International Cardiovascular Forum Journal 11 (2017)
DOI: 10.17987/icfj.v11i0.437

Preliminary Short-term Results of a Population of Patients Treated with MitraClip therapy: one Center Experience

R. Taravella[1], M. G. Cellura[2], G. Cirrincione[2], S. Asciutto[2], M. Caruso[2], M. Benedetto[2], R. Alduino[3], S. Novo[4].

1. Arnas Civico Hospital, Division of Interventional Cardiology, University Hospital "Policlinico P. Giaccone", Division of Cardiology.
2. Arnas Civico Hospital, Cardiology UTIC, Division of Interventional Cardiology.
3. PhD in Statistics.
4. University Hospital "Policlinico P. Giaccone", Full Professor Chief of Division of Cardiology.

Corresponding author:
Rossana Taravella,
Arnas Civico Cardiology UTIC, University of Palermo, Palermo, Italy.
Piazza Nicola Leotta 4,90127 Palermo,
Email: ross.taravella@gmail.com

Highlights

Objectives:
This retrospective analysis sought to evaluate 1-month outcomes and therapy effectiveness of a population of patients treated with MitraClip therapy. We describe in this article the preliminary results of primary effictiveness endpoint.

Background
Percutaneous Mitral Repair is being developed to treat severe mitral regurgitation (MR), with increasing real-world cases of functional MR (FMR). In the EVEREST (Endovascular Valve Edge-to-Edge Repair Study) II trial, percutaneous device showed superior safety but less reduction in MR at 1year. 4-year outcomes from EVEREST II trial showed no difference in the prevalence of moderate-severe and severe MR or mortality at 4years between surgical mitral repair and percutaneous approach.

Methods
We analysed retrospectively collected data from one center experience in Italy enrolled from January 2011 to December 2016. The study included 62 patients [mean age74±11 years, 43 men (69%)] with MR of at least grade 3+. All patients had functional MR, were in New York Heart Association (NYHA) functional class III or IV, with a large portion (78%) of mild-to-moderate Tricuspid Regurgitation (TR). One or more clips were implanted in 67 procedures (62 patients).

Results & Conclusions
Results and Conclusions: Severity of MR was reduced in all successfully treated patients,54(90%) were discharged with MR≤2+ (primary effictiveness endpoint). Clinical 1-month follow-up data showed an improvement in NYHA functional class (42 patients (70%) in NYHA class I-II). 60 of 62 (97 %) successfully treated patients were free from death and mitral valve surgery at 1-month follow-up. MitraClip therapy reduces functional MR with acute MR reduction to <2+ in the great majority of patients,with a large freedom from death, surgery or recurrent MR in a great portion of patients.

Keywords: MitraClip; Mitral Regurgitation; Catheter-based therapy; Heart valves; NYHA functional class.

Citation: Taravella R, Cellura MG, Cirrincione G, et al. Preliminary short-term results of a population of patients treated with MitraClip therapy: one center experience. International Cardiovascular Forum Journal. 2017; 11: 60-64 DOI: 10.17987/icfj.v11i0.437

Introduction

Functional mitral regurgitation (FMR) is increasingly common in elderly patients of real-world clinical experience with a large rate of comorbidities, almost all not suitable for surgical mitral valve repair. Morbidity and mortality are related to MR severity [1.2], and benefits from MitraClip therapy can often be seen through a reverse LV remodelling with LV dimension reductions [3]. Transcatheter implantation of the MitraClip device (Abbott, Abbott Park, IL, USA) is an important therapeutic strategy for patients with moderate-severe MR of functional etiology with a high surgical risk [4,5]. We sought to assess the feasibility, acute effectiveness , safety and short-term durability of MitraClip therapy in MR reduction and global clinical improvement in a population of 62 patients who underwent the percutaneous

* Corresponding author. E-mail: ross.taravella@gmail.com

ISSN: 2410-2636

procedures.

Materials and Methods

The MitraClip system

MitraClip is a catheter-based system made of a steerable 24-F guide catheter and the clip delivery system, which conducts the MitraClip polyester-covered mechanical device at its distal end [4]. Each clip has two arms and a 'gripper' adjacent to each arm. The procedure is performed in the cardiac catheterization laboratory with continuous echocardiographic and fluoroscopic guidance with the patient under general anesthesia. The distal end of the guide catheter reaches the left atrium through a transseptal-puncture approach. MitraClip effective position is held at the origin of main regurgitant jet, assessing the adequacy of the grasp, and if necessary placing a second device.

