SAGE-Hindawi Access to Research
Cardiology Research and Practice
Volume 2011, Article ID 739702, 4 pages
doi:10.4061/2011/739702

Case Report

Multimodality Imaging of Chronic Ischemia

Kiyotake Ishikawa, Dennis Ladage, Kleopatra Rapti, Leticia Fernandez-Friera, Ana Maria Garcia-Lopez, Javier Sanz, Roger J. Hajjar, Yoshiaki Kawase, and Mario J. Garcia

Cardiovascular Research Center, Mount Sinai School of Medicine, One Gustave L. Levy Place, P. O. Box 1030, New York, NY 10029-6574, USA

Correspondence should be addressed to Kiyotake Ishikawa, kiyotake1@hotmail.com

Received 31 August 2010; Accepted 5 October 2010

Academic Editor: Gregory Giamouzis

Although ischemic cardiomyopathy is commonly caused by chronic obstructive coronary disease, the mechanism of the cause is still under investigation. We present echocardiographic strain, magnetic resonance, and histology findings in a chronic ischemia model in preclinical study. This case illustrates the features of multimodality imaging in chronic obstructive coronary disease and gives us great insight into understanding the mechanism of ischemic cardiomyopathy.

1. Introduction

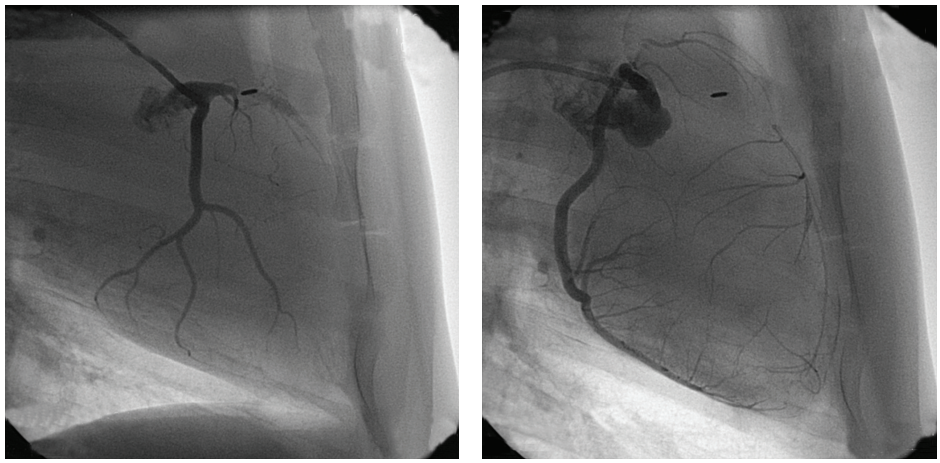
Ischemic cardiomyopathy, the most frequent cause of heart failure, is commonly caused by chronic obstructive coronary disease. The cardiomyocyte response to ischemia, the mechanism for ischemic cardiomyopathy, is still under investigation. On the other hand, imaging devices have developed rapidly over the past decade. We present successful images taken in a model with chronic coronary disease describing characteristic features of chronic ischemia.

2. Case Report

A Yorkshire pig (26 Kg) was studied for 2 months after a chronic implantation of customized occluder on the proximal left anterior descending (LAD) artery. Briefly, under isoflurane anesthesia, surgical access was achieved through the third left intercostal space. A plastic occluder of fixed diameter and 18 G copper wire were deployed around the proximal segment of the LAD. This model progresses a total occlusion of LAD artery with rich collaterals and minimum scar formation within 1 to 3 months after the occluder implantation. The study was performed in accordance with the Guidelines for the Care and Use of Laboratory Animals and was approved by the Subcommittee on Research Animal Care at Mount Sinai School of Medicine. Steady anesthesia using propofol 6 mg/kg/hr IV was maintained throughout each study point.

