# Prediction of mitral regurgitation resolution after coronary bypass graft surgery and cardiac resynchronization therapy by late gadolinium enhancement magnetic resonance imaging: a case report

## Mai Azuma<sup>1†</sup>, Shingo Kato<sup>2</sup>\*<sup>†</sup>, Kazuki Fukui<sup>2</sup>, and Kouichi Tamura<sup>3</sup>

<sup>1</sup>Department of Cardiology, Hodogaya Central Hospital, 43-1 Kamadaicho, Hodogaya, Yokohama, Kanagawa 240-8585, Japan; <sup>2</sup>Department of Cardiology, Kanagawa Cardiovascular and Respiratory Center, 6-16-1 Tomiokahigashi, Kanazawa, Yokohama, Kanagawa 236-0051, Japan; and <sup>3</sup>Department of Medical Science and Cardiorenal Medicine, Yokohama City University, 3-9 Fukuura, Kanazawa, Yokohama, Kanagawa 236-0004, Japan

Received 17 March 2018; accepted 20 October 2018; online publish-ahead-of-print 26 November 2018

Background	Appropriate surgical management of moderate functional mitral regurgitation (MR) at the time of coronary artery bypass graft (CABG) surgery remains controversial. A recent study demonstrated no survival benefit from adding mitral repair to CABG for patients with moderate functional MR. Preoperative prediction of reverse remodelling is crucial in making the decision to add mitral valve repair to CABG. Late gadolinium-enhanced magnetic resonance imaging (LGE MRI) offers a reference method to assess myocardial viability.
Case summary	A 60-year-old man with ischaemic cardiomyopathy was admitted to our hospital with exacerbation of heart failure symptoms. Left ventricular (LV) dilatation, severe impairment of LV systolic function, and moderate MR due to tethering were noted on transthoracic echocardiography. The mitral regurgitant jet was central. Intravenous administration of furosemide and human atrial natriuretic peptide was initiated. The patient experienced an episode of ventricular tachycardia, and coronary angiography demonstrated triple-vessel disease. On LGE MRI, subendocardial infarction with a transmural extent of 25–50% was revealed in the inferior, posterior, and lateral walls. Findings from LGE MRI suggested that myocardial viability had been preserved. After performing CABG and cardiac resynchronization therapy, LV volume was substantially decreased and moderate MR was significantly improved without surgical mitral repair. On speckle tracking echocardiography before surgery, a significant difference in the times to peak radial strain between the lateral wall (462 ms) and inferior wall (17 ms) indicated the presence of LV dyssynchrony. Left ventricular dyssynchrony was substantially improved after CABG and cardiac resynchronization therapy defibrillator implantation.
Discussion	In patients with ischaemic cardiomyopathy and moderate functional MR, acquisition of LGE MRI of the LV should be considered to evaluate the viability of LV myocardium. Findings from LGE MRI of the LV can potentially influence the surgical strategy. In patients with preserved viability of LV myocardium, functional MR could be improved after CABG without any surgical repair.

\* Corresponding author. Tel: +81 45 701 9581, Fax: +81 45 786 4770, Email: shingo.m12226@gmail.com

<sup>&</sup>lt;sup>†</sup> These authors contributed equally to this work.

Handling Editor: Matteo Cameli

Peer-reviewers: Georg Goliasch and Noémi Nyolczas

Compliance Editors: Anastasia Vamvakidou and Mark Philip Cassar

Supplementary Material Editors: Peregrine Green and Peysh Patel

<sup>©</sup> The Author(s) 2018. Published by Oxford University Press on behalf of the European Society of Cardiology.

This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (http://creativecommons.org/licenses/by-nc/4.0/), which permits non-commercial re-use, distribution, and reproduction in any medium, provided the original work is properly cited. For commercial re-use, please contact journals.permissions@oup.com

Keywords

Functional mitral regurgitation • Left ventricular remodelling • Late gadolinium enhancement • Viability assessment • Case report

#### Learning point

• Preoperative viability assessment using late gadolinium-enhanced magnetic resonance imaging might be useful for predicting postoperative reverse remodelling and improvement of ischaemic mitral regurgitation without surgical repair.