Patients

Data were collected retrospectively from one center in Italy between January 2011 and December 2016. A total of 62 patients [mean age 74±11 years, 43 men (69%)] underwent MitraClip therapy for MR of at least grade 3+, often with a poor clinical status [53 patients in NYHA functional class III-IV (85.5%)]. All patients had functional MR, with a high STS (Society of Thoracic Surgeons) risk score and EuroScore II during the baseline evaluation of the management of the valvular disease. As regards STS risk score, the lowest value was: Risk of Mortality: 0.33% and Morbidity or Mortality: 7.6% (Long Length of Stay: 2.31%, Short Length of Stay: 2.3%, Permanent Stroke: 0.45%, Prolonged Ventilation: 3.25%, DSW Infection: 0.1%, Renal Failure: 0.9%, Reoperation: 2.13% while the highest value was: Risk of Mortality: 35% (mean ± standard deviation 3,73 ± 4,7) and Morbidity or Mortality: 68.73% (mean ± standard deviation 25.1 ± 12) [Long Length of Stay: 53.2% (mean ± standard deviation 11.34 ± 8.3); Short Length of Stay: 64.2% (mean ± standard deviation 25.6 ± 14.8); Permanent Stroke: 5.2% (mean ± standard deviation 2.2 ± 1.04); Prolonged Ventilation: 54.2% (mean ± standard deviation 14.5 ± 9.5); DSW Infection: 1.04% (mean ± standard deviation 0.3 ± 0.16); Renal Failure: 47.4% (mean ± standard deviation 8.04 ± 8.7); Reoperation: 29.3% (mean ± standard deviation 9.8 ± 3.15)]. As concerns EuroScore II, the lowest value of Risk of In-Hospital Mortality was 3.4% while the highest value was 70.3% (mean ± standard deviation 32.1 ± 17.1). Due to the high surgical risk of the patients, MitraClip therapy was almost the only way to treat Mitral Regurgitation. Patients underwent transthoracic and transesophageal echocardiography to quantify MR and to evaluate the morphologic suitability for MitraClip implantation. All patients received optimal medical and device treatment, in respect of their comorbidities. Baseline demographic characteristics are shown in *Table 1*. The informed consent was obtained from each patient and the study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in a priori approval by the institution's human research committee.

Procedure

All the percutaneous interventions were performed using the protocol descrived above4,5. Briefly, the MitraClip system is carried to the left atrium by means of transseptal puncture, through the transfemoral venous route. The MitraClip polyester-covered mechanical device has 2 arms opened and closed thanks to the delivery catheter. The MitraClip system is positioned at the origin of the main regurgitant jet, and the device is grasped orthogonally to the plane of the mitral valve annulus. During the procedure , once the reduction of MR and the assessment of the diastolic transmitral gradient are detected with the use of transesophageal echocardiography, the clip can be deployed. The patient is under general anaesthesia throughout the intervention, monitoring the procedure by fluoroscopy and transesophageal 2- and 3-dimensional echocardiography. Procedural success was fixed as the implantation of at least one clip. The day before procedure, each patient was treated with a 300 mg clopidogrel loading dose and 100mg aspirin, while during procedure we used heparin and for the following 6 months patients were treated with clopidogrel (at a dose of 75 mg daily, for 30 days after procedure) and aspirin (at a dose of 100 mg daily).

Echocardiography

The severity of MR at baseline was graded according to the American Society of Echocardiography guidelines[6]. Post-intervention, the severity of MR was detected trough a quantitative assessment with the tecnique reported by Foster et al [7]. Left ventricular ejection fraction (LVEF) was assessed according to the biplane Simpson's method. The mitral valve orifice area was performed using the pressure half-time method.

Statistical Methods

Continuous variables are presented as mean ± standard deviation. Despite MR, TR and Aortic Regurgitation (AR) are ordinal variables, we took a comparison as continuous variables (just hypothetically), calculating the mean ± standard deviation grade of reduction of MR, TR, AR to quantify the mean grade of improvement of valvular regurgitations after MitraClip therapy. Categorical variables are presented as counts and percentages. Comparisons of continuous variables were performed by T test for paired samples; comparisons of categorical variables were performed by $\chi 2$ (chi-square) Test or McNemar Test, where appropriate, using SPSS software. A two-tailed p-value < 0.05 was regarded as statistically significant. Degenerative MR was defined as the presence of leaflet pathology (either anterior, or posterior or both), and functional MR was defined as the absence of leaflet pathology. No one of the patients had MR of degenerative etiology, while 23 patients (37%) had FMR with ischaemic aspects and 6 patients (9.7%) had FMR with degenerative aspects.