Coronary angiogram (CAG), left ventriculography (LVG), and echocardiography were performed at 2 weeks, 1 month, and 2 months. Although CAG showed only stenosis of LAD with normal flow at 2 weeks and 1 month with normal LVG and echocardiography, the stenosis developed to total occlusion with Rentrop grade 2 collateral flow from right coronary artery and antegrade bridge collateral flow at 2 months (Figure 1). At the point of occlusion, LVG showed slightly depressed anterior wall motion with ejection fraction (EF) of 59%.

Echocardiography at 2 months confirmed this abnormality (EF 58%). Using prototype Q-lab software (Philips Medical Systems, Andover, MA), two-dimensional images were analyzed for strain analysis using a speckle-tracking algorithm. Circumferential and radial strain (CS and RS, resp.) were analyzed at the level of papillary muscles, and both strain rates at anterior region showed relatively decreased but sustained value compared with other regions. (mean CS −19% versus −26%, mean RS 30% versus 46%, resp.) (Figure 2). After the echocardiography, the pig was transported to the magnetic resonance (MR) facility under anesthesia. Using a 1.5 Tesla magnet (Sonata, Siemens Medical Solutions, Erlangen, Germany), and with electrocardiographic gating, the same plane as during transthoracic



(a) (b)

Figure 1: Coronary angiography at 2 months. (a) Totally occluded left anterior descending artery with bridge collateral flow . (b) Rentrop degree 2 collateral flow from right coronary artery to left anterior descending artery.

