Left ventricular reverse remodeling after successful subannular mitral valve repair in end-stage heart failure: a case report

Jonas Pausch *, Tatiana Sequeira Gross, Hermann Reichenspurner, and Evaldas Girdauskas

Department of Cardiovascular Surgery, University Heart and Vascular Center Hamburg, Martinistraße 52, D-20246 Hamburg, Germany

Received 3 September 2019; first decision 2 October 2019; accepted 24 March 2020; online publish-ahead-of-print 27 April 2020

Background
Due to ongoing left ventricular (LV) remodeling and consecutive geometric displacement of both papillary muscles, end-stage heart failure is frequently associated with relevant functional mitral regurgitation (FMR) Type IIIb. Treatment strategies of FMR and their prognostic impact are still controversial.

Case summary
We present a case of an 80-year-old patient who suffered from recurrent symptoms of congestive heart failure due to dilated cardiomyopathy and concomitant severe FMR. To specifically address severe tethering of both mitral leaflets heart team decision was to perform minimally invasive mitral valve repair (MVR) including a subannular LV remodeling procedure, instead of an interventional edge-to-edge repair (MitraClip® procedure). In addition to mitral valve ring annuloplasty, standardized relocation of both papillary muscles was performed successfully, leading to a complete resolution of mitral leaflet tethering. There were no procedural complications and the patient was discharged with an excellent functional result without residual mitral regurgitation. Furthermore, after 12 and 24 months, he reported an increase of his functional exercise capacity and a remarkable reverse LV remodeling could be demonstrated.

Discussion
Novel subannular repair techniques, especially the relocation of both papillary muscles, specifically address mitral leaflet tethering in FMR and have an obvious potential to improve long-term competence of MVR. Therefore, they could be considered as a viable therapeutic option even in elderly patients presenting with end-stage cardiomyopathy and severe leaflet tenting.

Keywords
Functional mitral regurgitation • Heart failure • Reverse left ventricular remodelling • Minimally invasive mitral valve repair • Relocation of papillary muscles • Subannular repair • Case report

Learning points
• Geometric displacement of both papillary muscles due to left ventricular remodeling is a common phenomenon in ischaemic and non-ischaemic dilated cardiomyopathy that is associated with relevant functional mitral regurgitation (FMR).
• Relocation of both papillary muscles in addition to ring annuloplasty specifically addresses mitral leaflet tethering and may represent a viable treatment option in patients presenting with end-stage cardiomyopathy and severe FMR.
• In addition to patient characteristics and surgical risk, the pathogenesis and predominant mechanism of FMR should be evaluated by the heart team to define the best available treatment strategy.

* Corresponding author. Tel: +49 40 7410 50886, Email: j.pausch@uke.de
Handling Editor: Erik Holy
Peer-reviewers: Andre Dias and Domitilla Russo
Compliance Editor: Stefan Simovic
Supplementary Material Editor: Peysh A. Patel
© The Author(s) 2020. 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
Introduction

The optimal treatment of functional mitral regurgitation (FMR) with restricted leaflet motion during systole (Type IIIb) in heart failure patients is still controversial. Apart from guideline-directed optimal medical therapy (OMT), cardiac resynchronization therapy (CRT), and interventional mitral valve replacement, a durable mitral valve repair (MVR) has the potential to improve cardiac reverse remodeling and prognosis. In contrast to an isolated ring annuloplasty, which is associated with a high rate of late recurrent FMR, simultaneous sub-annular repair maneuvers have been shown to significantly improve long-term competence after MVR.

