does not differ in terms of average inhibition of platelet aggregation than clopidogrel. This again emphasizes that individual drug response more than average potency of the 2 tested drugs explain our findings. In keeping with our findings, only a minority (15%) of poor responders to clopidogrel displayed a normal response to the same drug after doubling the dose in a recent phase II study (2).

We strongly disagree that "The major take-home message conveyed to the readership is that clopidogrel-treated patients may be switched to ticlopidine if 'resistance' is determined by the platelet tests." Indeed, in keeping with the conclusion statement of our recent paper, our findings, especially in the current pre-prasugrel era, should affect the design of future trials rather than clinical practice. The observation that ticlopidine, at the currently recommended dosage, unlike clopidogrel at double regimen, overcomes resistance to clopidogrel in the great majority of cases may prompt randomized controlled studies where standard care after stenting (i.e., clopidogrel 75 mg/day) is compared with tailored antiplatelet treatment (clopidogrel 150 mg/day in nonresponders to clopidogrel standard regimen or ticlopidine in nonresponders to clopidogrel double dose). Until such a study becomes available, both the risks and benefits of tailoring treatment based on target platelet inhibition will remain hypothetical.

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Relationship Between Atrial Fibrillation and Left Atrial Size

The paper by Bangalore et al. (1) in a recent issue of the *Journal* evaluated the role of diastolic dysfunction as measured by left atrial (LA) size and the associated risk for adverse cardiovascular events in patients undergoing stress echocardiography. The authors report indexed LA size as a predictor of cardiac events independent of traditional clinical risk factors. Patients with significant mitral valve disease and with significant left ventricular systolic dysfunction were appropriately excluded from this study. However, atrial fibrillation (AF) is another important potential confounder, because is it known to affect LA remodeling and geometry (2) and is a known risk factor for cardiovascular events, particularly stroke. This remodeling effect is independent of loading conditions within the LA and can occur in both chronic and paroxysmal AF (3). It would be important to know whether AF was included in the multivariate analysis as well as the percent of patients who carried the diagnosis of AF. Furthermore, if LA size could predict prognosis in the subgroup of patients without AF to a similar extent as that reported in this study, this would lend further validity to the authors' argument to incorporate LA size into the prognostic interpretation of stress testing.

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Reply

We agree with the comment of Dr. Goldberg about the relationships between atrial fibrillation (AF) and left atrial (LA) size. In the AFFIRM (Atrial Fibrillation Follow-up Investigation of Rhythm Management) study of 4,060 patients with AF only 33% of patients had a normal LA size (1). Patients with dilated left atrium are more prone to AF, and patients with AF and a dilated left atrium are more likely to remain in AF than those with normal LA dimensions. Atrial fibrillation is also known to affect LA remodeling and geometry. In a prospective echocardiographic follow-up of patients with AF, atrial enlargement was shown to occur as a consequence of AF (2). Regardless of whether LA enlargement is a cause for or a consequence of AF, the prognosis is worse compared with patients with a normal LA size.

In our study cohort of 2,705 patients undergoing stress echocardiography (3), only 63 (2.3%) patients had either AF or atrial flutter. Analysis performed after excluding this cohort showed that LA size was able to further risk stratify patients undergoing stress echocardiography (Fig. 1). The results were similar for the multivariable analysis and incremental prognostic value analysis. Thus even after excluding patients with AF/atrial flutter, LA size provided independent and incremental value over standard risk factors, including left ventricular systolic dysfunction and ischemia, and was a powerful prognosticator. Therefore, it should be routinely used in the prognostic interpretation of stress echocardiography.