#### Introduction

The appropriate surgical management of moderate functional mitral regurgitation (MR) at the time of coronary artery bypass graft (CABG) surgery remains controversial. A recent randomized controlled trial identified no benefit from adding mitral repair to CABG surgery for patients with moderate functional MR.<sup>1</sup> The 2017 American Heart Association/American College of Cardiology guideline declared the usefulness of mitral repair as uncertain for patients with chronic, moderate, and functional MR undergoing CABG surgery (class of recommendation: IIb).<sup>2</sup> Late gadolinium-enhanced magnetic resonance imaging (LGE MRI) is an established method for assessing myocardial viability.<sup>3</sup> Compared with single photon emission computed tomography (SPECT), LGE MRI offers superior prediction of left ventricular (LV) reverse remodelling in patients with ischaemic cardiomyopathy after CABG.<sup>4</sup> In addition, LGE MRI is a useful modality for deciding the LV lead position and predicting LV reverse remodelling after cardiac resynchronization therapy (CRT).<sup>5</sup>

## Timeline

#### **Case summary**

A 60-year-old man with ischaemic cardiomyopathy, diabetes, hypercholesterolaemia, and chronic obstructive pulmonary disease was admitted to our hospital due to exacerbation of heart failure symptoms in July 2015. He was experiencing shortness of breath at rest [New York Heart Association (NYHA) Grade 4], but had no chest pain before admission. Upon arrival, respiratory rate was estimated at 26 breaths/min, peripheral oxygen saturation was 93% (room air), blood pressure was 100/54 mmHg, and heart rate was regular and 104 b.p.m. Physical examination revealed distended jugular veins and hepatojugular reflux. Thoracic auscultation showed pan-systolic murmur at apex (Levine III/VI), reduced breath sounds at the lung bases, an audible heart sound III, and lower thigh oedema. An electrocardiogram showed pathological Q waves in leads III and aVF, and complete left bundle branch block (QRS duration, 150 ms). Blood tests revealed that brain natriuretic peptide (BNP) was elevated to 1076 ng/mL (0-18.4 pg/mL), renal function was normal (creatinine, 0.85 mg/dL), and troponin T was not positive (<0.01 pg/dL). Chest X-ray showed cardiomegaly (cardiothoracic ratio 56%), mild congestion, and bilateral

2005	Angina pectoris, stent implantation for right coronary artery (RCA) mid-90% stenosis.
2006	Stent implantation for left anterior descending artery (LAD) proximal 75% stenosis.
2007	Stent implantation for RCA proximal 75% stenosis, RCA mid-in-stent 75% restenosis: plain old balloon angioplasty (POBA).
2012	RCA mid-in-stent 99% restenosis, POBA.
20 August 2015	Admission due to exacerbation of heart failure. Intravenous medical treatment initiated (human atrial natriuretic peptide and
	furosemide). Preoperative echocardiography was performed [severe left ventricular (LV) dysfunction, dyssynchrony, and moderate mitral regurgitation (MR)].
9 September 2015	Cardiac catheterization was performed.
	LAD proximal stent distal 75% stenosis, left circumflex artery proximal 90% stenosis, RCA mid-in-stent occluded, non-sus- tained ventricular tachyarrhythmia confirmed.
	On late gadolinium-enhanced magnetic resonance imaging, subendocardial infarction was revealed in the inferior and postero- lateral walls, and viability was preserved in the infarcted myocardial territory.
	Coronary artery bypass graft and cardiac resynchronization therapy (CRT) planned.
3 December 2015	Coronary artery bypass graft (LITA-LAD and Ao-SVG-OM) and implantation of epicardial LV lead for CRT performed by car- diovascular surgeons.
18 December 2015	Implantation of cardiac resynchronization therapy defibrillator.
29 December 2015	Discharge from hospital.
16 January 2017	Postoperative echocardiography performed (MR resolved).



**Figure I** Coronary angiogram shows significant coronary artery stenosis in the right coronary artery, left anterior descending artery, and left circumflex artery (red arrows).

pleural effusions. Transthoracic echocardiogram showed LV dilatation (LV diastolic diameter/LV systolic diameter 64.8/59.9 mm, LV enddiastolic volume 214 mL), severe impairment of LV systolic function [LV ejection fraction (EF), 16.4%], abnormal (akinetic) inferior wall motion, dyssynchrony, and moderate MR (right ventricle 23.8 mL, effective regurgitant orifice 0.16 cm<sup>2</sup>) due to tethering (tenting height 9.5 mm). The mitral regurgitant jet was central.