Timeline

| Date       | Event Description                                                                 |
|------------|-----------------------------------------------------------------------------------|
| October 2012 | First admission due to the symptoms of congestive heart failure [New York Heart Association (NYHA) Class II–III]. Exclusion of acute coronary syndrome by coronary angiogram and diagnoses of non-ischaemic dilated cardiomyopathy with consecutive mild to moderate functional mitral regurgitation (FMR) Type IIIb. |
| May 2016    | Second admission due to acute decompensated systolic heart failure (NYHA Class III) and moderate FMR Type IIIb. Exclusion of coronary artery disease by coronary angiogram. |
| April 2017  | Third admission due to acute decompensated heart failure (NYHA Class IV) and severe FMR Type IIIb. |
| October 2017 | Fourth admission due to acute decompensated heart failure (NYHA Class IV) and severe FMR Type IIIb despite OMT. Minimally invasive mitral valve repair including relocation of both papillary muscles combined with ring-annuloplasty. |
| April 2018  | 6-month post-operative follow-up. No signs of residual FMR. Improved functional exercise capacity (NYHA Class II). |
| October 2018 | 12-month post-operative follow-up. No residual FMR. Reverse left ventricular (LV) remodeling leading to improved systolic LV function as demonstrated by echocardiography and cardiac magnetic resonance. |
| October 2019 | 24-month post-operative follow-up. No residual FMR. Stable signs of reverse LV remodeling. |

Case presentation

An 80-year-old male patient presented with recurrent symptoms of severe congestive heart failure, including shortness of breath [New York Heart Association (NYHA) Class IV], peripheral oedema, and pleural effusions due to non-ischaemic dilated cardiomyopathy (DCM). Routine admission laboratory testing revealed signs of chronic left ventricular (LV) volume overload (NT-pro BNP 5784 ng/L) and chronic renal failure (creatinine 1.4 mg/dL). Apart from mild anaemia (haemoglobin 10.8 g/dL) no further relevant abnormalities were present. In his past medical history, he was diagnosed with insulin-dependent diabetes mellitus Type II, hypertension, and permanent atrial fibrillation. The latter could be confirmed by electrocardiogram, whereas no further relevant abnormalities occurred. Despite OMT, including bisoprolol, spironolactone, and sacubitril/valsartan, transthoracic echocardiography (TTE) revealed severe LV dilatation and dysfunction [LV end-diastolic diameter (LVEDD) 65 mm; LV end-systolic diameter (LVESD) 53 mm; LV ejection fraction (LVEF) 25%], which was confirmed by cardiac magnetic resonance (CMR) imaging [LV end-diastolic volume (LVEDV) 247 mL; LV end-systolic volume (LVESV) 192 mL; LVEF 22%] (Figure 1A and B). Furthermore, geometric displacement of both papillary muscles resulted in significant mitral leaflet tethering (tenting-height 11 mm; tenting-area 2.5 cm²; PML angle 41°) leading to severe Type IIIb FMR (EROA 0.22 cm²) and dilatation of the left atrium (left atrial volume 128.35 mL) (Figure 2). Cardiac resynchronization therapy was not indicated due to the absence of left bundle branch block and an QRS duration below 130 ms. Due to the absence of relevant ventricular arrhythmia, preventative implantation of a defibrillator was dismissed in this case by case decision. Interdisciplinary heart-team decision was to perform minimally invasive MVR and simultaneous cryoablation for atrial fibrillation with an occlusion of the left atrial appendage. In contrast to an interventional edge-to-edge repair (MitraClip) and standard surgical or catheter-based annuloplasty, surgical relocation of both papillary muscles was performed to actively re-remodel the left ventricle and thereby to specifically address severe leaflet tethering (Figures 2C and 3). The procedure was performed using a minimally invasive 3D full-endoscopic surgical approach. In addition to conventional mitral valve (MV) annuloplasty using an 28 mm ETlogix ring (Edwards Lifesciences, Irvine, CA, USA) two pledged 3-0 polytetrafluorethylene sutures were placed through the trunks of both papillary muscles (Figure 4A) and subsequently passed through the posterior mitral annulus (Figure 4B) and the adjacent annuloplasty ring (Figure 4C). After filling the left ventricle with cold saline stepwise traction was applied on both sutures until leaflet tethering disappeared. To create a stable distance between the papillary muscles and the mitral annulus both sutures were tightly knotted on the annuloplasty ring, while keeping the traction (figure 4D). There were no procedural complications and the patient was discharged fully recovered, with OMT including bisoprolol (5 mg twice daily), spironolactone (25 mg once a day), sacubitril/valsartan (97/103 mg twice daily), and oral anticoagulation (phenprocoumon). Transthoracic echocardiography at discharge revealed an excellent functional result without any residual MR, despite persisting LV dysfunction (LVEF 26%; LVEDD 63 mm; LVESD 51 mm). At 12 months follow-up, the patient reported a significantly improved functional exercise capacity (NYHA Class II). Furthermore, NT-pro-BNP levels decreased significantly in comparison to the baseline values (i.e. 1963 ng/L vs. 5784 ng/L). Transthoracic echocardiography revealed an improved LV function (LVEF 41%), as combined with a significant LV reverse remodeling (LVEDD 49 mm), as well as a competent MV without residual...
FMR (tenting-height <5 mm; tenting-area <1.0 cm²; PML angle 12°) (Figure 2D–F). Cardiac magnetic resonance confirmed a significant LV re-remodeling with an improved systolic LV function (LVEDV 133 mL; LVESV 87 mL; LVEF 35%) (Figure 1C and D). Twenty-four months after the surgery constant reverse LV remodeling could be demonstrated by TTE (LVEF 46%; LVEDD 51 mm; LVESD 42 mm) and CMR (LVEF 41%; LVEDV 167 mL; LVESV 99 mL).

