Published by Elsevier Inc.
ISSN 0735-1097/04/$30.00
doi:10.1016/j.jacc.2004.09.020

PRECLINICAL RESEARCH

Accurate and Objective Infarct Sizing by Contrast-Enhanced Magnetic Resonance Imaging in a Canine Myocardial Infarction Model

Luciano C. Amado, MD,* Bernhard L. Gerber, MD,* Sandeep N. Gupta, PHD,‡ Dan W. Rettmann, BS,‡ Gilberto Szarf, MD,† Robert Schock, PHD,§ Khurram Nasir, MD, MPH,* Dara L. Kraitchman, VMD, PHD,† João A. C. Lima, MD*

Baltimore, Maryland; Waukesha, Wisconsin; and Mahwah, New Jersey

OBJECTIVES To identify an accurate and reproducible method to define myocardial infarct (MI) size, we conducted a study in a closed-chest canine model of acute myocardial infarction, in which MI size was measured using different thresholding techniques and by imaging at different delay times after contrast administration.

BACKGROUND The MI size by contrast-enhanced magnetic resonance imaging (CE-MRI) is directly related to long-term prognosis. However, previous measurements were done using nonuniform methods and tended to overestimate nonviable areas.

METHODS Thirteen animals underwent 90 min of coronary artery occlusion, followed by reperfusion. The CE-MRI data were acquired within 24 h after reperfusion and compared with triphenyltetrazolium chloride pathology. In the first nine animals, images were obtained ~15 min after gadolinium diethylene triamine penta-acetic acid (Gd-DTPA) using an inversion-recovery gradient-echo pulse sequence. To identify the most accurate method, MI size by CE-MRI was measured visually and by semi-automatic thresholding techniques, using different criteria. In four additional animals, images were acquired every 6 min until 30 min after Gd-DTPA.

RESULTS Postmortem MI size was 13.5 ± 2.6% of left ventricular volume. Semi-automatic techniques, using full-width at half-maximum (FWHM) criterion, correlated best with postmortem data ($r^2 = 0.94$, $p < 0.001$; results confirmed by Bland-Altman plots). Using FWHM, there was no difference in MI size between different delay times after contrast (15.2 ± 2.9% to 14.5 ± 4.2% at 6 and 30 min, respectively; p = NS).

CONCLUSIONS When an objective technique is used to define MI size by CE-MRI, accurate infarct size measurements can be obtained from images obtained up to 30 min after contrast administration. (J Am Coll Cardiol 2004;44:2383–9) © 2004 by the American College of Cardiology Foundation

The extent of injury after an ischemic event and the distinction between viable and nonviable myocardium are important for treatment decision-making. Contrast-enhanced (CE) magnetic resonance imaging (MRI) is an imaging modality capable of high spatial resolution and able to assess the presence of viable myocardium in infarcted and poor contractile areas (1). In the chronic phase of myocardial infarction (MI), delayed hyperenhancement has been shown to correlate well with fibrosis and be a marker of irreversible injury (2). Also, measurements of MI extent determined by CE-MRI have been demonstrated to predict long-term prognosis and play a key role in treatment (3,4).

Various studies have shown that in the acute MI, CE imaging techniques tend to overestimate nonviable tissue (5–9). Many technical issues appear to be involved in this process. Previous studies using CE-MRI have utilized different methods, different pulse sequences for imaging acquisition, as well as different delays after contrast injection, making interpretation complex (1,5,6). Recently, a link between infarct overestimation and the delay time of imaging acquisition after contrast injection has been proposed (9). However, other previous studies have produced data suggesting that infarct size is reproducible between 10 and 30 min after contrast administration (10). The discrepancies observed between those studies could be attributed to methodologic differences and imply the need for an accurate and objective technique to define the extent of a delayed hyperenhanced region. Most studies have used arbitrary criteria to define the extent of infarcted tissue from CE-MRI (5,9,11). Until now, no one has validated an ideal technique to define infarct size by CE-MRI.

This study represents an attempt to find a uniform method to measure infarct size from delayed CE images.

From the Department of Medicine, Divisions of *Cardiology and †Radiology, Johns Hopkins University, School of Medicine, Baltimore, Maryland; ‡GE Medical Systems, Waukesha, Wisconsin; and §Datascope Corporation, Mahwah, New Jersey. The National Institutes of Health (NIH, National Heart, Lung and Blood Institute [NHLBI] grants RO1-HL63439 and RO1-HL66075-01) and Datascope Corporation funded this research. Dr. Kraitchman is supported by grant K02-HL04193 from the NHLBI. Drs. Kraitchman and Lima contributed equally to the concept and design of this study.