Both anterior and posterior leaflets of the mitral valve were tethered. As medical therapy for this patient, we administered furosemide and human atrial natriuretic peptide intravenously, along with oral medications comprising aspirin at 100 mg/day, carvedilol at 10 mg/day, losartan at 25 mg/day, furosemide at 20 mg/day, spironolactone at 25 mg/day, and digoxin at 0.125 mg/day. The digoxin was included as part of heart failure treatment. The patient had an episode of non-sustained ventricular tachycardia. After improvement of heart failure symptoms with pharmacotherapy, coronary angiography was performed. Multivessel coronary artery stenoses were demonstrated (in-stent occlusion was noted in the middle part of the right coronary artery and collaterals from left coronary arteries. In the left anterior descending artery, 75% stenosis was noted in the proximal stent edge, and 90% stenosis was identified in the proximal portion of the left circumflex artery) (Figure 1). Cardiac MRI was performed to evaluate myocardial viability. On LGE MRI, subendocardial infarction (transmural extent 25-50%) was revealed in the inferior and posterolateral walls (Figure 2). Based on findings from MRI, we assumed that viability was preserved in the infarcted myocardial territory. Prior to surgery, we had already provided guideline-directed medical therapy for this patient. No additional pharmacotherapy was performed after CABG and cardiac resynchronization therapy defibrillator (CRT-D) implantation. We planned CABG and CRT-D implantation for this patient. We did not plan to perform surgical mitral repair at the time of CABG, because we expected the MR would be resolved by LV reverse remodelling after surgery. Coronary artery bypass graft surgery and implantation of the LV lead were performed by the

cardiac surgeon. Fifteen days after CABG, CRT-D implantation was performed by a cardiologist (*Figure 3*). Follow-up echocardiographic examination was performed 1 year after surgery. We compared echocardiographic findings before and after CABG and CRT-D implantation. Figure 4 shows comparison of MR grade and degree of dyssynchrony (time to peak radial strain as evaluated by speckle tracking echocardiography) between pre- and post-CABG and CRT-D implantation. Mitral regurgitation disappeared after surgery (Figure 4A and B). Tethering of leaflets of the mitral valve was substantially improved, and the severity of MR was trivial. Time to peak radial strain in the lateral wall improved from 462 ms to 336 ms before and after intervention (Figure 4C and D). Left ventricular enddiastolic volume decreased from 214 mL to 164 mL and LVEF improved from 16.4% to 20.7%. On speckle tracking echocardiography before surgery, a significant difference in times to peak radial strain between the lateral wall (462 ms) and inferior wall (17 ms) indicated the presence of LV dyssynchrony. Time to peak radial strain was substantially improved after surgery. Tricuspid regurgitation decreased from moderate to trivial. One year after surgery, dyspnoea was improved (NYHA Grade 2). In addition, follow-up BNP levels have been approximately 200 ng/mL, and the patient has not required any hospitalizations for heart failure.

#### Discussion

Our case report suggested the possible utility of LGE MRI in deciding the surgical strategy for patients with ischaemic cardiomyopathy and moderate functional MR. In this patient, MR resolved without any surgical MR repair. Left ventricular reverse remodelling by revascularization and CRT might improve the geometry of the mitral valve and the synchrony of papillary muscles, leading to improvement of mitral valve function. In this regard, assessing myocardial viability and predicting the likelihood of LV reverse remodelling before cardiac surgery would be important. In a previous randomized controlled trial comparing CABG plus optimal medical therapy vs. medical therapy



Figure 2 Late gadolinium-enhanced magnetic resonance imaging shows subendocardial infarction in the inferior wall and posterior wall (red arrows).



