

A Nationwide Survey of Surgical Treatment for Severe Ischemic Mitral Regurgitation

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Objective: Mitral subvalvular procedures in addition to restrictive annuloplasty are promising for ischemic mitral regurgitation (IMR). However, the prevalence and efficacy of specific subvalvular repair in severe IMR have not been elucidated. This is the first nationwide survey regarding surgeons' attitudes toward IMR in Japan.

Methods: A questionnaire was sent to 543 institutions. From 2015 to 2019, numbers of elective first-time mitral valve replacement (MVR) with/without complete chordal preservation (CCP)/papillary muscle approximation (PMA) and mitral valvuloplasty (MVP) with/without papillary muscle relocation (PMR)/PMA in patients with severe IMR were collected. Concomitant procedures for coronary artery, tricuspid valve, and arrhythmia could be included but left ventricular reconstruction was excluded.

Results: Completed questionnaires were received from 286 institutions (52.7%). The majority (90%) had less than 20 cases within 5 years. The number of MVP (1413, 61.5%) surpassed MVR (886, 38.5%). CCP was performed in half of MVR (50.0%), while PMA was included in only 1.9% of MVR. PMA and PMR were also performed infrequently, in only 7.7% and 10.9% of MVP, respectively.

Conclusion: Japanese surgeons aggressively perform MVP for severe IMR. Subvalvular repair was also aggressively performed in addition to MVR, but not to MVP. A multi-center registry study is in progress.

Keywords: ischemic mitral regurgitation, mitral valvuloplasty, papillary muscle relocation, papillary muscle approximation, nationwide survey

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Introduction

There is still controversy regarding the most appropriate surgical treatment for secondary mitral regurgitation (SMR) represented by ischemic mitral regurgitation (IMR). Recent randomized clinical trial treating severe IMR from the Cardiothoracic Surgical Trials Network showed no significant difference between mitral valve replacement (MVR) and mitral valvuloplasty (MVP) in terms of left ventricular reverse remodeling or survival at 2 years, but the incidence of recurrence of mitral regurgitation (MR) was higher in MVP compared with MVR.¹⁾ The major concern with this study was the cause of frequent recurrence of MR after MVP, which was performed by annuloplasty alone in the majority of cases (additional subvalvular procedures in 11.9%), causing many adverse events related to heart failure and readmission. The underlying mechanism of IMR is characterized by displacement of the posterior papillary muscle associated with left ventricular dilatation due to myocardial ischemia causing tethering of the posterior leaflet.²⁾ Therefore, additional relocation of the posterior papillary muscle in addition to undersized annuloplasty has emerged as a promising novel surgical strategy for IMR, and favorable late outcomes have been reported.^{3,4)} Indeed, a meta-analysis of seven nonrandomized studies comparing ring annuloplasty with or without subvalvular repair for moderate-to-severe SMR showed efficacy of subvalvular repair in terms of mid-term mortality, recurrence of MR, reverse remodeling of the left ventricle, and NYHA class.⁵⁾

Nonetheless, subvalvular repair is still technically demanding and does not appear to have been widely adopted at the general community level. The emergence of novel catheter-based intervention to treat SMR has resulted in a paradigm shift toward more conservative therapy, although the real benefits of these alternatives for patients are unclear.⁶⁾ Therefore, we plan to launch a multicenter study to assess the real effects of subvalvular repair in severe IMR. Prior to this detailed study, we conducted a nationwide survey regarding surgical strategy for IMR in Japan because there have been few reports addressing this issue.

Methods

We mailed a survey questionnaire to 534 training institutions certified by the Japanese Board of Cardiovascular Surgery in June 2020. The numbers of elective first-time mitral valve surgeries for patients with severe IMR performed from 2015 to 2019 were collected. Details of operative procedures, such as MVR, MVR with complete preservation of the subvalvular structures, MVR with papillary muscle approximation (PMA) (**Fig. 1**), MVP, MVP with papillary muscle relocation (PMR), or MVP with PMA (**Fig. 2**), were also reported. Concomitant coronary artery bypass grafting, tricuspid valve surgery, and surgical ablation could be included, but cases of left ventricular reconstruction were excluded.