Manuscript received February 16, 2004; revised manuscript received August 5, 2004, accepted September 3, 2004.

JACC Vol. 44, No. 12, 2004
December 21, 2004:2383–9

Abbreviations and Acronyms

CE	= contrast-enhanced/enhancement
FWHM	= full-width at half-maximum
Gd-DTPA	= gadolinium diethylene triamine penta-acetic acid
LV	= left ventricle/ventricular
MI	= myocardial infarct/infarction
MRI	= magnetic resonance imaging
TI	= inversion recovery time
TTC	= triphenyltetrazolium chloride

For this purpose, we conducted a study with two main objectives: 1) to determine the most accurate and objective thresholding criterion to assess the presence and extent of viable myocardium in the acute phase of MI by delayed CE-MRI images; and 2) to examine whether the size of a hyperenhanced area remains constant as a function of time.

METHODS

Experimental protocol. All animal studies were approved by our Institutional Animal Care and Use Committee and complied with the "Guidelines for the Care and Use of Laboratory Animals" (National Institutes of Health [NIH] publication no. 80-23, revised 1985). Thirteen mongrel dogs (25 to 30 kg) were anesthetized, intubated, and mechanically ventilated. All animals received prophylaxis with antibiotics every 4 h.

Experimental MI. Catheter sheaths were placed in the right femoral artery (10-F) and right carotid artery (8-F). After this, the animals underwent heparinization (5,000 IU intravenously). A 6-F pigtail catheter was advanced through the femoral artery into the left ventricular (LV) cavity for ventriculography and pressure monitoring. A coronary angioplasty balloon (3.5-F, 20 mm) was advanced through the right carotid artery into the proximal left anterior descending coronary artery or left circumflex artery. Myocardial infarcts were created by inflating the angioplasty balloon for 90 min. After this period, the balloon was deflated and the artery reperfused.

The MRI protocol. To define the most accurate threshold technique to assess the extent of necrotic (nonviable) myocardium, images were obtained at 24 h after MI in the first nine animals. In the subsequent four animals, images were acquired at 1 h after MI to examine the extent of the hyperenhanced region over time, after contrast injection. One hour was chosen as the time necessary to stabilize the animal after MI. All images were acquired using a 1.5-T MR scanner (CV/i, GE Medical Systems, Waukesha, Wisconsin). Animals were placed in right decubitus with a phased-array surface coil wrapped around the chest.

Comparisons with infarct sizing methods. In the first nine animals, images were acquired 15 min after a 0.2-mmol/kg intravenous injection of gadolinium diethylene triamine penta-acetic acid (Gd-DTPA) (Magnevist, Berlex Laboratories, Montville, New Jersey), using an electrocardiographically gated, breath-hold, interleaved, inversion recovery, fast gradient echo pulse sequence: echo time of 3.3 ms, repetition time of 7.3 ms, 8-mm slice thickness/no gap, 28 × 21-cm field of view, 256 × 196-160 image matrix, 25° flip angle; two number of signals averaged, and 31.2-kHz bandwidth (12). The inversion recovery time (TI) was fixed at 200 ms for the first image acquisition. Two observers evaluated the quality of the first delayed enhancement image, and adjustments to the TI were done if necessary to achieve the best contrast between the normal and infarcted myocardium. The overall measured TI was 223 ± 9.2 ms.

Timing delay study. The same protocol was used for the time delay study. However, for this protocol, imaging acquisition was performed repeatedly starting immediately after contrast injection and continuing until 30 min after injection. Each set of images, covering the entire heart from base to apex, was acquired in ~6 min. A total of five sets of images, each containing eight to nine short-axis images, were obtained from each animal (n = 4). Small adjustments in TI were made to null the signal intensity from normal myocardium at different time points after contrast injection. The TI changed from 193.8 ± 6.3% to 212.5 ± 16.1% at 6 and 30 min after contrast injection, respectively (p = NS).