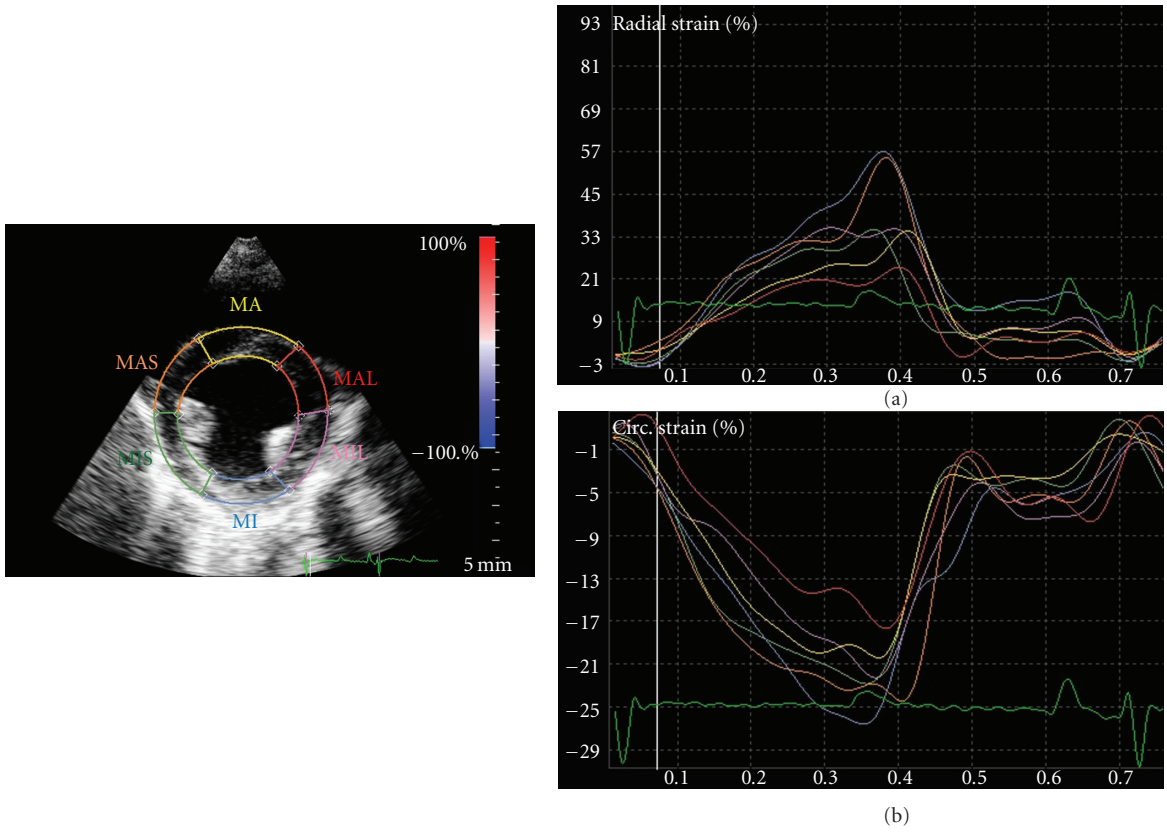


Figure 2: Strain analysis of equally divided six parts at the level of papillary muscles. Yellow and red lines are defined as anterior wall. Both radial strain (a) and circumferential strain (b) showed relatively decreased, yet preserved, strain rate compared with other regions.

echocardiography study was obtained. Delayed enhancement imaging was performed 15 minutes after the administration of 0.2 mmol/kg gadopentetate dimeglumine. T2-weighted image revealed limited intensified area in the subendocardium layer of the anterior wall, which indicates the presence of edema. However, no delayed enhancement was detected at the same region (Figure 3).

After a deep anesthesia with isoflurane, the pig was sacrificed and heart was sliced and subjected to triphenyltetrazolium chloride (TTC) staining to delineate the scar

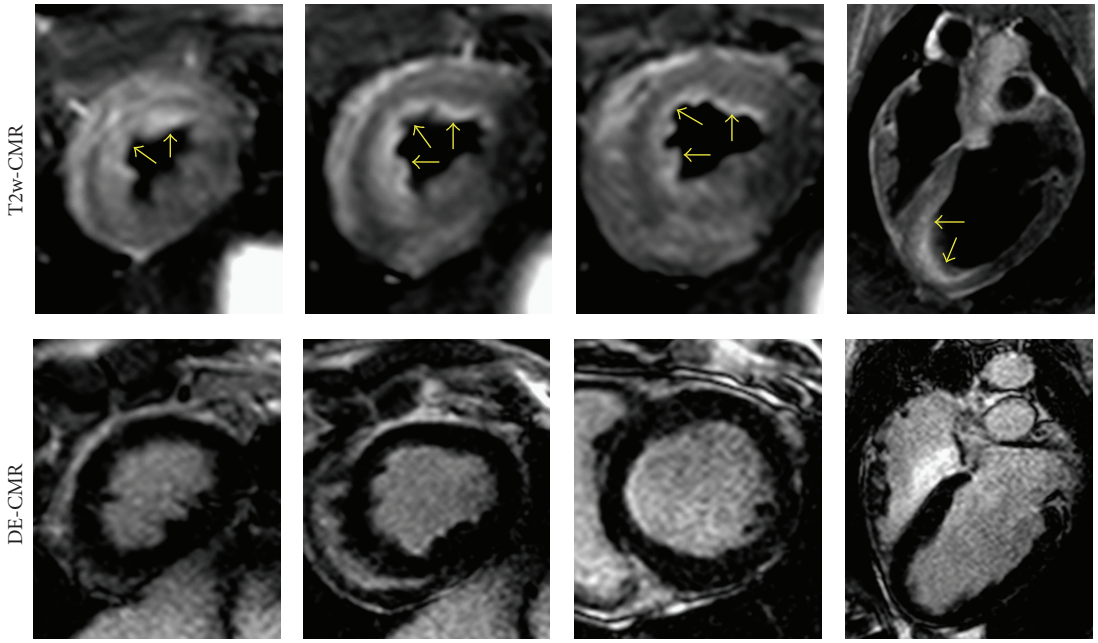


Figure 3: Corresponding short axis and long axis images obtained by CMR. T2w-CMR images showed uptake in the anterior wall (arrows), indicating myocardial edema from ischemia mainly in subendocardium (upper row). However, no specific change was found in delayed enhancement images (lower row). CMR: cardiac magnetic resonance DE: delayed enhancement.

