Detecting early arterial wall changes in premenopausal women with Metabolic syndrome by using black-blood DCE-MRI

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Introduction

The metabolic syndrome (MetS), a manifestation of insulin resistance, is associated with independent increased risk of CVD [1]. One of the early manifestations of MetS on the arterial wall is endothelial dysfunction, which may lead to altered contrast agent kinetics in dynamic contrast-enhanced (DCE) MRI. Because of the small size of the vessel wall early in the atherosclerotic process, blood suppressed DCE protocols are required, precluding extraction of the arterial input function (AIF) for kinetic modeling. Recently, a reference region approach for kinetic modeling without an AIF was demonstrated for a rabbit model of atherosclerosis [2]. In this study, we sought to test the ability of black-blood DCE-MRI to differentiate contrast agent kinetics in MetS versus healthy controls drawn from a population of premenopausal women.

Methods and Materials

Population For this study, 11 premenopausal women aged 35- 50 years of age with MetS and 19 age-matched controls were recruited. MetS was defined as having at least 3 of the following abnormalities: 1) abdominal obesity (waist circumference > 35 inches) 2) fasting triglycerides ≥ 150 mg/dL 3) HDL-C < 50 mg/dL, 4) systolic blood pressure (bp) >130 mm Hg and/or diastolic blood pressure >80 mmHg or physician diagnosed hypertension, and 5) fasting glucose > 100 mg/dL. This study was approved by the institutional review board and all subjects provided informed consent.

MR Imaging All subjects were imaged on a clinical 3T MRI scanner (Philips Achieva, Netherlands) using a custom 8-channel carotid coil. The MRI protocol included high-resolution T1-weighted black-blood imaging for measuring thickness of the common carotid artery wall and black-blood dynamic imaging to measure contrast agent kinetics due to vessel wall perfusion. Two slices were prescribed in the common carotid arteries immediately proximal to the carotid bulb on each side. High resolution T1-weighted images were obtained with a turbo spin echo (TSE) quadruple inversion recovery (QIR) sequence [3] with scan parameters: TR/TE=800/11ms, TI1/TI2=325/125ms, field-of-view (FOV)=14*14cm, matrix=400*400, echo train length=7, slice thickness=3mm, 2 nex. Black-blood DCE-MRI data were collected using a QIR TSE acquisition with scan parameters: TR/TE=900/13ms, TI1/TI2=325/125ms, FOV=16*4cm, matrix=240*60, echo train length=12, and slice thickness=3mm, 1 nex. The small FOV in the phase encode direction was enabled by the zoom feature for outer volume suppression and facilitated a temporal resolution of 6 seconds per slice. A total of 20 time points were obtained, wherein a bolus of Gd-DTPA (Magnevist, Bayer-Schering, Berlin) at 0.1mmol/kg was injected via power injector coincident with the third time point.

Image Analysis All images were analyzed using a custom program (CASCADE [4]). The T1-weighted images were independently analyzed by an expert to measure wall thickness by interactively defined contours for the lumen and outer wall boundaries. For DCE-MRI, we utilized a technique previously validated in a rabbit model of early atherosclerosis [2]. First, contours were mapped to each frame of the dynamic acquisition and adjusted as needed by an expert. Then, by assuming a linear relationship between the MRI signal and contrast concentration, the average intensity curve (SI(t)-SI(0), where SI(t) is the intensity at time t) of each artery was used as the contrast concentration curve for kinetic analysis. Because our use of black-blood sequence precluded the direct measurement of an arterial input function, a reference region method based on the Patlak model of kinetics was used for our analysis [2]:

$$v_p C_r(t) + K^{trans} \int_0^t C_r(\tau) d\tau = v_p^r C_v(t) + K_r^{trans} \int_0^t C_v(\tau) d\tau$$

