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Comparison of various methods for quantitative evaluation of myocardial infarct volume from magnetic resonance delayed enhancement data

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ABSTRACT

Background: Late gadolinium enhancement (LGE) cardiovascular magnetic resonance (CMR) enables the estimation of myocardial infarct (MI) extent. Nevertheless, manual quantification is time consuming and subjective. We sought to assess MI volume with different quantitative methods in both acute (AMI) and chronic MI (CMI).

Methods: CMR was performed 50 ± 21 h after MI in 52 patients and was repeated 100 ± 21 days later in a subgroup of 34 patients. Then, 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 left ventricular (LV) functional parameters: LV ejection fraction (LVEF), indexed end-diastolic (EDVi), end-systolic volumes (ESVi) and the number of hypokinetic segments (NbHk).

Results: For CMI, quantitative evaluation of infarct size using manual, +2SD, +3SD and fuzzy c-means provided equivalent results in terms of correlation coefficients for comparisons of MI volumes against LV function parameters (LVEF: $r>0.79$, $p<0.0001$; ESVi: $r>0.82$, $p<0.0001$, EDVi: $r>0.67$, $p<0.0001$, NbHk: $r>0.54$, $p<0.0009$). For AMI, +2SD and fuzzy c-means approaches provided higher correlations for comparisons of AMI volumes against biochemical markers (CK: $r>0.79$, $p<0.0001$,TnI: $r>0.77$, $p<0.0001$) and chronic LV function parameters (LVEF: $r>0.82$, $p<0.0001$, NbHk: $r>0.59$, $p<0.0002$).

Conclusions: 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 infarction (MI) predicts further ventricular remodeling, heart failure and death [1–3]. Hence, accurate quantification of infarct size is of great clinical interest. Cardiovascular magnetic resonance (CMR) late gadolinium enhanced (LGE) has been widely reported as an accurate method for identifying myocardial infarction. Indeed, animal and clinical studies demonstrated the excellent correlation of LGE-CMR with histopathological findings [4–6] as well as its effectiveness in determining the presence, location, and transmural extent of both acute (AMI) and chronic MI (CMI) [7–9]. These latter measurements are crucial in the management of patients with MI, because of the known relationship between the extent of necrosis and the left ventricular (LV) functional recovery after revascularization [4,10,11].

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 [12]. 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 [12] trained SCMR reader, 2) the widely used +2 to 6 Standard Deviation (SD) thresholding techniques [4,10,11,13], and 3) the unsupervised algorithm of the fuzzy c-means clustering, which have been previously used for MI quantification from LGE-CMR data [14,15].

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 [16,17]. Moreover, correlation between these enzymatic

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measurements and LGE-CMR quantification of necrosis has been previously shown [18–20]. In addition, the relationship between CMR quantifications of infarct size and both global and regional left ventricular (LV) contractility, which were defined as major predictors of mortality after MI was studied for both AMI and 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. Population

We prospectively enrolled 52 consecutive patients admitted to the Cardiology Intensive Care Unit for a first AMI as defined by the universal definition of AMI [21] based on increased TnI levels.

Patients were treated optimally as recommended by international guidelines. Coronary angiography was performed in all patients, and when necessary, percutaneous coronary intervention (PCI) was performed.

CK and TnI measurements were repeated every 6 h using commercially available immunoassays, until peak values were achieved. The cases in which these measurements decreased gradually after admission were excluded from comparisons against peak CK and TnI, assuming that the peak might have been reached prior to admission. Only two patients were in this category in our study group.

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. The study protocol was approved by the institutional review board and informed consent was obtained from all participants.

2.2. CMR protocol

CMR was performed using a 1.5 T system (Gyroscan Intera, Philips, Best, The Netherlands), 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 min 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 = 256 × 256, slice thickness = 6 mm, no gap), covering the whole left ventricle from base to apex. The inversion time (TI) was optimized using scouting Look–Locker sequence to minimize the signal in the remote myocardium (TI range was 170–200 ms).