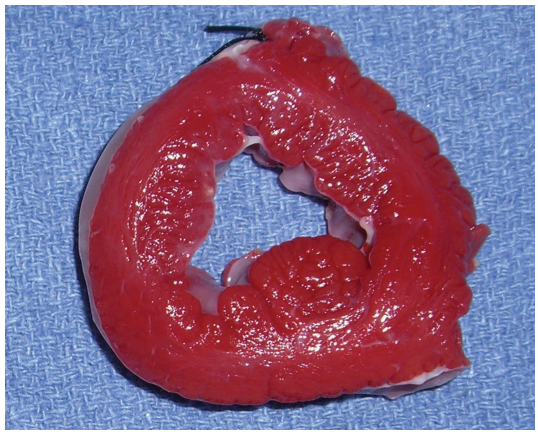


Figure 4: No macroscopic infarction was seen in postmortem TTC-stained myocardium. TTC: triphenyltetrazolium chloride.

area, and one of the slices was divided into 3 layers (endo, mid, and epi) to separately analyze the histopathological profile of each by hematoxylin and eosin (H&E), Masson's trichrome, and TUNEL stainings for further histological evaluation. No significant infarction was observed in TTC staining (Figure 4); however, H&E and Masson's trichrome stainings presented interstitial fibrosis in foci surrounded by apparently healthy myocardial tissue, as indicated by the presence of cardiomyocytes (Figures 5(a) and 5(b)). Furthermore, TUNEL staining showed ongoing mild apoptosis (Figure 5(c)), which was comparable with previous report in hibernated myocardium [1]. Both fibrosis and apoptosis were more apparent towards subendocardium, implying more impaired perfusion of subendocardium in hibernating myocardium.

3. Discussion

In this study, characteristic features of hibernated myocardium were successfully depicted using multiimaging modalities. Formative mechanism of hibernated myocardium is presumed as a complex adjustment to repetitive ischemia-reperfusion [2]. Although this is supported by changing patterns of flow-function relationship, no evidence of ongoing ischemia has been shown by in vivo imaging. Thus, our results further confirm the "adjustment to repetitive ischemia-reperfusion" hypothesis. Myocardial edema without delayed enhancement in cardiac MR suggests ischemia without irreversible change and can be regarded as a part of the process of adapting to chronically restricted blood flow over time. Decreased but maintained CS and RS in strain analysis can also be interpreted as an ischemic state of myocardium with preserved viability [3]. The above observation was further supported by the presence of no apparent infarction in TTC staining together with mild ongoing apoptosis as well as low-extent fibrosis.

3.1. Limitation. Due to the rather rapid progress of total occlusion when compared to humans, the ischemic response might be intensified in this model which led to the characteristic MR image. If we had performed resting perfusion with cardiac MR, it could have illustrated the reduction in flow.