where K^{trans} and v_p are the partial plasma volume and partial plasma volume of vessel wall, $C_v(t)$ and $C_r(t)$ are the measured concentrations for the vessel wall and reference region, respectively, and v_p^r and K_r^{trans} are the known values of the partial plasma volume (0.045 min^{-1}) and transfer constant (0.078) in the reference region (adjacent sternocleidomastoid muscle), respectively. The known values were measured on 6 subjects from a patient population imaged with bright blood DCE-MRI and analyzed by Patlak model. In DCE-MRI analysis, all slices meeting one of these criteria were excluded from analysis to avoid measurement bias introduced by artery obliquity or possible flow artifact: (1) a non-circular artery shape; (2) apparent localization within the carotid bulb; or (3) severe flow artifact.

Data Analysis Thickness measurements from multiple slices in the same artery were averaged to obtain individual measurements per artery. The maximum values of the vessel wall thickness and K^{trans} from left and right arteries were recorded. All data were compared between MetS group and control group using two-sided Student's t-tests.

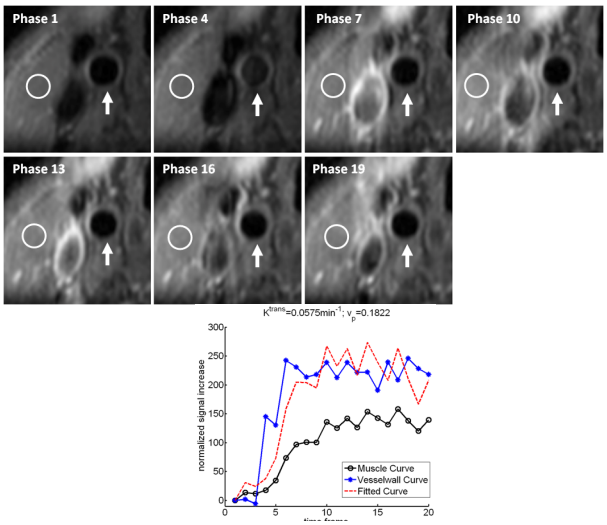

Fig 1. The black-blood DCE MR images of one slice of a representative case. The white arrow points the carotid artery, and the white circle shows the selected reference region in sternocleidomastoid muscle. The intensity versus time curves for the vessel wall and reference region were shown in the bottom image. The fitting results were: K^{trans}=0.058min^{-1}, v_p=0.1822.

Results

3 subjects with MetS and 2 controls were excluded due to artery obliquity for both arteries. Typical black-blood DCE-MRI images and intensity versus time curves for the vessel wall and muscle reference are shown in Figure 1 along with model fitting results. As summarized in Table 1, the maximal thickness measurements were significantly (P=0.02) higher in MetS group; and the maximal values of K^{trans} were significantly (P=0.03) lower in MetS group.

Table 1. MRI Findings comparing metabolic syndrome (MetS) group to normal control group.

	Maximum of both arteries		
	Control	MetS	P*
Thickness (mm)	0.692±0.061	0.754±0.051	0.02
K^{trans} (min^{-1})	0.033±0.016	0.017±0.015	0.03

*Significance by two-sided Student's t-test

Discussion and Conclusion

This study has shown that both increased thickness and reduced K^{trans} may be early manifestations of vessel wall disease in MetS. Furthermore, this study demonstrated the applicability of reference region modeling with a black-blood protocol in a human population for the first time. To date, black-blood DCE-MRI for early diseased vessel wall has only been reported in animal models, often using simplified area under the curve (AUC) analysis [5]. Clinically, the relatively young age of participants in this study also shows that vessel wall differences can be identified long before significant atherosclerotic disease is established by using MRI. Specifically, the previously demonstrated ability of MRI to measure vessel wall thickness [6] can be used to detect early intimal thickening. The reduction in K^{trans} observed here may be the result of intimal thickening without substantial neovascularization. In conclusion, this study shows that differences in vessel wall characteristics can be detected by MRI in premenopausal women with MetS. Thus, the proposed MRI techniques have potential for observing the effects of treatment or lifestyle interventions in MetS.

References:

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