Discussion

In contrast to degenerative mitral valve regurgitation, the most appropriate treatment for FMR Type IIIb remains controversial.1 Contradictory prognostic effects of interventional edge-to-edge repair (MitraClip®) in heart failure patients with severe FMR, including Type I and Type IIIb have been published and need further evaluation.9,10 Due to ongoing ventricular remodeling isolated annuloplasty is frequently associated with recurrent MR and failed to reduce mortality rates in comparison to OMT.4 To avoid the increased morbidity and mortality rates after mitral valve replacement, as well as prostheses-related complications, novel subannular repair techniques have been developed.11 By specifically addressing leaflet tethering, which represents the key role in the pathogenesis of FMR Type IIIb, supplemental relocation of both papillary muscles provides improved long-term durability as compared to isolated annuloplasty.6,7 Furthermore, it has the potential to promote reverse remodeling, conceivably resulting in a prognostic benefit.3,6,7

Conclusion

Standardized realignment of both papillary muscles combined with annuloplasty via a minimally invasive approach resulted in an excellent in-hospital and 2-year outcome in this 80-year-old patient with severe DCM and Type IIIb FMR. In addition to OMT and CRT, a durable MVR significantly reduces chronic LV volume overload, leading to clinical improvement and potential LV reverse remodeling. Therefore, in addition to baseline characteristics and surgical risk, the pathogenesis and predominant mechanism of FMR, including the severity of mitral leaflet tenting, should be considered by the heart team to provide the best possible treatment strategy.
Since his graduation at the University of Würzburg in 2015, Dr Jonas Pausch has been doing his clinical fellowship at the Department of Cardiovascular Surgery at the University Heart and Vascular Center Hamburg. His scientific interest includes advanced surgical treatment options for functional mitral regurgitation as well as mechanical circulatory support in chronic heart failure patients.

**Figure 2** Comparison of pre- and post-operative transthoracic echocardiography. Apical three (A) and four (B) chamber view: colour Doppler flow reveals severe functional mitral regurgitation Type IIIb (EROA 0.22 cm²). (C) Parasternal long-axis few: severe tethering of both mitral leaflets (tenting-height 11 mm; tenting-area 2.5 cm²; PML angle 41°; orange: PML; green: AML; blue: annular plane). Post-operative apical three (D) and four (E) chamber view: colour Doppler flow shows no residual functional mitral regurgitation. (F) Post-operative parasternal long-axis few: no residual tethering of mitral leaflets (orange: PML; green: AML; blue: annular plane).