Analysis of MRI data. COMPARISON OF INFARCT SIZING METHOD STUDY. To determine the most accurate technique of measuring infarct size by CE-MRI, images were transferred to a SUN workstation (Sun Microsystems, Santa Clara, California) and analyzed using a custom research software package (Cine Tool, GE Medical Systems). Endocardial and epicardial contours were traced manually. Once the myocardial contours were identified, infarct areas were traced manually by two different observers using both a visual qualitative approach and objective semi-automatic thresholding techniques. Various criteria based on the signal intensities of the normal and infarcted myocardium were used to semi-automatically threshold the infarct (Fig. 1).

N-STANDARD DEVIATIONS ABOVE REMOTE. With this technique, the mean and standard deviation of the signal intensity from the remote (noninfarcted) myocardium region of interest was determined, and infarcted regions were defined as areas presenting signal intensities above a certain number of standard deviations from the mean of the remote. Measurements were done using 1, 2, 3, 4, 5, and 6 standard deviations above the remote mean (Fig. 1) (1,9).

FULL-WIDTH AT HALF-MAXIMUM (FWHM). Measurements were also done based on FWHM criterion (13,14). The user clicked in the hyperenhanced region to provide a seed point, and a multi-pass region-growing algorithm was used to identify the infarct boundaries by using the FWHM criterion (Fig. 1).

VISUAL. Infarct size was also measured visually by two different observers, by manually defining the extent of

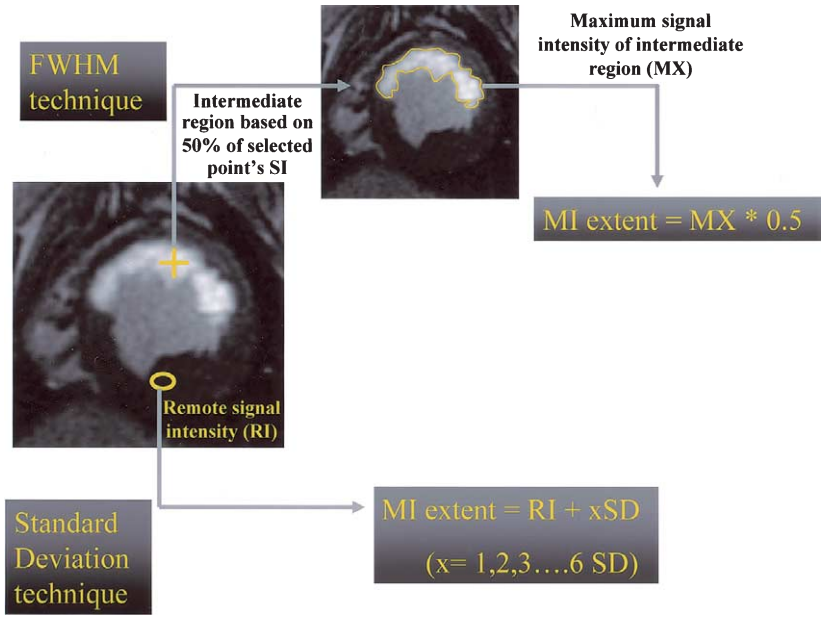

Figure 1. Delayed enhancement images and semi-automatic techniques using different criteria to quantify myocardial infarct (MI) extension: 1) the full-width at half-maximum (FWHM) criterion—an initial region is determined to grow to include all pixels with signal intensity (SI) >50% of a user selected point. The maximum signal intensity (MX) inside this initial region is then determined, and the final MI extent is defined as the area presenting with a signal intensity 50% above the maximum of the initial region (MI = MX * 0.5). 2) n-standard deviation (SD) criteria—the mean ± SD of remote signal intensity (RI) under the yellow circle was determined. The extent of MI was defined as areas presenting with signal intensities above the mean value from the remote (MI = RI + SD). Measurements were done using 1, 2, 3, 4, 5, and 6 SD above the mean value.

hyperenhanced area. Contouring was performed based on subjective visual identification of the infarct border.

Timing delay study. The most accurate method of measuring infarct size determined from the previous study was then employed to calculate MI size at different delay times in four additional animals. All measurements of infarct size were expressed as a percentage of LV volume, given by the sum of the volume of the hyperenhanced regions for all slices divided by the sum of the LV myocardial cross-sectional volumes for all slices.

Postmortem measurements. After image acquisition, animals were euthanized. The heart was excised and sectioned into 8-mm-thick short-axis slices and incubated in 2,3,5-triphenyltetrazolium chloride (TTC) for 20 min at 38°C to delineate viable myocardium (15). Each slice was photographed with a digital camera. Using a custom research software package (Cine Tool, GE Medical Systems), TTC-negative and LV borders were manually traced for each slice. Infarct size was determined as the percentage of LV volume.