This study has been approved by the institutional review board of the Jikei University School of Medicine (31-171(9670)).

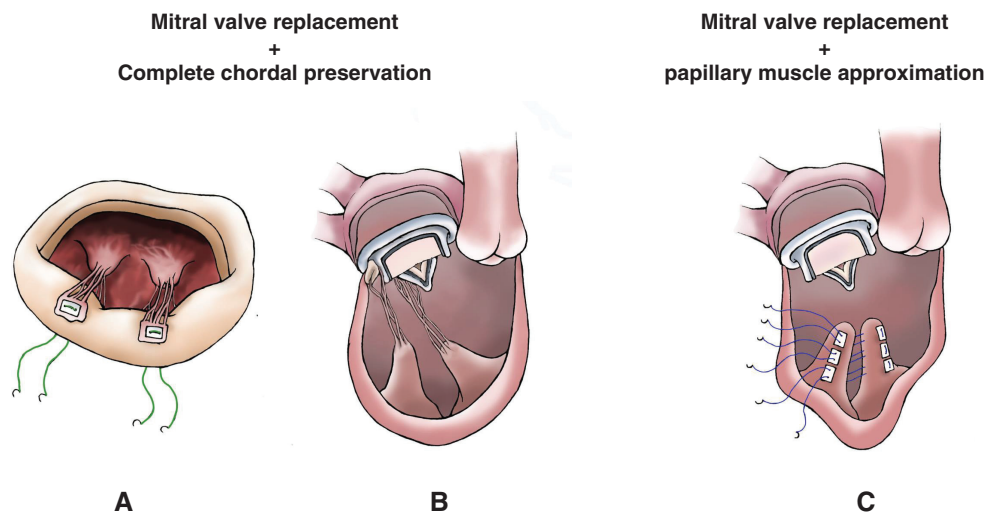


Fig. 1 Drawings illustrate subvalvular procedures; mitral valve replacement (MVR) + complete chordal preservation (**A** and **B**) and MVR + papillary muscle approximation (**C**). Chordae tendineae are not illustrated in **C**.

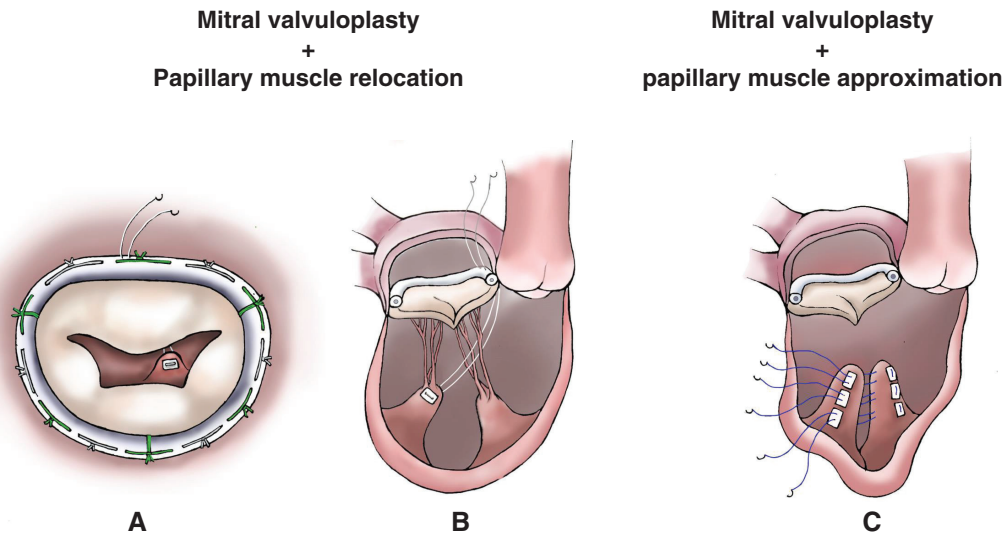


Fig. 2 Drawings illustrate subvalvular procedures; mitral valvuloplasty + papillary muscle relocation (**A** and **B**) and mitral valvuloplasty + papillary muscle approximation (**C**). Chordae tendineae are not illustrated in **C**.