Ethics

All patients included in the study were fully informed about the MitraClip procedure and signed a written consent form.

Results

Objectives

The primary objective of this study was to assess acute reduction of MR severity, TR severity, AR severity and the patients' clinical status at 1 month, as reflected by NYHA functional class (study primary effectiveness endpoint).

1-month (short term) outcomes

The 62 patients underwent a total of 67 interventions, with repeated procedures performed at 2018, 1537, 779, 693, and 446 days in 5 patients. 67 of 67 interventions (100%), were successful in 62 patients, with 2 nonprocedural deaths at 1 month. A single clip was implanted in 43 successful procedures (69%), whereas two clips per procedure were implanted in 19 successful procedures

International Cardiovascular Forum Journal 11 (2017)
DOI: 10.17987/icfj.v11i0.437

(31%). Successful clip implantation was associated with a reduction in MR severity by 1, 2, and 3 grades in 61% (*n*=37), 28% (*n*=17), and 8% (*n*=5) of procedures respectively, with an average reduction of 1,5 grades. Mitral regurgitation of grade 2+ or less was achieved in 54 successful procedures (90%). Five (8%) of the 62 successfully treated patients were discharged with MR severity reduced from 4+ to 3+.

The total device time, i.e. the time from septal puncture to withdrawal of the guide catheter from the left atrium, averaged ± standard deviation, minutes 254± 59.

A significant improvement in TR was observed with a reduction in TR severity of grade 2+ or less in 54 patients (92%). AR severity (100% mild-to-moderate before procedures) had neither great improvement nor significant worsening at 1 month.

Overall distributions of MR severity, TR severity, AR severity at baseline and at 1-month follow-up are shown respectively in *Table 2*. MR severity is also showed in *Figure 1*.

The patients successfully treated with MitraClip system showed an improvement in clinical status with a reduction in NYHA functional class to I-II class in 42 patients (70%). The overall distribution of NYHA functional class at baseline and at 1-month follow-up is shown in *Figure 2*.

Despite MR severity is an ordinal variable, if we take a comparison

Table 1. Baseline patient characteristics

	n = 62
Baseline patient characteristics	
Age, yrs, mean ± SD	73.8 ± 10.7
Sex , n (%)	
Male	43 (69.4)
Female	19 (30.6)
BMI classes, n (%)	
<18.5	2 (3.2)
[18.5 - 25)	24 (38.7)
[25 - 30)	30 (48.4)
≥30	6 (9.7)
Comorbidities and Risk Factors	
Family history of cardiovascular diseases, n (%)	19 (30.6)
Smoke, n (%)	
Yes	9 (14.5)
Former	3 (4.8)
Diabetes mellitus	23 (37.1)
Insulin therapy, n (%)	12 (19.4)
Hypertension, n (%)	45 (72.6)
Atrial fibrillation, n (%)	22 (37)
Congestive heart failure, n (%)	23 (38)
Hypercholesterolemia, n (%)	29 (46.8)
Chronic pulmonary disease (COPD), n (%)	8 (12.9)
GFR MDRD	58.0 ± 27.1
GFR < 60, ml/min, n (%)	33 (53.2)
Anemia, n (%)	32 (51.6)
Charlson Comorbidity Index > 1, n (%)	48 (77.4)
Prior myocardial infarction, n (%)	26 (41.9)
Prior PTCA, n (%)	25 (40.3)
Prior CABG, n (%)	14 (22)
Cerebrovascular Disease, n (%)	9 (14.5)
MR etiology, n (%)	
functional with ischaemic aspects	23 (37.1)
functional	33 (53.2)
functional with degenerative aspects	6 (9.7)
MR severity, n (%)	
1+ to 2+, mild-to-moderate	0 (0)
2+, moderate	0 (0)
3+, moderate-to-severe	8 (13)
4+, severe	54 (87)
TR severity, n (%)	
1+ to 2+, mild-to-moderate	27 (43)
2+, moderate	21 (34)
3+, moderate-to-severe	11 (18)
4+, severe	3 (5)
AR severity, n (%)	
1+ to 2+, mild-to-moderate	57 (92)
2+, moderate	5 (8)
3+, moderate-to-severe	0 (0)
4+, severe	0 (0)
LV ejection fraction (%± SD)	39 ± 12
LV end-diastolic volume, mL (mL± SD)	175 ± 60
Regurgitant Volume, mL/beat (mL± SD)	54 ± 9
Effective Regurgitant Orifice Area (EROA), cm² (cm²± SD)	0,35 ± 0.06
LA anterior-posterior diameter, mm (mm± SD)	45 ± 7.6
LA end-systolic Volume, mL (mL± SD)	93 ± 23
Vena Contracta, cm (cm± SD)	0.64 ± 0.08
PAPs , mmHg (mmHg± SD)	41 ± 9.6
NYHA functional class, n (%)	
I-II	9 (14.5)
III-IV	53 (85.5)
Electrical therapy, n (%)	
ICD	17 (27.4)
CRT	10 (16.1)

