Response to the Letter by Devaux et al

We thank Devaux et al1 for their interest in our work published in a recent issue of Circulation Research;3 We have carefully read their comments and replied to them.

First, we are afraid that there are some misunderstandings about our studies, including the study design. For the first screening in the study, we randomly selected 7 patients who experienced development of heart failure (HF) within a year after discharge from the hospital after acute myocardial infarction (AMI) and 7 matched control subjects who did not experience any cardiac events for 2 years after AMI using propensity score, as described in the Supplemental Materials of the original article.7 In the validation phase, we examined associations between HF development and circulating levels of candidate microRNAs (miRs) selected on the basis of the results of the first screening in a total of 86 post-AMI patients. Through these processes and additional experiments, we concluded that circulating levels of p53-responsive miRs were increased from the early convalescent stage (median, 18 days after onset) in post-AMI patients who survived the acute stage of AMI but developed HF within a year.2 Devaux et al claimed that our study had a limitation of statistical underpower without any calculation of statistical power of our study. However, if the statistical power was retrospectively calculated on the basis of the results of our study, the estimated sample size was 49 to detect a correlation of 0.35 (or −0.35) using a 1-sided hypothesis test with a significance level of 0.05 and a power of 80%, suggesting that our sample size (n=86) had enough power. Furthermore, it should be understood that the statistical power is the probability of the event of rejecting the null hypothesis in a future study (prospective power) and thus that post hoc (retrospective) calculation of the statistical power is meaningless, particularly once statistical significance is detected, regardless of sample size.3,4

As for the second comment, we agree with the point that the change in left ventricular diastolic dimension (LVDd) is another important factor to evaluate cardiac remodeling. However, cardiac remodeling should be assessed with several viewpoints. In our study, the absolute values of LVDd and left ventricular ejection fraction (LVEF) at 1 year were more excellently correlated with the development of HF than the change in LVDd from a median of 18 days after onset to 1 year (area under the receiver-operating characteristic curve [AUC]=0.746, r=0.335, P=0.010 for LVDd at 1 year; AUC=0.688, r=−0.334, P=0.010 for LVEF at 1 year; and AUC=0.679, r=0.236, P=0.086 for the change in LVDd), which was the reason why we showed the association between miR levels and LVDd or LVEF at 1 year but not the change in LVDd in the article.2 Indeed, the association of the change in LVDd with miR levels was less robust compared with those of absolute values of LVDd and LVEF at 1 year in the present study.

The third comment is somewhat misleading because our conclusions were that the levels of 3 p53-responsive miRs were elevated by the early convalescent stage of AMI in the sera of post-AMI patients who developed HF within 1 year of AMI onset and that further investigations are warranted to confirm the usefulness of these circulating miRs for predicting the risk of developing ischemic HF after AMI. However, we appreciate this comment because we had not shown the results of prediction analysis, as pointed out, because of the word limitation. Indeed, the description had been based on the results of receiver-operating characteristic analysis showing that the AUC was large enough to present associations between each miR level and HF development within 1 year (AUC=0.750, 0.716, and 0.676 for miR-194, miR-34a, and miR-192, respectively).

Finally, we refute the last claim. After careful reading of all of the excellent articles suggested,5–8 we again conclude that no miRs have been established as predictors of ischemic HF that develops after AMI. Zile et al5 and Devaux et al7,8 demonstrated relationships of miR levels with cardiac remodeling after AMI but just those with 1 parameter for each miR: miR-29a for left ventricular end-diastolic volume 90 days after AMI,5 miR-208b and miR-499 for LVEF <40%,7 and miR-150 for a change in left ventricular end-diastolic volume after AMI.1 Thus, although these articles elegantly suggested that several miRs are likely related to cardiac remodeling, none of them examined associations between miR levels and the development of HF in post-AMI patients.5,7,8 In this context, Eitel et al6 demonstrated that plasma miR-133a levels predicted a composite of death, HF, and reinfarction within 6 months after AMI. However, they also showed that there was no difference in incidence of HF between patients with lower and higher levels of miR-133a (4 of 108 patients [3.7%] for the lower miR-133a group versus 3 of 108 patients [2.8%] for the higher miR-133a group; P=NS). Overall, however, we totally agree with the last sentence by Devaux et al1 that the studies by us2 and others5–8 suggest that the potential of miRs as a prognostic biomarker in the secondary prevention setting of AMI deserves further testing.

Disclosures

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Letters to the Editor

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