Contrast-enhanced cardiac magnetic resonance (CE-CMR) imaging is becoming accepted as a reference “gold standard” for noninvasive estimation of myocardial infarct (MI) size against which other infarct sizing techniques, such as the electrocardiogram (ECG), are judged (1–3). The advantages of CE-CMR are obvious (4). However, as emphasized in an editorial by Engblom et al. (5), an essential step before considering CE-CMR as a “gold standard” is development of an accurate and reproducible method of actual process of MI size estimation among different laboratories. Fayn et al. (6) wrote an accompanying editorial outlining the interlaboratory collaborative process used for this purpose by the Common Standards for Quantitative ECG during the 1980s. A similar process is essential in any other method that is supposed to serve as a standard. Otherwise, the understanding and interpretation of the scientific results can be challenging, as would be emphasized in this editorial.

The study by Nijveldt et al. (7), published in this issue of JACC, has the ambitious goal of relating 3 ECG measures of a successful percutaneous coronary intervention (ST-segment resolution, residual ST-segment elevation, and Q waves) to 3 CE-CMR variables (left ventricular [LV] function, MI size, and microvascular obstruction [MVO]) during the 2- to 6-day window after acute thrombotic coronary occlusion. Two main aspects are considered in this editorial: first, the importance and challenges of presentation of the complex study design; and second, the persistent, unsolved challenges for using CE-CMR as the “gold standard” method for estimation of MI size.

Attention to detail in both definitions of terms and descriptions of methods are emphasized as essential prerequisites for reliability and reproducibility of research studies. For example, if patients with “unsuccessful PCI are excluded” but the criteria for success are not defined, or “patients with CK-MB <10× normal are excluded” but the timing of this observation is not mentioned; then the otherwise very important results cannot be clearly interpreted. Indeed, it seems inconsistent to exclude patients with the poor result of “less than optimal reperfusion” as well as those with the good result of “minimal biochemical marker elevation.”

When using “quantitative ECG parameters,” it is essential to know how these were determined. Was a single ECG core laboratory used, or were the data entered independently in the 4 study enrollment centers? What quality control method was used for the ECG measurements?

Description of the CE-CMR method used in measuring the MI size also would be strengthened by providing details. Because the CE-CMR data were determined with a “dedicated software package,” was any manual over-read performed? Because the endocardial and epicardial borders were “outlined manually;” was interobserver variability determined? There is particular variability in determination of “microvascular obstruction (MVO).” Because it is known that the central portion of a “hyperenhanced” region loses the “hypoenhancement” attributed to MVO during the days after the acute infarction, the 2- to 6-day window may be broad for comparison of true MVO: was there consistency in the MVO results between determinations performed on days 2 and 6?

The consideration of CE-CMR as a “gold standard” for MI size measurements has persisting chal-
Challenges. One is interlaboratory differences in the methods used for MI size measurement. Agreement of MI size measurements between observers from within the same institution has been established (8,9). However, because the reproducibility of these measurements might be influenced by local standards and conventions that are not explicitly stated, one cannot assume that measurements among observers from different institutions would achieve similar levels of agreement.

The MI size is assessed as a proportion of the overall LV volume; however, variability in measurement of LV volume has been documented (10). Some differences arise from the inclusion versus exclusion of papillary muscles and trabeculae in the overall LV volume. Another potential reason for the differences in the estimation of the MI size between observers from different laboratories is the estimation of the area with partial volume of infarcted myocardium. It is also known that the partial volume effect occurs in images when more than 1 tissue condition is present within a single voxel. The exact amount of the infarcted portion within areas with “partial volume” is difficult to assess. Currently, there is no interlaboratory consensus on the amount of these areas that should be designated as infarcted. The use of automatic methods was recently introduced as a solution to this problem (11). Also, there is a significant decrease in hyperenhanced myocardium during the first week after early reperfused MI, indicating that MI size might be overestimated if imaged early after MI (12).

Previous studies have documented artifacts that might appear on CE-CMR images as hyperenhanced areas. The LV outflow tract and apex have both been shown to be particularly challenging, because the nonlinear curvature of the myocardium produces “gray areas” similar to hyperenhanced areas. Also, there are many nonischemic cardiac conditions that cause lesions that can be visualized with CE-CMR. Even though differentiation of these conditions from ischemic changes has been previously studied, it is not always simple and does vary among observers (13,14).

Reasons for observer variability in the estimation of MI size by CE-CMR are numerous, and the potential for variability is present at all stages; from image acquisition to post-processing. The need for explicitly stated protocols used in measurements of MI size in research studies is a critical step toward the ability to compare results from different institutions. Detailed description of the method of each laboratory can help in defining variables that lead to differences in MI size measurements, so these determinations can be repeated with the same method.

The primary challenge is the standardization of methods among institutions. Comprehensive review of MI size measurement methods and publication of standards in appropriate journals is mandatory. Considerations of the rationale of each step in MI size measurements and development of consensus protocols are needed. Leading centers in CE-CMR should establish working groups to form consensus meetings dedicated to standardization of the MI size measurements.

This study by Nijveldt et al. (7) is an example of a scientifically important study that can be misinterpreted for reasons stated in this editorial. Therefore, it serves as a challenge for the clinical research community to provide a CE-CMR method to determine the precise quantifiable serial electrophysiologic changes that can be measured on the standard ECG as predictors of clinical outcome of sophisticated therapeutic interventions. This study emerges as a call for international leaders to develop standards that can be consistently applied for CE-CMR measurements. We encourage the authors of this key article to respond to the comments suggested by this editorial, so that a further step can be made in the process toward solving the problem created by the lack of methods that are standardized among different laboratories in the international scientific community.

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References


Key Words: cardiac magnetic resonance ● myocardial infarction ● electrocardiogram.