Statistical analysis

The results are reported as numbers (and percentages) or mean \pm standard deviation. Analyses were performed using Microsoft Excel (Microsoft Corporation, Redmond, WA, USA) and R version 3.6.2 (R Foundation for Statistical Computing, Vienna, Austria). The chi-squared test was used for analysis of caseload-dependent prevalence of sub-valvular repair. In all analyses, $P < 0.05$ was taken to indicate statistical significance.

Results

Completed questionnaires were obtained from 286 (53.6%) of the 543 institutions. Thirty-six institutions did not perform mitral valve surgery for severe IMR. A total of 886 MVR (38.5%) and 1413 MVP (61.5%) were performed during the study period at 250 other institutions. Of these MVR patients, subvalvular structures were completely preserved in 443 (50.0%) patients. Only 17 (1.9%) patients underwent PMA concomitantly with MVR. On the other hand, 154 (10.9%) and 109 (7.7%) of MVP patients had PMR and PMA, respectively (**Fig. 3**). Among 250 institutions, only one high-volume center conducted over 100 surgeries; however, 90% of institutions performed < 20 surgeries within 5 years (**Fig. 4, Table 1**). The institutional mean case volumes in 5 years were 3.5 ± 7.0 MVR, 1.8 ± 2.9 MVR with complete chordal preservation (CCP), 0.1 ± 0.6

MVR with PMA, 5.7 ± 6.2 MVP, 0.6 ± 1.6 MVP with PMR, and 0.4 ± 1.1 MVP with PMA.

In terms of caseload, the low-volume centers (< 10 cases) performed subvalvular procedures more aggressively than the high-volume center (**Table 2**). On the other hand, the frequency of MVP was similar regardless of caseload (61.5%).

Discussion

This is the first report of a nationwide survey to determine surgeons' attitude toward severe IMR in Japan. More than half of the institutions nationwide participated in this survey, and therefore we believe that the results are reliable and reflect real-world data in Japan.

There have been only a few studies regarding the epidemiology of IMR, which can be classified into two categories: cohort studies and surgical database studies. With regard to cohort studies, according to the Euro Heart Survey on Valvular Heart Disease conducted by the European Society of Cardiology in 2001, IMR was found in 7.3% of patients with moderate-to-severe MR.⁷⁾ Recently, many researchers have divided the etiology of MR as primary or degenerative MR and secondary or functional MR. In 2017, Euro Heart Survey II identified SMR and IMR in 32.5% and 17.1% of patients with severe MR, respectively.⁸⁾ Despite different inclusion criteria, the prevalence of IMR appears to have increased during the 16-year period between these surveys.

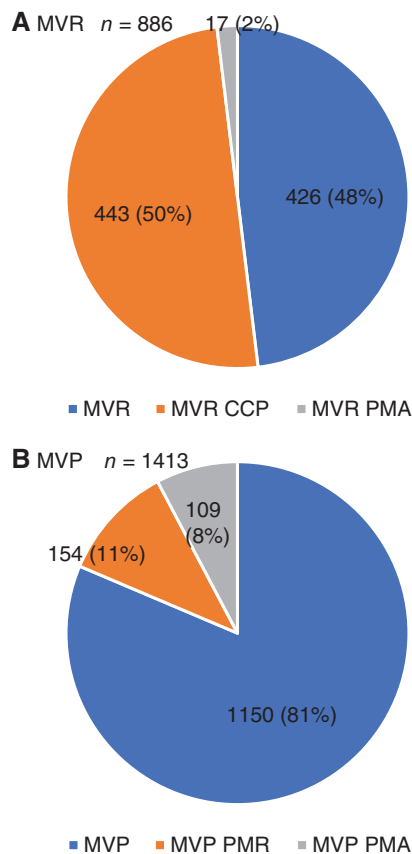


Fig. 3 Numbers and percentages of MVR (A) and valvuloplasty (B) performed for ischemic mitral regurgitation between 2015 and 2019 in Japan. Although half of MVR were performed with CCP, PMA and PMR were performed infrequently. CCP: complete chordal preservation; MVP: mitral valvuloplasty; MVR: mitral valve replacement; PMA: papillary muscle approximation; PMR: papillary muscle relocation

