Comparison of Methods for Quantification of Myocardial Infarct Size from Delayed Enhancement Magnetic Resonance Data

Nadjia Kachenoura[1], Nicolas Baron[1,2], Philippe Cluzel[3], Frédérique Frouin[1], Alain Herment[1], Philippe Grenier[3], Gilles Montalescot[2], Farzin Beygui[2]

[1] Laboratoire d'Imagerie Fonctionnelle, Inserm U678/UPMC Univ Paris 6, Paris, France
[2] Cardiology department, Inserm u937, Pitie-Salpetriere Medical Center, Paris, France
[3] Radiology Department, Pitie-Salpetriere Medical Center, Paris, France

Abstract

We sought to assess myocardial infarct (MI) volume with different quantitative methods in both acute (AMI) and chronic MI (CMI) from CMR late Gadolinium Enhancement images. CMR exam was performed 50±21 hours after MI in 52 patients and was repeated 100±21 days later in a subgroup of 34 patients. Necrosis volumes were quantified using: 1) manual delineation, 2) automated fuzzy c-means method, and 3) +2 to 6SD thresholding approaches. Results were compared against peak values of serum Troponin I (TnI), creatine kinase (CK) and LV functional parameters. For CMI, quantitative evaluation of infarct size using manual, +2SD, +3SD and fuzzy c-means provided equivalent results for comparisons of MI volumes against LV function parameters ($r>0.79$, $p<0.0001$). For AMI, +2SD and fuzzy c-means approaches provided higher correlations for comparisons of AMI volumes against biochemical markers ($r>0.77$, $p<0.0001$) and chronic LV function parameters ($r>0.59$, $p<0.0002$). The fuzzy c-means and +2SD methods provided highest correlations with biochemical MI quantification as well as LV function parameters. The fuzzy c-means approach which does not require an arbitrary identification of the remote myocardium is fast and reproducible. It may be clinically useful in the evaluation of patients with MI.

1. Introduction

The extent of myocardial infarct (MI) predicts further ventricular remodeling, heart failure and death [1]. Hence, accurate quantification of infarct size is of great interest. Late Gadolinium Enhancement (LGE) has been widely reported as an accurate method for identifying MI. Determining the presence, location, and extent of both acute (AMI) and chronic MI (CMI) is crucial in the management of patients with MI, because of the known relationship between necrosis extent and LV functional recovery after revascularization [2].

Quantification of the amount of myocardial necrosis is commonly based on the time-consuming manual delineation of the MI while repeating manipulations of the contrast window. This process results in a subjective decision, which might be influenced by the operator training and experience [3]. Our study was designed to evaluate the ability of several approaches to accurately quantify the volume of myocardial necrosis in both AMI and CMI. The tested approaches included: 1) the manual delineation of the MI by a level 1 [3] trained SCMR reader, 2) the widely used+2 to 6 Standard Deviation (SD) thresholding techniques [2], and 3) the unsupervised algorithm of the fuzzy c-means clustering, which have been previously used for MI quantification from LGE-CMR data.

For AMI, the accuracy of the quantitative measurements was assessed while comparing MI volumes against biochemical quantification of the infarct size, based on plasma peak levels of CK and troponin I (TnI) that were widely demonstrated as predictors of mortality after MI [4]. In addition, the relationship between CMR quantifications of infarct size and global left ventricular (LV) contractility parameters, which were defined as major predictors of mortality after MI was studied for CMI. Finally, the relationship between AMI volumes and LV function parameters measured during the chronic phase was studied to assess the functional significance of AMI size quantifications.

2. Methods

2.1. Study population

We prospectively enrolled 52 consecutive patients admitted to the Cardiology Intensive Care Unit for a first AMI. Coronary Angiography was performed in all patients, and when necessary, Percutaneous Coronary Intervention (PCI) was performed.

CK and TnI measurements were repeated every 6 hours using commercially available immunoassays, until

peak values were achieved. Patients with unstable hemodynamic status or a contraindication to CMR were excluded from the study. The remaining patients had a first CMR exam during the acute phase of the MI and a second CMR exam during the chronic phase of the MI. patients who had another event between the two exams were excluded from the analysis performed in the chronic setting.