Statistical analysis. Analysis was performed using STATA software (Stata Corp., College Station, Texas). Infarct size is expressed as the mean value ± SEM. Pearson correlation and linear regression analysis were used to compare between the different MRI measurements and MRI measurements against postmortem measurements. Results were confirmed with repeated measurements analysis of variance and Bland-Altman plots (16). The Bland-Altman repeatability analysis method was used to compare semi-automatic and visual techniques. A level of $p < 0.05$ was considered statistically significant.

RESULTS

Figure 2A shows excellent correspondence of the infarct size measured by delayed CE-MRI images and TTC pathology. The mean infarct size by TTC was 13.5 ± 2.6% of the LV volume.

Comparison of infarct sizing method study. Table 1 summarizes the results of MI size measured by different thresholding techniques, compared with postmortem infarct extent. Compared with the postmortem data, the best correlation was achieved with MRI measurements based on the FWHM thresholding technique ($y = 1.1x + 2.3$; $r^2 = 0.94$) (Fig. 2A). Regression and Bland-Altman analysis confirmed the superiority of the FWHM technique (bias of 4.1% of LV; $p < 0.001$) (Fig. 2B), compared with the other semi-automatic thresholding techniques tested (Fig. 3).

Figure 2C demonstrates the results of Bland-Altman analysis of interobserver reproducibility from semi-automatic and visual techniques. A much better reproducibility was achieved with FWHM compared with visual techniques (bias of −0.1% and −3.4% of LV for FWHM and visual measuring techniques, respectively).

Timing delay study. Infarct size measurements from delayed enhancement images acquired with different delay times were segmented using the FWHM criterion. There was no significant difference in MI size (as percentage of LV volume) between different delay times after contrast injection (from 15.2 ± 2.9% to 14.5 ± 4.2% at 6 and 30 min after contrast injection, respectively; p = NS).

Figure 4 depicts delay CE images at five different time points after contrast injection, from three different animals,