A recent echocardiography-based study (EuMiClip) investigated both etiologies of MR in Europe and observed SMR in 30.1% of moderate-to-severe MR patients, of whom 51.4% had IMR (15.5% of overall MR), which was similar to Euro Heart Survey II.⁹⁾

Mayo Clinic and Rochester Epidemiology Project from 2000 to 2010 in the USA reported a prevalence of SMR of 56% in patients with moderate-to-severe MR. Of these, only 5% of SMR patients underwent mitral valve surgery.¹⁰⁾ Subgroup analysis, targeting patients with digitally recorded echocardiography for review, showed that SMR and IMR were observed in 65% and 26% of cases of moderate-to-severe MR, respectively. Only 3%–4% of patients with SMR had mitral valve surgery in their lifetime.¹¹⁾

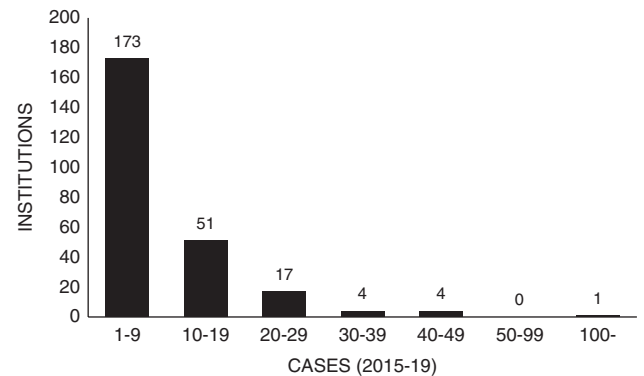


Fig. 4 Stratified numbers of institutions conducting mitral valve surgeries for ischemic mitral regurgitation between 2015 and 2019. Most of the institutions (90%) had <20 cases within 5 years.

Among patients with heart failure and ischemic or non-ischemic dilated cardiomyopathy recruited in four Italian centers, mild-to-moderate and severe SMR were observed in 49% and 24% of cases, respectively. Severe SMR was independently associated with mortality and hospitalization.¹²⁾

The sixth national adult cardiac surgical database report by the Society for Cardiothoracic Surgery in Great Britain and Ireland between 2004 and 2008 indicated that IMR was found in 13.1% of patients who underwent mitral valve surgeries for MR. MVP was aggressively performed in 75.2% of these cases, but postoperative mortality was unknown.¹³⁾

According to the French national database between 2014 and 2016 and the Euro Heart Survey II, SMR was observed in 16.2% and 24.3% of patients who underwent mitral valve surgeries, with in-hospital mortality rates of 7.8% and 4.9%, respectively.^{8,14)} Recently, surgeons are more reluctant to perform MVP for 38.9% and 36.8% of patients with SMR, respectively. The French national database reported that the in-hospital mortality rates of patients with isolated valve surgery for SMR were 2.2% after MVP and 7.1% after MVR.¹⁴⁾ Importantly, transcatheter intervention was performed at the same rate as MVP according to the Euro Heart Survey II (32.2%).⁸⁾

A report from The Society of Thoracic Surgeons Adult Cardiac Surgery Database from 2011 to 2016 indicated that only 4.2% and 1.3% of mitral valve surgeries were for SMR and IMR, respectively.¹⁵⁾ Compared to the population-based prevalence, the surgical undertreatment of SMR/IMR is remarkable.