BMI, Body Mass Index; eGFR, estimating Glomerular Filtration Rate; MDRD, Modification of Diet in Renal Disease; CABG, coronary artery bypass graft surgery; MR, Mitral Regurgitation; TR, Tricuspid Regurgitation; AR, Aortic Regurgitation; PAPs stimated Pulmonary Artery Pressure; LV, Left ventricular; LA, Left atrial; NYHA, New York Heart Association; ICD, implantable cardioverter defibrillator; CRT, cardiac resynchronization therapy.

Table 2.

n = 60			
	before-MitraClip	1-month after-MitraClip	p
Mitral Regurgitation	3.9 ± 0.3	1.5 ± 0.8	<0.001
normal/mild/mild-to-moderate n (%)	0 (0)	54 (90)	
moderate-to-severe/severe n (%)	60 (100)	6 (10)	
Tricuspid Regurgitation (n=59)	1.8 ± 0.9	1.3 ± 0.8	<0.001
normal/mild/mild-to-moderate n (%)	46 (78)	54 (92)	
moderate-to-severe/severe n (%)	13 (22)	5 (8)	
Aortic Regurgitation	0.6 ± 0.6	0.7 ± 0.6	0.088
normal/mild/mild-to-moderate n (%)	60 (100)	60 (100)	
moderate-to-severe/severe n (%)	0	0	

Despite MR, TR and AR are ordinal variables, we take a comparison as continuous variables (just hypothetically), calculating the mean ± standard deviation grade of reduction of MR, TR, AR to quantify the changes from baseline to 1 month in MR, TR , AR severity of successfully treated patients.

as a continuous variable (just hypothetically) using mean ± standard deviation, we find a decrease from 3.9 ± 0.3 at baseline to 1.5 ± 0.8 at 1-month follow-up ($p < 0{,}001$) in MR grade in 60 successfully treated patients. A statistically significant reduction was also noted in TR severity, with the same comparison, with a decrease from 1.8 ± 0.9 at baseline to 1.3 ± 0.8 at 1-month follow-up ($p< 0.001$) in these patients.

Of the 60 patients with clinical follow-up data, 42 (70%) had improved from NYHA functional class III or IV at baseline to NYHA functional class I or II , while 18 (30%) remained in NYHA functional class III or IV with no great functional improvement, despite MR being reduced by 1 and even 2 grades.

Discussion

Main findings

This observational, retrospective one-center investigation of 62 patients with severe MR showed that MitraClip therapy is feasible and effective in these patients. Acutely, clip implantation achieved MR grades of ≤ 2+ in the vast majority of patients. At 1-month follow-up, 40 of the 60 successfully treated patients followed clinically, had improved by at least one NYHA functional class. The preliminary results of these findings satisfy our primary efficacy endpoint.

Our study suggests that the majority of patients with severe FMR will experience a clinical benefit from MR reduction by MitraClip therapy, particularly important for the severity of both ischaemic and non-ischaemic cardiomyopathy often present in these patients3. Clinical benefits are expressed for both the mitral valvular disease and the underlying heart failure disease3.

Treatment options for severe functional mitral regurgitation

The management of current real-world patients with severe FMR, is an hard challenge, because of their high STS risk score and EuroScore II, together with their old age and several comorbidities. When optimized medical, and, where appropriate, cardiac resynchronization therapy, fail to reduce MR in these patients, MitraClip is almost the only way to treat them [8]. However, we wait for new insights on safety and effectiveness of MitraClip system during long-term follow-up, to highlight, if true, long-term durability of MR reduction, functional improvement, survival and quality of life of these patients. In the present study, concordant with other observational MitraClip studies,[5,9] MR grades of 2+ or less were acutely achieved in 90% of successful procedures. This rate is noticeably higher than the 74% reported in EVEREST (Endovascular Valve Edge-to-Edge REpair Study) [4] and suggests the hypothesis that FMR may be treated with MitraClip with a greater effectiveness than degenerative MR. The chance to reverse maladaptive remodelling is a major determinant of long-term prognosis in these patients [10,11]. 4-year outcomes from EVEREST II trial showed no difference in the prevalence of moderate-severe and severe MR or mortality at 4 years between surgical mitral repair and percutaneous approach, despite a number of cases treated with MitraClip required surgery to treat residual MR [13]. Clearly, the acute reduction in MR severity in our patients was accompained at 1 month by significant improvement in NYHA functional class.