2.3. Post processing and image analysis

For both acute and chronic CMR datasets, images were reviewed by a single expert blinded to all clinical data. The extreme basal slices containing bright areas corresponding to the aortic outflow tract were excluded from the analysis. Besides, endocardial and epicardial contours were traced using the Philips computer assisted software for each slice.

.2.3.1. Quantitative evaluation of infarct size

2.3.1.1. Manual quantification. A first analysis is manually performed on the Philips Viewforum software. A level-1 SCMR trained operator manually outlined the myocardial hyper-enhanced regions introducing corrections while varying the contrast window. Besides, when present, areas corresponding to microvascular obstructions (defined as the hypointensity within a hyperintense region in patients with MI) were included in the infarct zone.

2.3.1.2. Semi-automated 2 to 6SD quantification. As a first step, a region of interest (ROI) was manually defined on the remote myocardium, as large as possible 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 $M + k \cdot SD$ (with $k = 1$ to 6).

2.3.1.3. Semi-automated fuzzy c-means quantification. As previously described [14,15], the fuzzy c-means algorithm (see Appendix A for more details) 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. Of note, clustering was achieved independently on each slice to avoid misclassification related to eventual inter-slice differences in signal intensity. Moreover, it was achieved on a region including myocardium and LV cavity as previously described [14] to avoid misclassifications especially in slices without scar. Indeed, in normal slices, when LV cavity is included, the two expected classes of pixels (enhanced and non-enhanced voxels) can always be defined.

For the unsupervised fuzzy clustering approach, 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 (i.e. number of voxels with a measure of membership above the threshold value) was plotted according to the threshold values (Fig. 1). The value corresponding to the flat portion of this curve was defined as the optimal threshold, which was then used for myocardial necrosis delineation (Fig. 1). The flat portion of the curve was used for the definition of the threshold so that the amount of necrosis would not be affected by slight variations around the optimal threshold. No manual corrections were applied to both thresholding and fuzzy c-means approaches.

2.3.1.4. Absolute and relative infarct size. 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).

.2.3.2. Evaluation of LV function

An independent operator, blinded to LGE and clinical data, used Simpson's formula to measure LV global end-diastolic (EDV) and end-systolic (ESV) volumes, mass and LV ejection fraction (LVEF) after endocardial and epicardial border tracing using a computer assisted approach on each short axis slice of the b-SSFP dynamic sequences. Body surface area adjusted EDV (EDVi) and ESV (ESVi) were also calculated. Regional contractility was quantified on the basis of the AHA/ACC LV segmentation model [22]. For each, myocardial segment, myocardial thickening was estimated as the mean difference between end-diastolic and end-systolic thicknesses. A segment was considered hypokinetic if its thickening was <5 mm (<−2SD of normal value assessed in normal segments in our CMR laboratory). All LV function measurements were performed using the Phillips Viewforum software.

2.4. 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

3.1. Population

A total of 52 patients were included and underwent a first CMR exam 50 ± 21 h 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. The remaining group of 18 patients comprised patients who had a second event before the date planned for the second CMR exam and patients who did not came to the second CMR exam. All LGE-CMR images were considered interpretable and included in the analysis. Clinical, biological and angiographic characteristics as well as CMR data, for both the acute and the chronic phases, are detailed in Tables 1 and 2, respectively, showing a standard acute coronary syndrome population with relatively low risk profile (preserved LVEF, no cardiogenic shock and very few with signs of heart failure). As indicated in Table 1, percutaneous coronary intervention was attempted in 84% of the patients and was successful in only 91% of these patients.

3.2. Infarct size quantification

Fig. 2 describes mean values and standard deviations of infarct mass measured by the seven LGE quantification techniques in AMI and CMI. As expected, the infarct mass decreased consistently between the acute and the chronic phases. When tested on the 34 subjects who had both CMR exams, using a Wilcoxon paired test, this expected decreasing trend was found to be statistically significant only for the manual ($p<0.0002$), the fuzzy c-means ($p<0.0002$), the +2SD ($p=0.004$) and the +3SD ($p=0.02$) approaches.