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Letters to the Editor

Reply to Kawada—N-Terminal Pro B-Type Natriuretic Peptide, High-Sensitivity Cardiac Troponin T and the Extent of Hibernating Myocardium

To the Editor:

We thank Dr Kawada for his interest in our research, which represents a first step toward understanding the relationship of N-terminal pro B-type natriuretic peptide (NT-proBNP) and high-sensitivity cardiac troponin T (hs-cTnT) to hibernating myocardium in patients with ischemic heart failure.[1] We now reemphasize, as was stated in the report, that this work is a "first step" and further studies are needed.

We agree with Dr Kawada that overfitting can be a risk with logistic regression models.[2] We noted that age, left ventricular ejection fraction, and estimated glomerular filtration rate were selected *a priori* as covariates because these parameters are known to affect the levels of NT-proBNP and hs-cTnT.[3,4] Because of the clinical importance of the listed covariates and the magnitude of their effects on biomarkers, it was deemed necessary to include them in the model. We did acknowledge the risk of overfitting the logistic regression model in the Discussion (*Study Limitations* section).[1] The smallest subgroup modelled had a reasonable sample size of 29 (Table 4). We also presented the results of the multiple regression model with the covariates (including hibernation and biomarkers) as continuous variables (Table 3), and kept these 4 covariates for the analysis. Furthermore, we also acknowledged in the *Discussion* that this subgroup analysis was post hoc, and as such, "…should be interpreted with caution. Further studies are required to support these findings and are ongoing."[1] In the multiple regression model, the adjusted R^2 was not presented because a model of prediction was not our concern. At this stage, we were simply interested in the relationship with hibernation/scar adjusted for the other variables.

In reference to the receiver operating characteristic curve analysis, Dr Kawada correctly notes that the accuracy of NT-proBNP and hs-cTnT predict hibernating myocardium was moderate. That there is some predictive ability for these biomarkers is very provocative, but we agree that confirmatory studies are needed to support this novel observation.

Finally, Dr Kawada raises the important point that a combination of biomarkers for predicting hibernation would be useful; we agree. In the present study, however, NT-proBNP and hs-cTnT were not modelled together, because: (1) of the risk of overfitting that was previously identified; (2) it was more important to first establish their independent association with hibernation and scar; and (3) this important line of investigation should be reserved for higher-powered confirmatory studies, because a substantial increase in sample size would be required. This concept is an important area of our ongoing investigations.

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