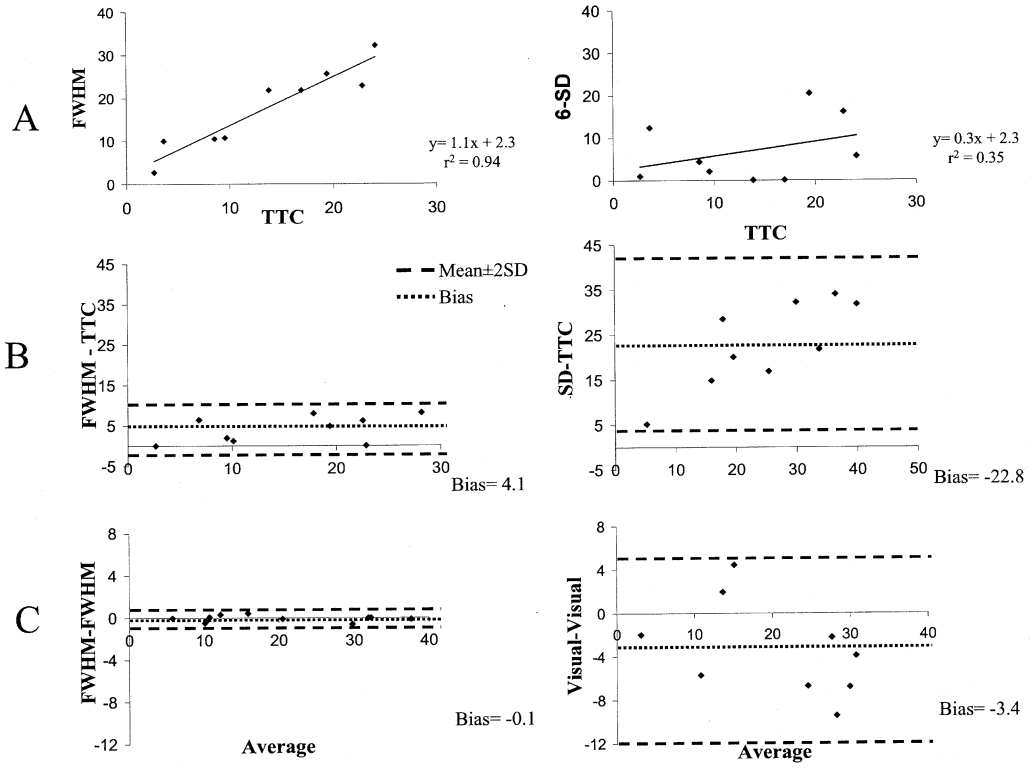

Figure 2. Infarct size measured by delayed contrast-enhanced magnetic resonance imaging using different criteria. **(A)** The best full-width at half-maximum (FWHM) and worst (6 SD) correlations against triphenyltetrazolium chloride (TTC) pathology. **(B)** Bland-Altman analyses show the level of agreement between infarct size measured by the different criteria against TTC (FWHM and 1 SD for best and worst, respectively). **(C)** Bland-Altman analyses of interobserver reproducibility studies obtained from visual and semi-automatic criteria methods.

demonstrating excellent concordance of infarct size measurements over time. Indeed, there was high agreement of MI size between the first set of images until 30 min after contrast injection ($y = 1x - 0.8$; $r^2 = 0.97$, when measurements obtained at 6 and 30 min were compared). Results were confirmed by Bland-Altman analysis (bias of −0.2% of LV) (Fig. 5).

DISCUSSION

This study was designed to identify an accurate and objective method to measure infarct size from delayed CE-MRI scans. Our results can be summarized as follows: 1) the semi-automatic thresholding technique based on the FWHM criterion is an accurate and reproducible segmentation method to define infarct size on delayed CE images; 2) when using an accurate objective segmentation criterion, the delay time of image acquisition after contrast injection is not an important factor in the accuracy of infarct size measurements; and 3) using an accurate method to describe delayed hyperenhanced regions, no significant overestimation of the infarct size is observed compared with postmortem.

CE-MRI for myocardial viability. The extent of MI and the ability to differentiate viable from nonviable tissue are important variables for treatment decision-making. In cardiology, measurements of infarct size by CE-MRI have been validated as prognostic indicators after acute MI (3). However, there is ongoing debate regarding the potential overestimation by the CE-MRI technique to assess local viability and contractile functional recovery after an acute event or treatment intervention (2,5,8).

Although delayed contrast hyperenhancement has been shown to accurately reflect myocellular necrosis, and therefore to be a definite marker of absent myocardial viability on ex vivo imaging, studies have reported an overestimation of infarct size (7,17). More specifically, some studies have demonstrated improvement in circumferential shortening between one and seven weeks after MI in regions presenting with delayed hyperenhance-

Table 1. Statistical Analysis

	FWHM	1 SD	2 SD	3 SD	4 SD	5 SD	6 SD	Visual
Pearson correlation (r^2)	0.94	0.85	0.79	0.71	0.56	0.42	0.35	0.69
Linear regression (p value)	<0.001*	<0.05*	<0.05*	<0.05*	NS	NS	NS	<0.05*
Bland-Altman plot (bias†)	4.1 ± 1.1%	22.8 ± 3.2%	11.8 ± 2.5%	6.0 ± 2.1%	6.6 ± 1.7%	8.1 ± 1.8%	8.7 ± 2.1%	8.6 ± 1.9%

*Compared with postmortem data. †Bias expressed as percentage of left ventricle (mean ± SD).
FWHM = full-width at half-maximum; NS = not significant; SD = standard deviation.