The annual report by the Japanese Association for Thoracic Surgery did not focus on IMR.¹⁶⁾ In 2017, a

Table 1 Numbers of institutions and surgeries classified according to the number of mitral valve surgeries performed in 5 years

No. of operations	No. of institutions	MVR					MVP				
		All MVR	MVR with CCP		MVR with PMA		All MVP	MVP with PMA		MVP with PMR	
		No.	No.	% of MVR	No.	% of MVR	No.	No.	% of MVP	No.	% of MVP
1–9	173	286	192	67.1	10	3.5	456	55	12.1	66	14.5
10–19	51	223	129	57.8	1	0.4	494	32	6.5	44	8.9
20–29	17	137	66	48.2	0	0.0	278	11	4.0	31	11.2
30–39	4	57	18	31.6	0	0.0	89	4	4.5	8	9.0
40–49	4	104	27	26.0	0	0.0	75	7	9.3	5	6.7
100–	1	79	11	13.9	6	7.6	21	0	0.0	0	0.0
Total	250	886	443	50.0	17	1.9	1413	109	7.7	154	10.9

CCP: complete chordal preservation; MVP: mitral valvuloplasty; MVR: mitral valve replacement; PMA: papillary muscle approximation; PMR: papillary muscle relocation

Table 2 Proportion of subvalvular procedures stratified by institutional total case numbers

Surgical procedures	Case number (%)*		P-value
	<10	≥10	
Institutional case volume			
Overall	742	1557	
MVR	286 (38.5)	600 (38.5)	
+ CCP	192 (67.1)	251 (41.8)	<0.001
+ PMA	10 (3.5)	7 (1.2)	0.04
MVP	456 (61.5)	957 (61.5)	
+ PMA	55 (12.1)	54 (5.6)	<0.001
+ PMR	66 (14.5)	88 (9.2)	0.004

*MVR, MVP; % indicates ratio among overall mitral valve surgeries. + CCP, + PMA, + PMR; % indicates ratio among MVR or MVP. CCP: complete chordal preservation; MVP: mitral valvuloplasty; MVR: mitral valve replacement; PMA: papillary muscle approximation; PMR: papillary muscle relocation

total of 11517 mitral valve surgeries were performed, of which 295 cases (2.6%) with MR were performed at more than 2 weeks after the onset of myocardial infarction. The details of surgeries (repair or replacement) were unknown, and the in-hospital mortality rate was 9.8%.¹⁶⁾ The total case numbers of our survey within 5 years were 2299 (average 460 cases/year), which seemed to collect majority of surgical cases for IMR in Japan.

Compared with these findings summarized in **Table 3**, Japanese surgeons seem to be aggressive in preserving the native mitral valve even in cases with severe IMR. Although the object was limited to severe IMR, the mitral valve was preserved in nearly two thirds of cases. The importance of subvalvular apparatus was widely accepted through the relatively high rate of CCP in cases undergoing MVR (50%). However, PMA and PMR were performed in only 7.7% and 10.9% of MVP cases, respectively, which were similar to the rate in the CTS net study (11.9%).¹⁾ The reason for this low frequency of subvalvular repair is unclear, but there are several

possible explanations. First, this procedure is neither standardized nor reproducible, and is therefore still technically demanding. Alternatively, there is no clear evidence of clinical benefit to the patients. As described previously, a meta-analysis identified survival benefit of subvalvular repair in SMR.⁵⁾ On the other hand, the latest meta-analysis found no significant survival difference between restrictive annuloplasty alone and additional subvalvular repair, although subvalvular repair was favorable in terms of adverse composite endpoints.¹⁷⁾

Interestingly, low-volume centers were more aggressive in performing subvalvular procedures than high-volume centers. Although the real reason for this finding is unclear, we speculate that the low-volume centers may have ample time to perform such complex surgeries, while high-volume centers may prefer simple and quick surgeries. On the other hand, surgeons' attitude to preservation of the native mitral valve seems quite similar regardless of caseload. It can be inferred that the background of this finding may be Japanese surgeons' distrust of prosthetic valves.

