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## REPLY

We appreciate the letter from Thomas et al. for emphasizing the emerging value of measuring fat around the heart. However, we respectfully disagree with the primary assertion in the letter, since we in fact did study epicardial fat as defined by the letter authors. On computed tomography (CT), our designation of pericardial fat was “all adipose tissue detected within the pericardium,” which matches the definition of epicardial fat specified by Iacobellis et al. (1). A closer look at our work will additionally reveal that we separately studied the volume of adipose tissue inside and outside of the pericardium. In doing so, we showed that only fat inside the pericardium held predictive power for the risk of future cardiovascular events.

Although some investigators performing CT-based research have defined pericardial fat as we did (2–4), others have used pericardial fat to encompass adipose tissue both inside and outside of the pericardium (5,6). Undoubtedly this nonuniform labeling creates confusion. Given the increasing attention paid to fat surrounding the heart and coronary arteries, standardization of terminology may be in order. This notwithstanding, readers of the literature should cautiously examine the methodology to ensure understanding of the exact fatty depot being measured.

The ability to derive additional prognostic information from standard noncontrast calcium scoring CT by quantifying fat volume inside the pericardium is important. We look forward to understanding further the impact of this measure through future investigations.

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## Prognostic Significance of Strain Imaging in Amyloidosis

In the interesting article in a recent issue of *JACC* by Koyama et al. (1), tissue Doppler (TD) longitudinal strain measured at the left ventricular (LV) base was reported to be an independent predictor of outcome in patients with cardiac amyloid light-chain (AL) amyloidosis. These findings point out an interesting potential clinical application of strain imaging for risk stratification in these subjects. However, caution is needed in accepting the independent prognostic role of basal strain, as a number of established prognostic factors, such as LV ejection fraction, New York Heart Association functional class, natriuretic peptide plasma concentration, cardiac troponins, indexed left atrial volume, the ratio of mitral peak velocity of early filling to early diastolic mitral annular velocity, right ventricular dysfunction, and renal failure, were not considered in survival analyses. Several evidences confirmed a major impact of these factors on clinical outcome in patients with cardiac AL amyloidosis (2). This may be of particular importance because nearly 70% of cardiovascular events (15 of 22) occurred in group 3 (cardiac amyloidosis with clinical evidence of heart failure), where the relative contribution of these variables to clinical outcome is expected to be relevant. Even if a subgroup analysis showed a borderline significant association of basal strain with outcome among patients with no clinical evidence of heart failure, it should be considered that most of these variables are important determinants of outcome in the pre-clinical stages of heart failure as well (3).

In addition, we believe that the evaluation of strain imaging as a prognosticator in cardiac AL amyloidosis should not be limited to the assessment of baseline deformation values. We recently reported an early improvement in both average longitudinal strain and systolic dyssynchrony after treatment with melphalan and dexamethasone, an aspect that was not detectable by color TD (4). Because response to therapy is an important predictor of survival in these patients, the prognostic meaning of changes in strain pattern after therapy might be an intriguing issue to investigate. The clinical impact of myocardial dyssynchrony—a controversial question in cardiac amyloidosis, for which, to date, 3-dimensional echocardiography and color TD have yielded conflicting results, ranging from increased dyssynchrony to abnormal hypersynchronization—may also represent an interesting application of strain imaging. Lastly, the promising role of speckle tracking imaging should be pointed out. Very recent

preliminary data suggest that longitudinal strain measured by speckle tracking may be a powerful independent predictor of mortality in patients with primary amyloidosis and normal LV ejection fraction (5).

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## REPLY

We appreciate Dr. Ballo's letter concerning our recent article (1) on the prognostic significance of strain Doppler imaging in light-chain (AL) amyloidosis. The correspondent's major concern pertains to the perception that "established prognostic factors," such as left ventricular (LV) ejection fraction, New York Heart Association functional class, natriuretic peptide level, cardiac troponins, indexed left atrial volume, mitral annular velocity determined by pulsed tissue Doppler (TD) imaging, right ventricular function, and renal function, were not considered in our study.

We did not intend to suggest in our article (1) that strain imaging should be the sole technique for assessing prognosis in AL amyloidosis. Certainly, the prognostic value of cardiac biomarkers is well established, and these measurements may be useful in clinical assessment. However, the emphasis of our work is on cardiac function assessed by echocardiographic techniques. Our data were a continuation of our previous published work on this topic. As mentioned in the introduction to our study, we previously demonstrated that systolic dysfunction can be detected in cardiac amyloidosis by using strain/strain rate Doppler imaging, when dysfunction is not apparent by other echocardiographic techniques (2). No report on the prognostic value of strain and strain rate Doppler imaging in AL amyloidosis has yet been published; therefore, we further developed these methods to test the hypothesis that strain

and strain rate Doppler imaging may be additional tools for defining prognosis in this disease. Ejection fraction was addressed in our previous reports and showed no significant difference among the 3 groups studied (3,4); thus, we excluded the parameter from prognostic analysis. Mitral annular velocity was indeed assessed in the current study (early diastolic tissue velocity at base in Fig. 2, Table 2, and Table 3), but the prognostic value was found to be poor. Although renal function was not directly assessed, it is well recognized that cardiac involvement in AL amyloidosis is the predominant negative prognostic factor of any organ, a feature again noted in our study. The clinical impact of myocardial dyssynchrony has yielded conflicting results and needs to be validated in a large population of AL amyloidosis. In contrast to the more "traditional" prognostic factors described on echocardiography, strain imaging is highly sensitive to minor changes in cardiac function, and basal longitudinal strain value clearly detected differences of longitudinal LV myocardial deformation among the 3 groups. For this reason, we selected basal LV strain as a representative of LV longitudinal strain in contrast to mid- and apical LV strain. We are certainly interested in speckle tracking imaging, and LV torsion may be a key parameter as a prognosticator in AL amyloidosis (5). With current techniques of strain imaging, LV strain can be easily and quickly obtained and our data confirmed, and it may become a useful additional prognostic tool in this uncommon but potentially treatable disease.

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