**Figure 3** Cardiac resynchronization therapy defibrillator was implanted in this patient.

alone for patients with LVEF  $\leq$ 35% and coronary artery disease amenable to CABG [the Surgical Treatment for Ischaemic Heart Failure (STICH) trial], CABG plus medical therapy did not significantly reduce the rate of all-cause mortality in comparison to medical therapy alone.<sup>6</sup> The STICH Extension Study (STICHES),<sup>7</sup> a long-term follow-up (median of 9.8 years) study of STICH cohort, demonstrated the lower rate of all-cause mortality in the CABG group compared with the medical therapy group. Based on these results, combination of CABG and medical therapy would be more beneficial than medical therapy alone for patients with coronary artery disease and LVEF  $\leq$ 35%. Late gadolinium-enhanced magnetic resonance imaging offers a reference standard to assess myocardial viability (>75% LGE has a 100% negative predictive value for functional recovery after revascularization).<sup>3</sup> However, the utility of viability assessment before the CABG is controversial. For example, in the Heart Failure Revascularisation Trial (HEART), viability assessment by imaging modality (e.g. stress echocardiography, SPECT, angiocardiography, and positron emission tomography) did not show the clinical merit to select patients for revascularization (percutaneous coronary intervention or CABG).<sup>8</sup> Further study is required to assess the utility of viability assessment using LGE MRI before CABG. Regarding the treatment for functional MR, a recent study showed that surgical mitral repair at the time of CABG did not improve mortality.<sup>1</sup> Possible reasons for this result include differences in expertise and own preferences amongst operators and longer cardiopulmonary bypass time associated with worse clinical outcomes. From this point of view, debate continues regarding surgical mitral repair for functional MR. In this patient, the area of myocardial infarction was not extensive on LGE MRI. We, therefore, thought that LV reverse remodelling would occur and surgical mitral repair would not be necessary. In addition, LGE MRI is useful to decide LV lead position and predict responders to CRT. Left ventricular lead positions over scar were associated with poorer CRT response, higher risk of cardiovascular death, heart failure hospitalizations, and sudden cardiac death.<sup>9</sup> Our patient showed subendocardial infarction with transmural extent of 25–50% on LGE MRI in the lateral wall. This finding suggested the high probability of LV reverse remodelling after surgery. Beyond LGE, other MRI parameters might play an important role for CRT-D implantation. For example, contrast-enhanced magnetic resonance venography can visualize the coronary vein branch used to select optimal LV lead position.<sup>10</sup> Myocardial extracellular volume fraction as quantified by the T1 mapping technique can predict LV reverse remodelling and clinical outcome in non-ischaemic cardiomyopathy.<sup>11</sup> In addition, improvement of papillary muscle dyssynchrony might be an important mechanism in the disappearance of functional MR in this patient. A previous study using two-dimensional speckle tracking echocardiography demonstrated that CRT can acutely reduce MR in patients with dyssynchrony involving the papillary muscles. Interruption of CRT at 6 months of follow-up resulted in acute loss of resynchronization with recurrence of MR.<sup>12</sup> In our case,



**Figure 4** Comparison of degree of mitral regurgitation (A, B) and dyssynchrony (C, D) between pre-operation and post-operation. Mitral regurgitation resolved after the surgery (A, B). Time to peak radial strain was improved after surgery (ranging from 0 ms to 480 ms before surgery, 336 ms after surgery).

the significant difference in times to peak radial strain between the lateral wall (462 ms) and inferior wall (17 ms) suggested the presence of papillary muscle dyssynchrony before surgery.

## Conclusions

С

In conclusion, our case report suggested the possible utility of preoperative viability assessment by LGE MRI for predicting postoperative reverse remodelling and improvement of functional MR without surgical repair.

In addition, LGE MRI is useful to decide LV lead position and predict responders to CRT. By evaluating both of them, we thought that it will lead to further improvement of functional MR.

## Supplementary material

Supplementary material is available at *European Heart Journal - Case* Reports online.

#### Acknowledgements

The authors are grateful to Naka Saito, MT for his efforts in data collection.

#### Funding

S.K. receives research grant from MSD Life Science Foundation and Public Interest Incorporated Foundation; research grant from Japanese Circulation Society.

**Slide sets:** A fully edited slide set detailing this case and suitable for local presentation is available online as Supplementary data.

**Consent:** The author/s confirm that written consent for submission and publication of this case report including image(s) and associated text has been obtained from the patient in line with COPE guidance.

Conflict of interest: none declared.

#### References

- Michler RE, Smith PK, Parides MK, Ailawadi G, Thourani V, Moskowitz AJ, Acker MA, Hung JW, Chang HL, Perrault LP, Gillinov AM, Argenziano M, Bagiella E, Overbey JR, Moquete EG, Gupta LN, Miller MA, Taddei-Peters WC, Jeffries N, Weisel RD, Rose EA, Gammie JS, DeRose JJ, Puskas JD, Dagenais F, Burks SG, El-Hamamsy I, Milano CA, Atluri P, Voisine P, O'Gara PT, Gelijns AC. Two-year outcomes of surgical treatment of moderate ischemic mitral regurgitation. N Engl J Med 2016;**374**:1932–1941.
- Nishimura RA, Otto CM, Bonow RO, Carabello BA, Erwin JP, Fleisher LA, Jneid H, Mack MJ, McLeod CJ, O'Gara PT, Rigolin VH, Sundt TM, Thompson A. 2017 AHA/ACC focused update of the 2014 AHA/ACC guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol 2017;**70**:252–289.

