomas.