tant "extreme" left ventricular dilation, surgical replacement of the valve is not necessarily contraindicated because the increased diastolic dimension is not in itself a marker of irreversible ventricular dysfunction. In multivariate analysis, preoperative left ventricular ejection fraction was the only significant predictor of postoperative ventricular function, and diastolic chamber dimension, as measured by M-mode echocardiography, was not predictive.

Although it has been suggested by others (2) that surgical treatment for aortic insufficiency may be recommended on the basis of preoperative chamber size without adjustment for body surface area, can the present investigators truly support the use of two-dimensional chamber diameter to predict outcome from a study of only 31 patients without acknowledging the subjects' size? It is possible that the subjects were of large enough body habitus to make the two-dimensional diameter measurement relatively less significant. The reason that the study group included only men was quite likely also related to body size. Because women in general have smaller ventricles than men, they would be unlikely to develop an end-diastolic chamber size ≥80 mm. In women (or for that matter, any person of small stature) "extreme" left ventricular dilation might occur at a diastolic dimension of 70 mm, for example. Ejection phase indexes are predictive of outcome and postoperative ventricular function because they are independent of body size.

It would be very interesting to look at the end-diastolic volume index as a variable in this study to see whether it has any predictive value.

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Reply

We appreciate Miller's interest in our recent article (1). He raises important points regarding the management of aortic regurgitation:

1. The rationale for including extreme left ventricular dilation as an indication for operation in patients with severe aortic regurgitation is based on the observation of occurrence of sudden death treated medically with this extreme left ventricular dilation (2,3). However, the postoperative outcome of these patients was poorly defined. As mentioned in our report, the number of patients mentioned in published reports with preoperative extreme left ventricular dilation and followed up postoperatively is very limited, and their outcome was usually described as dismal but was not formally analyzed. Our study (1) fills this gap of knowledge by demonstrating that the postoperative outcome of these patients with extreme left ventricular dilation is acceptable, although mild excess late mortality is observed due to associated left ventricular dysfunction.

Indeed "only" 31 patients had extreme left ventricular dilation based on an end-diastolic diameter ≥80 mm. However, this degree of left ventricular enlargement is unusual, and the present series is, to our knowledge, the largest published. We concur that patients with this degree of left ventricular dilation deserve operation without delay.

2. A very important issue is the problem of the potential bias introduced by using left ventricular diameters unadjusted for body size. We certainly agree that using unadjusted diameters is a problem, particularly for women. We have presented in abstract form (4) a study that is in the process of publication regarding aortic regurgitation in women. Briefly, it shows, as Miller may have suspected, that utilization of unadjusted left ventricular diameters as surgical criteria, either 55 mm at end-systole or 80 mm at end-diastole, is irrelevant in women with aortic regurgitation because they almost never reach this extent of ventricular dilation. This has important consequences for the outcome of women with aortic regurgitation.

3. End-diastolic volume index was not measured, but diameters normalized to body surface area have no better prognostic value than nonnormalized diameters. Therefore, we cannot specifically recommend using the body surface area-adjusted left ventricular diameters for the timing of operation. The ejection phase indexes are predictive of the outcome, not only because they are dimensionless, but mostly because they reflect the reduced myocardial contractility.

4. We think that the good outcome after operation observed in patients operated on early in the course of their disease, as demonstrated in our study (1), should lead to the reassessment of the optimal timing of operation in patients with severe aortic regurgitation. In particular, in light of the poor survival of the patients operated on with New York Heart Association class III or IV symptoms (5), even mild dyspnea or angina should lead to the consideration of operation.

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Measurement of QT Interval

In the January issue of the Journal, Molnar et al. (1) reported exceptionally long QT intervals in their article on the diurnal variation of the correct QT interval (QTc). They measured the QT interval manually from QRS-T wave templates representing 5-min averages obtained from 24-h Holter recordings. However, they do not discuss the reasons why their QT intervals are radically longer than those usually reported. For example, in the Framingham study data (2), which Molnar et al. use in heart rate correction, the measured QT intervals are ~50 ms shorter at respective heart rates. Figure 1 shows the average measured QT intervals at different heart rates in the

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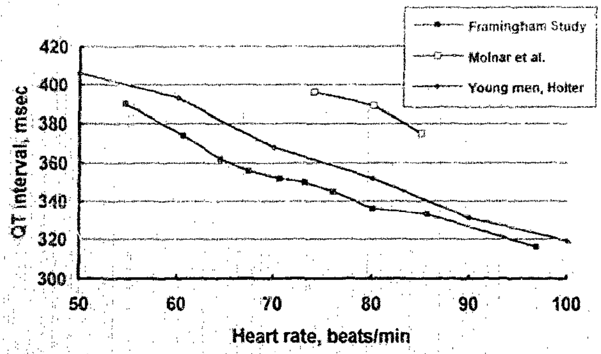

Figure 1. Measured QT intervals at different heart rate levels in the study of Molnar et al., the Framingham study and a Holter study of young healthy men.

Framingham study (one QT measurement/subject [all men], manual measurement of the longest QT interval on the 12-lead rest electrocardiogram, paper speed 25 mm/s) and in the study of Molnar et al. (measured from their Fig. 3 for the time between 11 AM and 8 PM, when all subjects were awake). The 21 subjects of Molnar et al. also included 10 women and were somewhat older (mean 57 years, range 36 to 76) than those in the Framingham Study (mean 44 years, range 28 to 62). However, according to the data of Rautaharju et al. (3), this age and gender difference would be responsible for only ~5 ms of the difference in measured QT intervals. To exclude the role of the ambulatory situation in QT measurement, we also included in Figure 1 our QT interval data for 100 young healthy men (18 to 30 years old) measured at stable heart rates 50, 60, 70, 80, 90, 100, 110 and 120 beats/min from 24-h Holter recordings (4). These QT intervals are 30- to 40-ms shorter at respective heart rates than those reported by Molnar et al. (the effect of age and gender differences is expected to be <5 ms [3]). Thus, the reason for the clear differences between these three studies must lie in the methodology of QT measurement. If Molnar et al. consider the manual QT measurements of the Framingham study incorrect, it is surprising that they use the formula derived from the Framingham study data in the heart rate correction of their QT intervals, without discussing the correctness of this procedure.

We think that the data presented by Molnar et al. emphasize the importance of publishing the QT interval measurement algorithms used in the commercial Holter analysis systems. Only then will it be possible to try to standardize the methodology of the automatic QT interval measurement and obtain QT data that can be compared from one study to another.

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Reply

We thank Mäntysaari et al. for their interest in our report and for their comments regarding the comparability of our data with those published elsewhere. We share their concern about the lack of standardized methodology for QT interval measurement.

The values for each of the curves in their Figure 1 were obtained using different methods: For the curve showing the Framingham data (1), the mean QT intervals were calculated for gender-specific deciles of RR values. For the curve showing data from the study by Viitasalo and Karjalainen (2), the QT intervals were collected at stable heart rates. Regarding our study (3), Mäntysaari et al. graphically interpreted hourly mean RR and QT interval data from our Figure 3. We have two major concerns about this data interpretation:

1. Data points from our study represent something different than those from the other two studies, in which QT values were measured at specific heart rates. Our data, in contrast, represent hourly average QT and RR intervals, and, as such, there is a wide range of values underlying them.
2. The relation between heart rate and RR interval is not linear. Therefore, average RR intervals, as reported in our Figure 3, cannot be readily converted into average heart rate, as the Mäntysaari et al. have done with our data. For example, for two QT intervals measured at heart rates of 60 beats/min (RR 1 s) and 100 beats/min (RR 0.6 s), the average QT interval would be plotted at the average heart rate of 80 beats/min. However, if the average heart rate is determined from RR intervals that have been converted to heart rate, the resulting rate is 75 beats/min [(1 s + 0.6 s)/2 = 0.8 s = 75 beats/min]. Thus, details of the method by which data are analyzed can produce differing results, thereby shifting the position of the QT interval versus RR curve.

We reanalyzed the data cited in the letter of Mäntysaari et al. using, as much as possible, comparable analytic techniques for each of the three studies. We assessed the QT intervals from our study (3) as a function of the RR interval and fitted them using the Framingham formula. The regression lines, as well as the regression line for men from the Framingham study (1) and the actual values of "Young men, Holter" of Viitasalo et al. (2) are shown in our Figure 1. The heart rate data of

Figure 1. QT versus RR relationship from three studies using Holter monitoring and 12-lead electrocardiogram (see text for details).