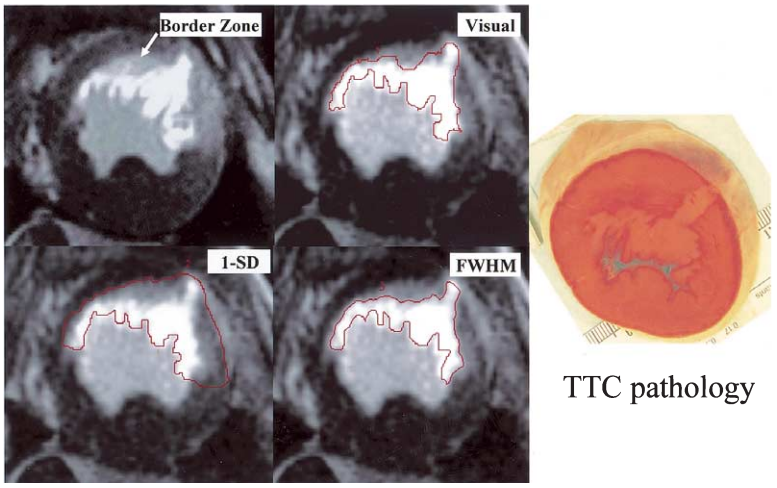

Figure 3. Comparison of infarct size measured from short-axis images by delayed contrast-enhanced magnetic resonance imaging (MRI) using different techniques. The **arrow** demonstrates the border zone, areas with partial enhancement on the edge of the infarct, which may lead to visual ambiguity in assessing the delayed hyperenhanced area. The infarcted region was delineated by the different techniques using different criteria, as shown by contours in **red**: 1 = visual; 2 = standard deviation (1 SD); and 3 = full-width at half-maximum (FWHM). Significant variability among segmentation methods is noted, especially related to the inclusion of the border zone on the analysis. The MRI infarct size was compared with postmortem measurements (triphenyltetrazolium chloride [TTC] pathology).

ment (5), and others have confirmed this inotropic response in up to 41% of hyperenhanced segments (18), suggesting viability. A potential explanation of these findings is the presence of a nontransmural infarction. In this regard, Garot et al. (19) have shown that the improvement in contractile function in regions of hyperenhancement are related to the presence of nontransmural infarction, suggesting a tethering to neighboring viable regions. Additionally, Kim et al. (1) demonstrated that hyperenhanced regions tend to decrease in the range of approximately three-fold from three days to eight weeks after MI. This shrinkage effect can lead to erroneous interpretation in the differentiation of nontransmural (defined as <50% of LV wall extension) from transmural (>50% of LV wall) at the acute phase of MI. These data combined support the need for an accurate technique to measure the extent of the necrotic area at the acute phase of MI.

The reasons for infarct size overestimation by MRI are not completely understood. Partial volume effects intrinsic to slice thickness limitation are likely responsible for most of the infarct size overestimation. Potential mechanisms might also include the possibility that myocardial edema without cell necrosis could produce late tissue hyperenhancement through an increase in the extracellular distribution of the contrast agent (20,21). In theory, an interstitial water increase due to plasma infiltration after the hyperemic stage of acute MI could explain the infarct size overestimation observed in clinical and experimental studies. However, the presence of extracellular edema is difficult to document, and its magnitude is even harder to quantify.

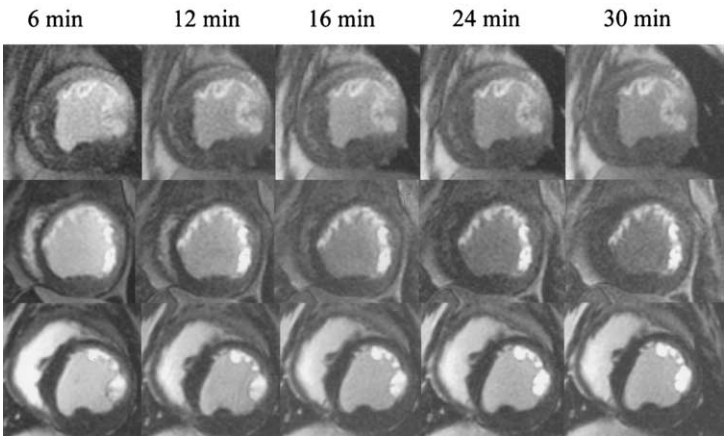

Figure 4. Differences in infarct size over time. This figure depicts delayed enhancement short-axis images from three different animals. Images were obtained every 6 min after contrast injection until 30 min after contrast. The presence, location, and size of the hyperenhanced region were similar for all time points. There were high levels of agreement in measurement of myocardial infarct size between the first set of images at 6 min and all others up to 30 min after contrast injection.

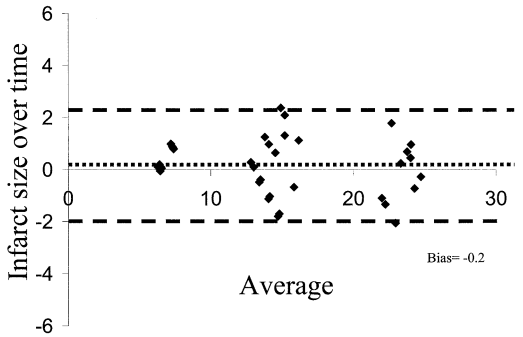

Figure 5. Bland-Altman analysis demonstrates no important differences in infarct size measurements over time (bias of −0.2% of left ventricle).

