LETTER TO THE EDITOR

The Diagnostic Performance of Multifunction Cardiogram (MCG) in Functional Myocardial Ischemia

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Ann Noninvasive Electrocardiol 2015;xx(x):1–3

IN REPLY

Dr. Imhoff and Dr. Rainford raised several issues regarding the clinical trial: Multifunction cardiogram Evaluation in Diagnosis of Functional coronary Ischemia sTudy (MED-FIT).[1] We respond to the raised issues as follows:

- A relevant selection bias could not be ruled out because of the small number of patients and the high mean age.

We should admit that the number of patients enrolled in MED-FIT was small. We strictly excluded those patients with acute coronary syndrome, prior coronary artery bypass grafting, severe valvular heart disease, electrocardiographic evidence of prior myocardial infarction, and patients taking medications such as nitrates and β-blockers, in whom multifunction cardiogram (MCG) score might not be applicable in predicting myocardial ischemia. Otherwise, nearly consecutive patients planned for diagnostic coronary angiography were enrolled in this study. Regarding dominance of elderly patients, the mean age (71.2 years) in this study was very comparable to those in prior Japanese large registries enrolling consecutive patients undergoing coronary stent implantation.[2,3]

- Hemodynamically relevant collateral circulation was apparently not considered in the analysis of the CAG finding.

In this study, we used the invasively evaluated fractional flow reserve (FFR) as the primary end point. The FFR values incorporate the influence of collateral circulation in evaluating functional myocardial ischemia.[4] Therefore, in 39 patients who actually underwent the invasive FFR measurement, we could exclude the possibility of negative MCG results due to hemodynamically relevant collateral circulation. In 23 patients with high-grade (≥99%) angiographic stenosis who did not undergo invasive FFR measurement, we could not exclude the possibility of negative MCG results due to hemodynamically relevant collateral circulation. Actually, we found angiographically visible collateral in 10 (43.5%) of 23 patients without invasive FFR measurement. However, a previous study suggested that significant myocardial ischemia usually persists even with abundant collateral circulation.[5]

- The authors chose not to perform FFR on the subset with 30% or less obstruction, assuming FFR was negative.

We agree that we could not deny the presence of myocardial ischemia in patients with 30% or less obstruction. However, this approach is the current standard practice in using FFR as a diagnostic tool. Furthermore, the area under the receiver operating characteristics curve evaluated in 39 patients who actually underwent FFR measurement, was only

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DOI:10.1111/anec.12299

0.65, which was not far from the value 0.51 in the entire study population.

- It should also be noted that the calculation of a mean severity score for the assessment of CAD does not comply with the instruction for use of MCG.

MCG records a resting ECG for 82 seconds in each session. From the ECG data, we can receive MCG severity score and supplemental reports for session analysis. In instructions of MCG, the MCG severity scores should be dealt with session analysis for detecting various heart diseases. However, severity scores could vary in each session and the descriptive results from the session analysis could not be used to categorize the severity score objectively and quantitatively in the clinical study. Previous reports suggesting the high accuracy of MCG severity score in detecting coronary artery stenosis did not adequately describe the methodologies to derive the certain severity score for a given patient from the scores obtained in several sessions.[6–9] In an attempt to follow an objective methodology, we selected the average and maximum value of MCG severity score among two or three sessions for the current analysis in MED-FIT.

- It is very difficult to conclude that the investigative methods of four prior independent studies involving larger and more diverse patient selection were in error.

In the previous four studies evaluating MCG, the angiographic end point was ≥50% diameter stenosis by visual estimation, which was well known to be unreliable in evaluating myocardial ischemia.[6–9] Invasive FFR used in MED-FIT is currently regarded as more reliable in detecting myocardial ischemia than coronary angiography.[10,11] Furthermore, the "independence" of the previous four studies might be questioned, because all the four studies were published from the same group and presented in the similar format.

- Another recent study by Amano et al. comparing MCG also with CAG and FFR reached conclusions that were very comparable to the MCG validation studies.

In the study by Amano et al.,[12] more than 80% of patients had >50% stenosis. Therefore, the study population was quite different from our study. Also, unlike our study, FFR value was used as an additional index on diameter stenosis by visual estimation, which was not the standard method in using FFR for detection of myocardial ischemia.

- A study by Strobeck et al. comparing MCG with SPECT and CAG concluded that MCG had high predictive value for the presence of hemodynamically relevant CAD.

In the study by Strobeck et al.,[13] the angiographic end point was ≥70% diameter stenosis also by visual estimation. The results from a study using the angiographic end point by visual estimation are hardly comparable to those from our study using invasive FFR as the end point.

- In the most recent analysis published by Kawaji et al. using the same dataset, the authors came to the contrasting conclusion.

This study showed poor diagnostic performance of MCG for functional myocardial ischemia and angiographically significant stenosis (≥50% by quantitative coronary angiography). However, we reported high sensitivity to detect angiographic coronary atherosclerosis (defined as coronary stenosis ≥30% by visual estimation, which was the threshold % diameter stenosis to perform invasive FFR measurement in MED-FIT) in a post hoc subanalysis using the MED-FIT data.[14] These are not contrasting conclusions.

Therefore, we believe that the MED-FIT study added important information about the clinical utility of MCG.

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