2.2. CMR protocol

CMR was performed using a 1.5 Tesla system (Gyroscan Intera, Philips, Best, The Netherland), with a five-element phased array thoracic coil and the SENSE technique. All acquisitions followed a standard protocol with T2 weighted Short Tau Inversion Recovery (STIR)-Black-Blood imaging, cine-SSFP dynamic acquisitions in short and long axis (2 and 4 chambers), first pass perfusion imaging, and LGE sequences. LGE-CMR was performed 10 to 20 minutes after the intravenous Dimeglumine Gadobenate injection (0.2 ml/kg). Between 12 and 16 short-axis slices were acquired (TR=4 ms, TE=2 ms, flip angle=20°, matrix size=256x256, slice thickness= 6 mm, no gap), covering the whole left ventricle from base to apex. The inversion time (TI) ranged between 170 and 200 ms.

2.3. Quantitative evaluation of infarct size

For both acute and chronic CMR datasets, images were reviewed by a single expert blinded to all clinical data. Endocardial and epicardial contours were traced using the Philips computer assisted software for each slice.

A first analysis is manually performed on the Philips Viewforum software. A trained operator manually outlined the myocardial hyper-enhanced regions introducing corrections while varying the contrast window. Besides, when present, areas of microvascular obstructions were included in the infarct zone.

A second method consisted in a semi-automated 2 to 6SD quantification. As a first step, a region of interest was manually defined on the remote myocardium, and mean value (M) and standard deviation (SD) of intensity within this region were computed. Then, these values were used to set-up an abnormality threshold equal to M + k.SD (with k = 1 to 6).

The third approach consisted in semi-automated fuzzy c-means quantification. As previously described [5], the fuzzy c-means algorithm was first used to classify LV voxels into two classes, “enhanced voxels” and “non-enhanced voxels”. This process was applied to each slice to enable the estimation of two parametric maps containing probabilities of membership of each voxel to the “enhanced cluster” and to the “non-enhanced cluster”. These probabilities of membership were comprised between 0 and 1. Measures of membership to the enhanced class, which were comprised between 0 and 1, were calculated for each slice. Then, for the entire myocardium, the threshold was varied between 0.25 and 0.5 and the curve representing the amount of necrosis was plotted according to the threshold values. The value corresponding to the flat portion of this curve was defined as the optimal threshold, which was then used for myocardial necrosis delineation.

For all LGE quantification techniques, total necrosis volume was calculated, after the automated or the manual delineation of the enhanced zones. Besides, total infarct mass was determined from the product of infarct volume and the myocardial density. Quantitative LGE results were also expressed as relative infarct volume (total infarct volume/total myocardial volume).

2.4. Evaluation of LV function

An independent operator, blinded to LGE and clinical data measured body surface area adjusted LV global end-diastolic (EDVi) and end-systolic (ESVi) volumes as well as LV mass and ejection fraction (LVEF) from b-SSFP dynamic sequences, using the Phillips Viewforum software. Regional contractility was quantified on the basis of the AHA/ACC LV segmentation model. And a segment was considered hypokinetic if its thickening was < 5mm (<-2SD of normal value assessed in normal segments in our CMR laboratory).

2.5. Statistical analysis

Data are expressed as means ± standard deviation or percentage (%) for relative measurements. Comparisons between variables were performed using the non-parametric paired Wilcoxon test, and values of $p < 0.05$ were considered statistically significant. Correlations between measurements were assessed using the Pearson’s correlation test.

3. Results

A total of 52 patients were included and underwent a first CMR exam 50±21 hours after admission for MI and a second CMR exam 100±21 days after admission for MI. The subgroup that had both CMR exams comprised 34 patients. All LGE-CMR images were considered interpretable and included in the analysis.

3.1. Acute myocardial infarction

Correlations coefficients for comparisons between both CK and TnI peak levels and LGE-CMR quantified infarct size in AMI are summarized in figure 1. For comparisons against peak TnI and CK levels, the manual,

the +2SD, +3SD and the unsupervised fuzzy c-means quantification methods resulted in higher correlation coefficients, with a slight superiority for the fuzzy c-means approach. For the SD thresholding techniques the correlation coefficients and their significance levels decreased gradually while increasing the threshold values resulting in only fair correlations for the +4 to +6 SD, approaches.

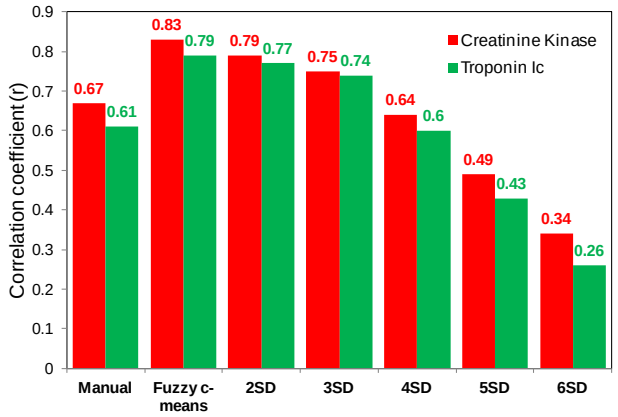

Figure 1. Comparisons between CMR quantified relative volumes of necrosis and biological markers of necrosis during the acute phase. All comparisons reached statistical significance.