Table 3 Epidemiology of ischemic/SMR

	Population	Investigation period	Etiology	Frequency among MR patients	Frequency among MV surgeries	Rate of repair	In-hospital mortality
Cohort study							
Euro Heart Survey ⁷⁾	92 centers, 5001 adults with VHD ≥ moderate	2001	IMR	64/877 (7.3%)			
Euro Heart Survey II ⁸⁾	222 centers, 7724 patients with severe VHD	2017	SMR	368/1114 (32.5%)	87/358 (24.3%)	32/87 (36.8%); 28/87 (32.2%)	11/368 (3.0%), post-intervention 4/82 (4.9%)
European registry (EuMiClip) ⁹⁾	19 centers, 63463 patients, MR ≥ moderate	Published in 2018	IMR SMR IMR	190/1114 (17.1%) 1010/3309 (30.5%) 519/3309 (15.7%)			
Mayo Clinic & Rochester Epidemiology Project ^{10,11)}	1294 isolated MR ≥ moderate	2000–2010	SMR	723/1294 (56%)		Rate of surgery 34/723 (5%)	
HF registry in 4 Italian centers ¹²⁾	1256 HF with ischemic or non-ischemic DCM	Published in 2011	SMR	Mild-to-moderate 49%, severe 24%			5-year survival 30% for IMR
Nationwide surgical database							
GB and Ireland national database ¹³⁾	8219 MV surgeries for MR	2004–2008	IMR		1079/8219 (13.1%)	811/1079 (75.2%)	
French national database ¹⁴⁾	18167 MV surgeries, 56 centers	2014–2016	SMR		2935/18147 (16.2%)	1141/2935 (38.9%)	229/2935 (7.8%), isolated MVP 10/463 (2.2%), isolated MVR 69/968 (7.1%)
JATS annual report ¹⁶⁾	11517 isolated MV surgeries	2017	MR after MI		295/11517 (2.6%)		Overall 9.8%
STS adult cardiac surgery database ¹⁵⁾	87214 isolated MV surgeries, 1125 centers	2011.7–2016.9	IMR		785/60185 (1.3%)	58.20%	

DCM: dilated cardiomyopathy; HF: heart failure; IMR: ischemic mitral regurgitation; JATS: Japanese Association for Thoracic Surgery; MR: mitral regurgitation; MV: mitral valve; MVP: mitral valvuloplasty; MVR: mitral valve replacement; SMR: secondary mitral regurgitation; STS: Society of Thoracic Surgeons; VHD: valvular heart disease

Our primary purpose is to identify the real clinical role of specific subvalvular repair for severe IMR. Based on this survey, we will launch a multicenter registry study to address this goal.

Limitations

This work was based on a nationwide questionnaire collecting surgical cases for severe IMR. However, the definition of severity was dependent on each institution. Backgrounds and prognoses of participants were not surveyed in this study. This survey collected only the

number of cases who underwent MVR with CCP, based on the hypothesis that most of surgeons preserved at least posterior leaflet in this setting. In addition, we did not differentiate PMR, suspension, and preservation in detail. More detailed survey with regard to the number of preserved chordae might be ideal. Number of mitral valve leaflet augmentation was not collected in this survey because relatively small number of cases was expected. One of our purposes of this survey is to identify institutions aggressive to perform subvalvular repair in addition to ring annuloplasty in IMR to recruit to future registry study. The lack of detailed clinical data

and outcomes in this survey prevented us from clarifying real benefits of subvalvular repair in this setting. Further retrospective studies using detailed echocardiography data and propensity score-matched studies using data from the National Clinical Database will be performed in the near future.

Conclusion

This was the first nationwide survey to determine surgeons' attitude toward IMR in Japan. Japanese surgeons aggressively perform MVP in patients with severe IMR. Subvalvular repair was also performed aggressively in addition to MVR (i.e., CCP), but not to MVP (i.e., PMA or PMR). A multicenter registry study with sufficient caseload to identify the real clinical role of specific subvalvular repair for severe IMR is warranted.