Accurate method for infarct sizing. Our study supports the importance of choosing an accurate technique to measure infarct size by CE-MRI. As shown in Table 1, important variations in MI size measurements were observed in our study when using different thresholds for myocardial hyperenhancement (bias from 4.1 ± 1.1% to 22.8 ± 3.2% of LV for FWHM and 1 standard deviation criteria, respectively).

Our results illustrate the ability of the FWHM criterion to accurately measure infarct size by CE-MRI, compared with the other semi-automatic criteria. Most of the semi-automatic techniques previously published utilized the signal intensity of areas outside the infarct to define hyperenhanced regions. Surface coil intensity variations may confound the segmentation criteria when using a remote region to calculate the segmentation threshold. The FWHM criterion is based solely on the signal intensity inside the infarcted area. Therefore, even in the case of spatial variations in intensity, the boundary determined by this approach does not change, as it is relative to the local infarct signal maximum. Consequently, this approach should be less susceptible to surface coil intensity variations (Fig. 1).

Measurements using the semi-automatic FWHM technique demonstrate a reduction in interobserver variability compared with non-automatic visual techniques (bias of −3.4 and −0.1% of LV for Bland-Altman repeatability analysis for visual and FWHM techniques, respectively) (Fig. 4). These results reinforce the importance of using objective techniques to reduce the possibility of human error.

Even when using the most accurate technique—FWHM—differences in infarct size measured by CE-MRI and at postmortem were still observed. This can be partly explained by differences between the two techniques: MRI infarct size measurements are based on the extension of the contrast (Gd-DTPA) penetration into the necrotic tissue, whereas the TTC staining technique is related to the extension of tissue capable of reacting to the stain (TTC).

Also, problems with the TTC staining technique should be considered. For example, potential limitations of slicing the anatomic piece preceding the TTC staining are intrinsic to this method; TTC staining requires a thermal-conditioning step that can dehydrate the myocardium and consequently alter the infarct configuration, making it difficult to accurately delineate the infarct's true dimensions. Finally, as a result of the thermal-conditioning step, myocardial dehydration can lead to imprecise weighting of the slices, as well as inaccuracies in infarct size measurements normalized by LV mass.

Delayed time study. In our study, no significant differences in MI extent were noted among CE-MRI measurements performed between 6 and 30 min after contrast injection. These results support the findings of Mahrholdt et al. (10), who reported that infarct size measured as the hyperenhanced area on CE-MRI does not change between 10 and 30 min after contrast. Conversely, our findings diverge from another recent report by Oshinski et al. (9), who found a decrease from 60% of LV at 3 min to 30% of LV at 40 min after contrast injection.

The different results found in our study and the study by Oshinski et al. (9) can be partly related to differences in species, specific collateral flow, or edema formation secondary to different degrees of reperfusion injury (22). In addition, these discrepancies could be due to differences in the MRI pulse sequences utilized in those studies (12). The importance of the TI (delay time between the inversion pulse and data acquisition) to null the normal and noninfarcted myocardium has been emphasized in past studies (12). In our study, TI adjustments were performed for adequate image acquisition (Fig. 4).

Furthermore, our study highlights a new and important factor: the use of objective criteria to delineate the extension of hyperenhanced myocardium defined by CE-MRI. As shown by our findings, subjective measurements demonstrated a variance as high as ±300% (from 6.0 ± 2.1 to 22.8 ± 3.2 for bias of 3 and 1 standard deviation techniques, respectively) among different methods. These findings reinforce the importance of choosing an accurate technique to measure infarct size in a clinical setting.

Conclusions. This study documents the accuracy and reproducibility of the semi-automatic technique based on the FWHM criterion to measure infarct size by CE-MRI. In addition, the study demonstrates that by using an objective segmentation technique, the delay time after contrast injection is not an important factor to the accuracy of infarct size measurements by CE-MRI. Finally, our results suggest that future studies using CE-MRI to measure the extent of MI should consider the use of the FWHM criterion. These findings might have important implications to the interpretation of CE-MRI methods to measure infarct size in a clinical setting.

Acknowledgment

We thank Danielle Fritzges for her assistance in the implementation of the study.

Reprint requests and correspondence: Dr. João A. C. Lima, Associate Professor of Medicine, Cardiology Division (Blalock 569), Johns Hopkins Hospital, 600 N. Wolfe Street, Baltimore, Maryland 2187-6568. E-mail: jlima@jhmi.edu.