3.2. Chronic myocardial infarction

As shown in figure 2, relative infarct size quantified in CMI by the 7 methods correlated significantly with LVEF, EDVi, ESVi. Correlation coefficients obtained for the manual technique were slightly higher, although very close to those obtained for the fuzzy c-means and the +2SD and +3SD thresholding techniques. For the chronic phase comparisons, correlation coefficients and their levels of significances were less sensitive to the increase in threshold values. Indeed all comparisons including +5SD and +6SD resulted in significant correlations.

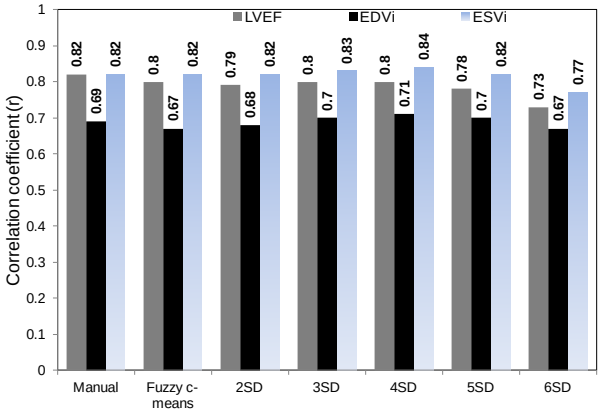

Figure 2. Comparisons between CMR quantified relative volumes of necrosis and the global LV functional parameters during the chronic phase. All comparisons reached statistical significance.

3.3. Functional consequences of the acute MI size

To evaluate the functional consequences of the AMI quantified volumes, their relationship with LV functional parameters measured during the chronic phase was studied. Figure 3 shows the correlation coefficients obtained from such analysis. Correlation coefficients obtained for the fuzzy c-means quantification method were slightly higher, although very close to those obtained for the +2SD, +3SD and manual methods. Again, comparisons against +4SD, +5SD and +6SD resulted in fair correlations.

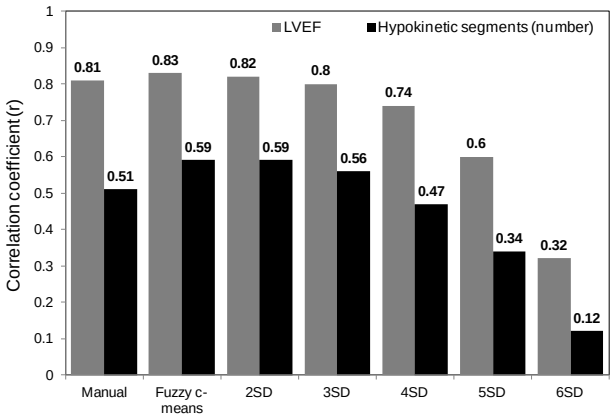

Figure 3. Functional consequences of the AMI. Relationships between MI volumes quantified during the acute phase and the LV functional parameters measured during the chronic phase. All comparisons reached statistical significance except for +5 and +6 SD methods.

4. Discussion

Our data showed that the quantitative evaluation of infarct size using manual, +2SD, +3SD and fuzzy c-means approaches resulted in high and significant correlations for: 1) comparison of the AMI volumes against the biochemical markers of infarct size, 2) comparison of MI volumes and LV global functional parameters in CMI, and 3) comparison between AMI volumes and the LV functional parameters measured during the chronic phase. While these four approaches provided equivalent results during the chronic settings, a slight superiority was obtained for the fuzzy c-means and the +2SD approaches during the acute settings. The aforementioned relationship between infarct size in AMI and the LV functional parameters measured during the chronic phase complies with the known relationship between the infarct size and the LV functional recovery.

Although LGE-CMR is routinely used to assess

myocardial infarct size, there is no gold standard for quantitative analysis of such data. Most studies have used time-consuming (23.7±5.7 minutes were reported by Mewton [6]) and poorly reproducible manual delineation of infarct area. Moreover, as previously reported, higher infarct sizes were obtained with the manual approach in our data. However, differences between methods in terms of infarct volume and correlation with other clinical measurements were less pronounced in CMI probably because of the more homogeneous nature of the infarct in the chronic setting. Indeed the heterogeneous AMI might be more sensitive to the arbitrary choice of visualization parameters such as image contrast and brightness, which would affect manual quantification leading to subjective measurements.