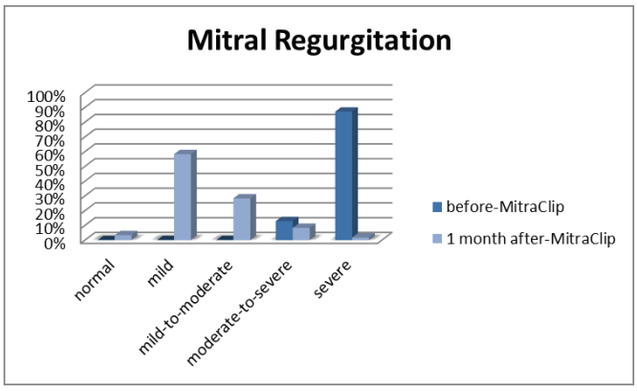

Figure 1. Mitral Regurgitation at baseline and at 1-month follow-up.

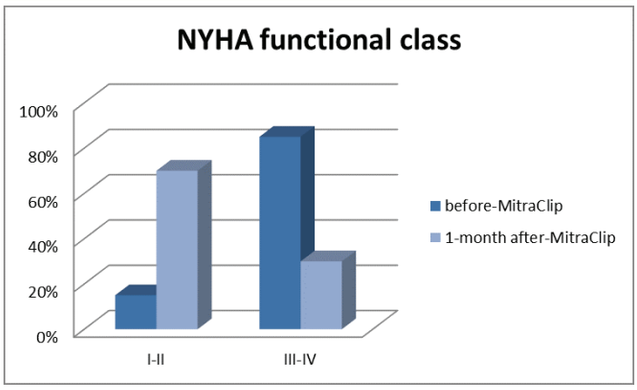

Figure 2. NYHA functional class at baseline and at 1-month follow-up.

International Cardiovascular Forum Journal 11 (2017)
DOI: 10.17987/icfj.v11i0.437

Survival

Considering the adverse baseline characteristics of our patients, particularly focusing on age, NYHA functional class, LV ejection fraction, the presence of coronary artery disease and ischaemic cardiomyopathy, it is a good result to observe a 30-day mortality rate of 3.2% (1-month follow-up changes in echocardiographic variables, electrocardiographic parameters and postprocedural rate of complications will be discussed in a forthcoming analysis about secondary safety endpoint). 26 patients (42%) had a prior myocardial infarction, 14 patients (22%) underwent a coronary artery bypass grafting (CABG) surgery and 25 patients (40%) underwent a percutaneous transluminal coronary angioplasty (PTCA) in their past medical history; this was relevant in their comorbidities, global clinical status, baseline evaluation of the surgical risk, and also for a prediction of survival and prognosis during the long-term follow-up. *Franzen et al* [3] in a group of patients with severe LVEF reduction heart failure treated with MitraClip reported a 30-day mortality rate of 6%. *Braun et al* [12] observed in a group of patients with coronary artery disease who underwent MitraClip therapy a perioperative mortality of 8%. In our population 33 patients (53%) had annular dilation of mitral valve while 25 patients (39.7%) had papillary muscle disfunction, complicating the functional etiology and the management of these patients. Post-procedural close haemodynamic monitoring of each individual patient in Coronary Intensive Care Unit is mandatory because MitraClip therapy can alter the balance of preload and afterload [3].

Limitations

We recognize the retrospective nature of this study, the bit small number of patients and short-term follow-up at 1-month as major limitations. As a consequence, there were no study protocol strictly adhered at the enrollement of different patients, together with logistic limitations inside the hospital. The echocardiographic assessment of MR severity was performed only at rest, and there wasn't an independent dedicated core laboratory. Furthermore, a complete insight on our study will be provided with the secondary safety endpoint analysis.