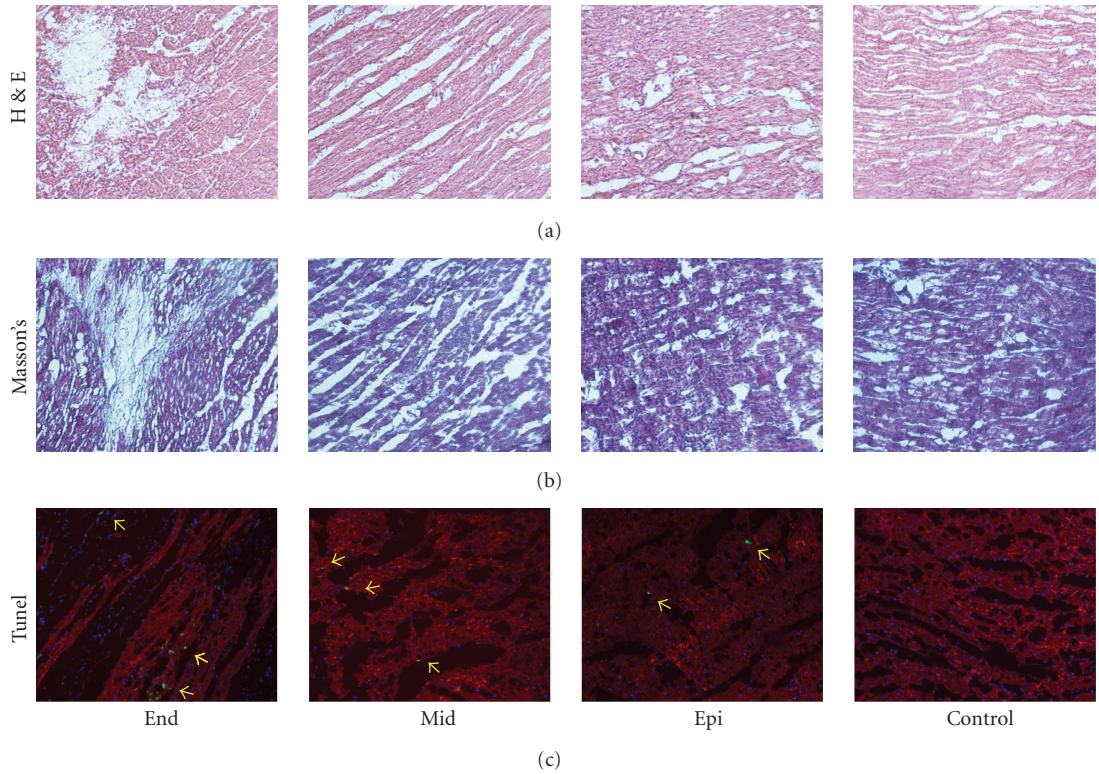


Figure 5: (a, b): General histopathology as assessed by H&E (upper) reveals cardiac lesion. Further characterization by Masson's trichrome (middle) staining shows interstitial fibrosis, which is more severe towards the subendocardium. (c) TUNEL staining for apoptosis analysis of myocardial tissue sections. TUNEL positive nuclei are stained with FITC (green; arrows). Cardiomyocytes were identified by α actinin immunostaining (red). Nuclei were stained with DAPI (blue). Percentages of TUNEL positive nuclei were 0.40%, 0.26%, 0.12%, and 0.03% for endo, mid, epi, and control endo, respectively. H&E: hematoxylin and eosin, FITC: fluorescein isothiocyanate, DAPI: 4'-6'-diamidino-2-phenylindole.

4. Conclusion

We believe that this study is the first to show characteristic features of concurrent multiple images from an identical animal that brought out development of ischemia in chronic obstructive coronary disease. Despite a case report from only one animal, this report gives us a comprehensive understanding in images of chronic ischemia, and at the same time, provides great insight into understanding the mechanism of ischemic cardiomyopathy.

Acknowledgment

This paper was supported by Grants from the National Institutes of Health (1P20HL100396 and 5R01HL083156).

References

[1] C. Chen, L. Ma, D. R. Linfert et al., "Myocardial cell death and apoptosis in hibernating myocardium," *Journal of the American College of Cardiology*, vol. 30, no. 5, pp. 1407–1412, 1997.

[2] G. Heusch, R. Schulz, and S. H. Rahimtoola, "Myocardial hibernation: a delicate balance," *American Journal of Physiology*, vol. 288, no. 3, pp. H984–H999, 2005.

[3] M. Becker, A. Lenzen, C. Ocklenburg et al., "Myocardial deformation imaging based on ultrasonic pixel tracking to identify reversible myocardial dysfunction," *Journal of the American College of Cardiology*, vol. 51, no. 15, pp. 1473–1481, 2008.