- Kim RJ, Wu E, Rafael A, Chen EL, Parker MA, Simonetti O, Klocke FJ, Bonow RO, Judd RM. The use of contrast-enhanced magnetic resonance imaging to identify reversible myocardial dysfunction. N Engl J Med 2000;343: 1445–1453.
- Skala T, Hutyra M, Vaclavik J, Kaminek M, Horak D, Novotny J, Zapletalova J, Lukl J, Marek D, Taborsky M. Prediction of long-term reverse left ventricular remodeling after revascularization or medical treatment in patients with ischemic cardiomyopathy: a comparative study between SPECT and MRI. Int J Cardiovasc Imaging 2011;27:343–353.
- Bilchick KC, Kuruvilla S, Hamirani YS, Ramachandran R, Clarke SA, Parker KM, Stukenborg GJ, Mason P, Ferguson JD, Moorman JR, Malhotra R, Mangrum JM, Darby AE, Dimarco J, Holmes JW, Salerno M, Kramer CM, Epstein FH. Impact of mechanical activation, scar, and electrical timing on cardiac resynchronization therapy response and clinical outcomes. J Am Coll Cardiol 2014;63:1657–1666.
- Velazquez EJ, Lee KL, Deja MA, Jain A, Sopko G, Marchenko A, Ali IS, Pohost G, Gradinac S, Abraham WT, Yii M, Prabhakaran D, Szwed H, Ferrazzi P, Petrie MC, O'Connor CM, Panchavinnin P, She L, Bonow RO, Rankin GR, Jones RH, Rouleau JL. Coronary-artery bypass surgery in patients with left ventricular dysfunction. N Engl J Med 2011;364:1607–1616.
- 7. Velazquez EJ, Lee KL, Jones RH, Al-Khalidi HR, Hill JA, Panza JA, Michler RE, Bonow RO, Doenst T, Petrie MC, Oh JK, She L, Moore VL, Desvigne-Nickens P,

Sopko G, Rouleau JL. Coronary-artery bypass surgery in patients with ischemic cardiomyopathy. N Engl J Med 2016;**374**:1511–1520.

- Cleland JG, Calvert M, Freemantle N, Arrow Y, Ball SG, Bonser RS, Chattopadhyay S, Norell MS, Pennell DJ, Senior R. The Heart Failure Revascularisation Trial (HEART). *Eur J Heart Fail* 2011;**13**:227–233.
- Leyva F, Taylor RJ, Foley PW, Umar F, Mulligan LJ, Patel K, Stegemann B, Haddad T, Smith RE, Prasad SK. Left ventricular midwall fibrosis as a predictor of mortality and morbidity after cardiac resynchronization therapy in patients with nonischemic cardiomyopathy. J Am Coll Cardiol 2012;60:1659–1667.
- Lam A, Mora-Vieira LF, Hoskins M, Lloyd M, Oshinski JN. Performance of 3D, navigator echo-gated, contrast-enhanced, magnetic resonance coronary vein imaging in patients undergoing CRT. *J Interv Card Electrophysiol* 2014;41:155–160.
- Puntmann VO, Carr-White G, Jabbour A, Yu CY, Gebker R, Kelle S, Hinojar R, Doltra A, Varma N, Child N, Rogers T, Suna G, Arroyo Ucar E, Goodman B, Khan S, Dabir D, Herrmann E, Zeiher AM, Nagel E. T1-mapping and outcome in nonischemic cardiomyopathy: all-cause mortality and heart failure. *JACC Cardiovasc Imaging* 2016;**9**:40–50.
- Ypenburg C, Lancellotti P, Tops LF, Bleeker GB, Holman ER, Pierard LA, Schalij MJ, Bax JJ. Acute effects of initiation and withdrawal of cardiac resynchronization therapy on papillary muscle dyssynchrony and mitral regurgitation. J Am Coll Cardiol 2007;50:2071–2077.