**Figure 3** Standardized relocation of both papillary muscles using two pledged 3-0 polytetrafluoroethylene sutures in addition to conventional mitral valve annuloplasty to completely resolve leaflet tethering.
Supplementary material

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

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

1. Trochu JN, Dillon R, Gustafsson F, Mitchell SA, Mitrovic V, Alfieri O. Mitral regurgitation—unmet need for improved management strategies. Int J Cardiol Heart Vasc 2014;5:26–41.
2. Nishimura RA, Otto CM, Bonow RO, Carabello BA, Erwin JP, Flesher 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. Circulation 2017;135:e1159–e1195.
3. De Bonis M, Lapenna E, Verzini A, La Canna G, Grimaldi A, Torracca L, Maisano F, Alfieri O. Recurrence of mitral regurgitation parallels the absence of left ventricular reverse remodeling after mitral repair in advanced dilated cardiomyopathy. Ann Thorac Surg 2008;85:932–939.
4. Goldstein D, Moskowitz AJ, Gelijns AC, Alawadi G, Parides MK, Perrault LP, Hung JW, Voisine P, Dagenais F, Gillinov AM, Thourani V, Argenziano M, Gammie JS, Mack M, Demers P, Atluri P, Rose EA, O’Sullivan K, Williams DL, Bagella E, Michler RE, Weisel RD, Miller MA, Geller NL, Taddei-Peters WC, Smith PK, Moquette E, Overbey JR, Kron IL, O’Gara PT, Acker MA. Two-year outcomes of surgical treatment of severe ischemic mitral regurgitation. N Engl J Med 2016;374:344–353.
5. Girdauskas E, Pausch J, Harmel E, Gross T, Detter C, Sinning C, Kubitz J, Reichenspurner H. Minimally invasive mitral valve repair for functional mitral regurgitation. Eur J Cardiothorac Surg 2019;55:17–25.
6. Harmel E, Pausch J, Gross T, Petersen J, Sinning C, Kubitz J, Reichenspurner H. Girdauskas E. Standardized subannular repair improves outcomes in type IIB functional mitral regurgitation. Ann Thorac Surg 2019;108:1783–1792.
7. Pausch J, Harmel E, Sinning C, Reichenspurner H, Girdauskas E. Standardized subannular repair for type IIB functional mitral regurgitation in a minimally invasive mitral valve surgery setting. Eur J Cardiothorac Surg 2019;56:968–975.
8. Beigel R, Wunderlich NC, Kar S, Siegel RJ. The evolution of percutaneous mitral valve repair therapy: lessons and implications for patient selection. J Am Coll Cardiol 2014;64:2688–2700.
9. Stone GW, Lindenfeld J, Abrahm WT, Kar S, Lim DS, Mishell JM, Whisenant B, Grayburn PA, Rinaldi M, Kapadia SR, Rajagopal V, Sarembock IJ, Brieke A, Marx SO, Cohen DJ, Weissman NJ, Mack MJ; for the COAPT Investigators. Transcatheter mitral-valve repair in patients with heart failure. N Engl J Med 2018;379:2307–2318.
10. Obadia J-F, Messika-Zeitoun D, Leurent G, Iung B, Bonnet G, Pirio N, Lefèvre T, Piot C, Rouleau F, Carré D, Nejari M, Ollmann P, Leclercq F, Saint Etienne C, Teger E, Leroux L, Karam N, Michel N, Giral G, Donal E, Trochu J-N, Cormier B, Armoiry X, Coutie F, Masscott-Boulch D, Barel C, Samson G, Guepin P, Vahanian A, Mewton N; for the MITRA-FR Investigators. Percutaneous repair or medical treatment for secondary mitral regurgitation. N Engl J Med 2016;375:2297–2306.
11. Harmel EK, Reichenspurner H, Girdauskas E. Subannular reconstruction in secondary mitral regurgitation: a meta-analysis. Heart 2018;104:1783–1790.