Conclusions

This study suggests that severe FMR can be successfully reduced by MitraClip implantation, with clinical benefits at 1 month. We need to integrate our results, with present and future national and multinational registries (including the Italian GIOTTO, in which our hospital is a participant center), to validate our outcomes and to assess the long-term durability of MR reduction, long-term survival and of quality of life of patients treated with MitraClip therapy during the following scheduled follow-up visits.

Declarations of Interest

The authors declare no conflict of interest.

Acknowledgements

There's no funding source. The authors state that they abide by the "Requirements for Ethical Publishing in Biomedical Journals" [14].

References

1. Robbins JD, Maniar PB, Cotts W, Parker MA, Bonow RO, Gheorghiade M. Prevalence and severity of mitral regurgitation in chronic systolic heart failure. Am J Cardiol 2003;91:360–362. DOI: 10.1016/S0002-9149(02)03172-7.
2. Trichon BH, Felker GM, Shaw LK, Cabell CH, O'Connor CM. Relation of frequency and severity of mitral regurgitation to survival among patients with left ventricular systolic dysfunction and heart failure. Am J Cardiol 2003;91:538–543. DOI: 10.1016/S0002-9149(02)03301-5.
3. Franzen O,van der Heyden J, Baldus S et al. MitraClip therapy in patients with end-stage systolic heart failure. European Journal of Heart Failure 2011;13;569-576. DOI: 10.1093/eurjhf/hfr029.
4. Feldman T, Kar S, Rinaldi M, et al. EVEREST Investigators. Percutaneous mitral repair with the MitraClip system: safety and midterm durability in the initial EVEREST (Endovascular Valve Edge-to-Edge REpair Study) cohort. J Am Coll Cardiol 2009;54:686–694. DOI: 10.1016/j.jacc.2009.03.077.
5. Tamburino C, Ussia GP, Maisano F, et al. Percutaneous mitral valve repair with the MitraClip system: acute results from a real world setting. Eur Heart J 2010;31:1382–1389. DOI: 10.1093/eurheartj/ehq051.
6. Zoghbi WA, Enriquez-Sarano M, Foster E et al. Recommendations for evaluation of the severity of native valvular regurgitation with two-dimensional and Doppler echocardiography. J Am Soc Echocardiogr 2003;16:777–802. DOI: 10.1016/S0894-7317(03)00335-3.
7. Foster E, Wasserman HS, Gray W et al. Quantitative assessment of severity of mitral regurgitation by serial echocardiography in a multicenter clinical trial of percutaneous mitral valve repair. Am J Cardiol 2007;100:1577–1583. DOI: 10.1016/j.amjcard.2007.06.066.
8. Nishimura RA, Otto CM, Bonow RO, et al. 2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease, Mitral Regurgitation:Recommendations. Circulation. 2014;129. DOI: 10.1161/CIR.0000000000000031.
9. Franzen O, Baldus S, Rudolph V, et al. Acute outcomes of MitraClip therapy for mitral regurgitation in high-surgical-risk patients: emphasis on adverse valve morphology and severe left ventricular dysfunction. Eur Heart J 2010;31:1373–1381. DOI: 10.1093/eurheartj/ehq050.
10. Kotlyar E, Hayward CS, Keogh AM, Feneley M, Macdonald PS. The impact of baseline left ventricular size and mitral regurgitation on reverse left ventricular remodelling in response to carvedilol: size doesn't matter. Heart 2004;90:800–801. DOI: 10.1136/hrt.2002.009696.
11. Liang YJ, Zhang Q, Fung JW, et al. Impact of reduction in early- and late-systolic functional mitral regurgitation on reverse remodelling after cardiac resynchronization therapy. Eur Heart J 2010;31: 2359–2368. DOI: 10.1093/eurheartj/ehq134.
12. Braun J, Bax JJ, Versteegh MI, et al. Preoperative left ventricular dimensions predict reverse remodeling following restrictive mitral annuloplasty in ischemic mitral regurgitation. Eur J Cardiothorac Surg 2005;27:847–853. DOI: 10.1016/j.ejcts.2004.12.031.
13. Mauri L, Foster E, Glower DD, et al. 4-Year Results of a Randomized Controlled Trial of Percutaneous Repair Versus Surgery for Mitral Regurgitation. Journal of the American College of Cardiology. Vol. 62, No. 4, 2013. DOI: 10.1016/j.jacc.2013.04.030.
14. Shewan LG, Coats AJS, Henein M. Requirements for ethical publishing in biomedical journals. International Cardiovascular Forum Journal 2015;2:2. DOI: 10.17987/icfj.v2i1.4.