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Disclosure Statement

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References

- 1) Goldstein D, Moskowitz AJ, Gelijns AC, et al. Two-year outcomes of surgical treatment of severe ischemic mitral regurgitation. *N Engl J Med* 2016; **374**: 344–53.
- 2) Otsuji Y, Levine RA, Takeuchi M, et al. Mechanism of ischemic mitral regurgitation. *J Cardiol* 2008; **51**: 145–56.
- 3) Kron IL, Green GR, Cope JT. Surgical relocation of the posterior papillary muscle in chronic ischemic mitral regurgitation. *Ann Thorac Surg* 2002; **74**: 600–1.
- 4) Langer F, Groesdonk HV, Kunihara T, et al. Dynamic RING + STRING for ischemic mitral regurgitation: papillary muscle repositioning and modification of the septal-lateral diameter in the loaded beating heart under echocardiographic guidance. *J Thorac Cardiovasc Surg* 2011; **141**: 1315–6.
- 5) Mihos CG, Larrauri-Reyes M, Santana O. A meta-analysis of ring annuloplasty versus combined ring annuloplasty and subvalvular repair for moderate-to-severe functional mitral regurgitation. *J Card Surg* 2016; **31**: 31–7.
- 6) Praz F, Grasso C, Taramasso M, et al. Mitral regurgitation in heart failure: time for a rethink. *Eur Heart J* 2019; **40**: 2189–93.
- 7) Iung B, Baron G, Butchart EG, et al. A prospective survey of patients with valvular heart disease in Europe: The Euro Heart Survey on valvular heart disease. *Eur Heart J* 2003; **24**: 1231–43.
- 8) Iung B, Delgado V, Rosenhek R, et al. Contemporary presentation and management of valvular heart disease: The EURObservational Research Programme Valvular Heart Disease II Survey. *Circulation* 2019; **140**: 1156–69.
- 9) Monteagudo Ruiz JM, Galderisi M, Buonauro A, et al. Overview of mitral regurgitation in Europe: results from the European Registry of mitral regurgitation (EuMiClip). *Eur Heart J Cardiovasc Imaging* 2018; **19**: 503–7.
- 10) Dziadzko V, Clavel MA, Dziadzko M, et al. Outcome and undertreatment of mitral regurgitation: a community cohort study. *Lancet* 2018; **391**: 960–9.
- 11) Dziadzko V, Dziadzko M, Medina-Inojosa JR, et al. Causes and mechanisms of isolated mitral regurgitation in the community: clinical context and outcome. *Eur Heart J* 2019; **40**: 2194–202.
- 12) Rossi A, Dini FL, Faggiano P, et al. Independent prognostic value of functional mitral regurgitation in patients with heart failure. A quantitative analysis of 1256 patients with ischaemic and non-ischaemic dilated cardiomyopathy. *Heart* 2011; **97**: 1675–80.
- 13) Bridgewater B, Keogh B. The Society of Cardiothoracic Surgery in Great Britain & Ireland Sixth Adult Cardiac Surgical Database Report 2008. July 2009, ISBN 1-903968-23-2.
- 14) Messika-Zeitoun D, Candolfi P, Enriquez-Sarano M, et al. Presentation and outcomes of mitral valve surgery in France in the recent era: a nationwide perspective. *Open Heart* 2020; **7**: e001339.
- 15) Gammie JS, Chikwe J, Badhwar V, et al. Isolated mitral valve surgery: The society of thoracic surgeons adult cardiac surgery database analysis. *Ann Thorac Surg* 2018; **106**: 716–27.
- 16) Committee for Scientific Affairs, The Japanese Association for Thoracic Surgery, Shimizu H, et al. Thoracic and cardiovascular surgeries in Japan during 2017: Annual report by the Japanese Association for Thoracic Surgery. *Gen Thorac Cardiovasc Surg* 2020; **68**: 414–49.
- 17) Nappi F, Antoniou GA, Nenna A, et al. Treatment options for ischemic mitral regurgitation: a meta-analysis. *J Thorac Cardiovasc Surg* 2020. s0022-5233(20)31262-9. ahead of print.