Thresholding methods have also been widely used in clinical studies focused on infarct quantification using LGE-CMR images. The threshold values used in the previous studies vary from 1 to 6 SD. However, the values of +2 or +3SD are most commonly used [2] and this usefulness was confirmed in our study. However, this superiority of +2SD and +3SD approaches was more pronounced in the acute settings while in the chronic settings, correlations between MI volumes and the LV functional parameters were less sensitive to the threshold value. Again, this might be due to the more homogeneous nature of the infarct in the chronic setting. Furthermore, the +2SD and +3SD approaches provided infarct mass in the same range with those provided by the manual approach while the approaches using threshold values up to +4SD resulted in substantially lower infarct mass. This phenomenon was accentuated in the acute setting probably because of the heterogeneous nature of the MI in this phase which increases the sensitivity of the measurements to the threshold value.

Compared to thresholding methods, the fuzzy c-means method used in the present study has the advantage of not being based on the arbitrary identification of a remote region. It automatically affects voxels to normal or enhanced class. Because classification was achieved on the cavity and the myocardial wall, any prior knowledge on whether a considered slice had an infarcted area or not is not necessary. Also, classification on each individual slice allows decreasing the dependence of our technique on surface coil intensity variations. Finally, our technique complies with clinical requirements in terms of reproducibility, objectivity and processing time (few seconds for each patient).

Similar to all techniques that are based on signal intensity analysis, automated techniques did not take into account areas of microvascular obstruction (MVO), which are not enhanced after gadolinium contrast injection. This technical limitation may lead to a potential underestimation of the infarct size, however, this was minimal in the present study since MVO was observed in only 5/52 patients. In addition, methods that presented higher performances in the acute setting were those which provided the higher performances in the chronic setting, reflecting the minor effect of MVO in our database.

The manual, fuzzy c-means, +2SD and +3SD methods provided high correlations with biochemical infarct size quantification as well as LV global and regional function parameters with a slight superiority for the fuzzy c-means and the +2SD methods in the acute settings. Conversely to the +2SD thresholding technique for which an arbitrary area within the remote myocardium should be defined, the fuzzy c-means method is based on an original unsupervised clustering algorithm, which enables an objective and reproducible quantification of infarct size in both AMI and CMI .Accordingly, the fuzzy c-means based method may lead to a more accurate assessment and a better prediction of LV remodeling. It may be of clinical usefulness for the management of patients with MI.

References

[1] White HD, Norris RM, Brown MA, et al. Effect of intravenous streptokinase on left ventricular function and early survival after acute myocardial infarction. N Engl J Med 1987; 317:850-855.

[2] Fieno DS, Kim RJ, Chen EL, Lomasney JW, Klocke FJ, Judd RM. Contrast-enhanced magnetic resonance imaging of myocardium at risk: distinction between reversible and irreversible injury throughout infarct healing. J Am Coll Cardiol 2000; 36:1985-1991.

[3] Pohost GM, Kim RJ, Kramer CM, Manning WJ. Task Force 12: training in advanced cardiovascular imaging (cardiovascular magnetic resonance [CMR]): endorsed by the Society for Cardiovascular Magnetic Resonance. J Am Coll Cardiol 2006; 47:910-914.

[4] Knight CJ, Keeble TR, Wilson S, et al. Short term prognosis of patients with acute coronary syndromes: the level of cardiac troponin T elevation corresponding to the "old" WHO definition of myocardial infarction. Heart 2005; 91:373-374.

[5] Kachenoura N, Redheuil A, Herment A, Mousseaux E, Frouin F. Robust assessment of the transmural extent of myocardial infarction in late gadolinium-enhanced MRI studies using appropriate angular and circumferential subdivision of the myocardium. Eur Radiol 2008; 18:2140-2147.

[6] Mewton N, Revel D, Bonnefoy E, Ovize M, Croisille P. Comparison of visual scoring and quantitative planimetry methods for estimation of global infarct size on delayed enhanced cardiac MRI and validation with myocardial enzymes. Eur J Radiol; 78:87-92.

Address for correspondence.

Nadjia Kachenoura
Laboratoire d'Imagerie Fonctionnelle, INSERM U678
91 Bd de l'Hôpital, Paris, France
Nadjia.kachenoura@inserm.fr