REFERENCES

1. Kim RJ, Fieno DS, Parrish TB, et al. Relationship of MRI delayed contrast enhancement to irreversible injury, infarct age, and contractile function. Circulation 1999;100:1992–2002.
2. Kim RJ, Wu E, Rafael A, et al. The use of contrast-enhanced magnetic resonance imaging to identify reversible myocardial dysfunction. N Engl J Med 2000;343:1445–53.
3. Wu KC, Zerhouni EA, Judd RM, et al. Prognostic significance of microvascular obstruction by magnetic resonance imaging in patients with acute myocardial infarction. Circulation 1998;97:765–72.
4. Kramer CM, Rogers WJ, Theobald TM, et al. Remote noninfarcted region dysfunction soon after first anterior myocardial infarction: a magnetic resonance tagging study. Circulation 1996;94:660–6.
5. Rogers WJ Jr., Kramer CM, Geskin G, et al. Early contrast-enhanced MRI predicts late functional recovery after reperfused myocardial infarction. Circulation 1999;99:744–50.
6. Schaefer S, van Tyen R, Saloner D. Evaluation of myocardial perfusion abnormalities with gadolinium-enhanced snapshot MR imaging in humans. Work in progress. Radiology 1992;185:795–801.
7. Saeed M, Bremerich J, Wendland MF, et al. Reperfused myocardial infarction as seen with use of necrosis-specific versus standard extracellular MR contrast media in rats. Radiology 1999;213:247–57.
8. Kramer CM, McCreery CJ, Semonik L, et al. Global alterations in mechanical function in healed reperfused first anterior myocardial infarction. J Cardiovasc Magn Reson 2000;2:33–41.
9. Oshinski JN, Yang Z, Jones JR, et al. Imaging time after Gd-DTPA injection is critical in using delayed enhancement to determine infarct size accurately with magnetic resonance imaging. Circulation 2001; 104:2838–42.
10. Mahrholdt H, Wagner A, Holly TA, et al. Reproducibility of chronic infarct size measurement by contrast-enhanced magnetic resonance imaging. Circulation 2002;106:2322–7.
11. Kim RJ, Judd RM, Chen EL, et al. Relationship of elevated 23Na magnetic resonance image intensity to infarct size after acute reperfused myocardial infarction. Circulation 1999;100:185–92.
12. Simonetti OP, Kim RJ, Fieno DS, et al. An improved MR imaging technique for the visualization of myocardial infarction. Radiology 2001;218:215–23.
13. Hoffmann KR, Dmochowski J, Nazareth DP, et al. Vessel size measurements in angiograms: manual measurements. Med Phys 2003; 30:681–8.
14. Hoffmann KR, Nazareth DP, Miskolczi L, et al. Vessel size measurements in angiograms: a comparison of techniques. Med Phys 2002; 29:1622–33.
15. Rochitte CE, Lima JA, Bluemke DA, et al. Magnitude and time course of microvascular obstruction and tissue injury after acute myocardial infarction. Circulation 1998;98:1006–14.
16. Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. Lancet 1986;1:307–10.
17. Schaefer S, Malloy CR, Katz J, et al. Gadolinium-DTPA-enhanced nuclear magnetic resonance imaging of reperfused myocardium: identification of the myocardial bed at risk. J Am Coll Cardiol 1988;12:1064–72.
18. Dendale P, Franken PR, Block P, et al. Contrast enhanced and functional magnetic resonance imaging for the detection of viable myocardium after infarction. Am Heart J 1998;135:875–80.
19. Garot J, Bluemke DA, Osman NF, et al. Transmural contractile reserve after reperfused myocardial infarction in dogs. J Am Coll Cardiol. 2000;36:2339–46.
20. Lima JA, Judd RM, Bazille A, et al. Regional heterogeneity of human myocardial infarcts demonstrated by contrast-enhanced MRI: potential mechanisms. Circulation 1995;92:1117–25.
21. Judd RM, Lugo-Olivieri CH, Arai M, et al. Physiological basis of myocardial contrast enhancement in fast magnetic resonance images of 2-day-old reperfused canine infarcts. Circulation 1995;92:1902–10.
22. Jennings RB, Schaper J, Hill ML, et al. Effect of reperfusion late in the phase of reversible ischemic injury: changes in cell volume, electrolytes, metabolites, and ultrastructure. Circ Res 1985;56:262–78.