Folia Cardiologica 2022
vol. 17, no. 3, pages 157–162
DOI: 10.5603/FC.a2022.0032

ISSN 2353–7752
e-ISSN 2353–7760

The rationale for closing the iatrogenic atrial septal defect during the MitraClip procedure

Uzasadnienie zamknięcia jatrogennego ubytku przegrody międzyprzedsionkowej podczas zabiegu MitraClip

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Abstract

Introduction. The formation of an iatrogenic septal defect (iASD) during the MitraClip procedure may be associated with adverse consequences, including right ventricular (RV) volume overload resulting in worsening heart failure, hospitalizations, and increased mortality.

The aim of the study is to evaluate the effects of closing the iASD simultaneously during MitraClip on the RV function.

Material and methods. Four patients who underwent the MitraClip procedure were analysed. The resulting iASD was closed using an Amplatzer occluder during the indexed procedure. The patients were followed up for 12 months.

Results. The complete iASD closure was achieved in all patients. There were no deaths during 12 months of observation. In all cases, the RV dimensions decreased, on average, from 38 ± 5.35 mm to 34.35 ± 5.06 mm. No patient had progression of tricuspid regurgitation to significant regurgitation (TR ≥ 3+). Right ventricular systolic pressure (RVSP) decreased from an average of 47.50 ± 7.82 mm Hg to 38.00 ± 8.57 mm Hg.

Conclusions. The results indicate a beneficial effect of concomitant closure of iASD during the MitraClip procedure by reducing RV exposure to volume overload and the associated severity of tricuspid valve regurgitation and pulmonary hypertension.

Key words: MitraClip, iatrogenic atrial septal defect, atrial septal defect closure

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Introduction

Transcatheter reduction of mitral regurgitation procedures is frequently used in clinical practice. It can be expected that the latest American College of Cardiology and European Society of Cardiology guidelines while upgrading the recommendations to class IIa for functional mitral regurgitation, will result in an even more frequent qualification for this procedure. The MitraClip procedure requires puncture of the atrial septum and passage through it with large

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diameter catheters (24 F). The result is fairly frequent iatrogenic defects in the atrial septum. Ussia [1] and Saitoh [2] demonstrated the presence of iatrogenic septal defect (iASD) in over 80% of patients in short-term follow-up. Smith [3] and Ikenaga [4] showed that iASD is present in 43% to 57% of patients after one month. Although iASD closes spontaneously in some cases, the iASD presence 12 months after the procedure is described by other authors in up to 50% of patients [5].

The presence of iASD in patients undergoing MitraClip procedures may be associated with several adverse effects. Schueler et al. [5] draw attention to the possibility of right heart volume overload, RV failure, and hence hospitalization and deaths. Also, Tayoma et al. [6] showed an increased frequency of hospitalizations due to worsening heart failure in patients with iASD. The direction of flow through the iASD affects the frequency of adverse events and the prognosis of patients. The iASD with the reverse right-to--left flow is also the cause of acute arterial deoxygenation [7, 8]. In turn, Ikenaga showed that iASD is associated with lower left ventricular (LV) ejection fraction, larger diastolic and systolic LV volumes, and right heart enlargement [4]. So far, the results of iASD closure in the case of persistent iASD and immediate in the case of acute deoxygenation have been published [9–11]. The validity of closing the iASD during MitraClip treatment has not been assessed before the leftover leakage led to adverse effects. This study presents the results of 4 patients who underwent iASD occlusion during the MitraClip procedure, regardless of the flow direction between the atria.

Material and methods

The paper presents the procedures performed in 4 patients with simultaneous reduction of mitral regurgitation and closure of the iASD resulting from the procedure. Patient characteristics are given in Table 1. The iASD closure procedures were performed with the Amplatzer occluder

Table 1. Clinical characteristics and echocardiographic parameters assessing prior to MitraCip procedure

	Patient 1	Patient 2	Patient 3	Patient 4	Mean ± SD
Age [years]	71	59	65	70	66.25 ± 4.76
MR range	4+	4+	4+	4+	
LVDD [mm]	59	77	71	61	67.0 ± 7.35
LVSD [mm]	47	66	64	51	57.0 ± 8.15
LVEDV [mL]	136	217	231	169	188.25 ± 37.93
LVED/BSA [mL/m^2]	70.45	90.02	101.45	84.50	86.60 ± 11.15
LVEF [%]	30	26	26	31	28.25 ± 2.28
ERO [cm^2]	0.6	0.3	0.2	0.47	0.39 ± 0.15
RVD [mm]	41	43	42	35	38.0 ± 5.35
TR range	3+	2+	1	2+	–
TAPSE [mm]	11	15	21	15	15.6 ± 3.2
PVR [WU]	5.36	4.2	3.56	3.2	4.10 ± 0.80
RVSP [mm Hg]	32	63	37	46	44.5 ± 11.80
TAPSE/sPAP [mm/mm Hg]	0.23	0.25	0.56	0.32	0.24 ± 0.13
(TR dP/dt)/TR V_{max}	100.42	68.77	97.00	68.18	88.59 ± 12.29
RVEe [mm/WU]	2.05	3.57	5.89	4.57	4.02 ± 1.40
6MWT [m]	281	409	120	177	246 ± 110.07
Max O^2 consmp. [mL/kg]	12.6	20.6	13.4	17.1	15.53 ± 3.6
NT-proBNP pre [ng/mL]	3782	841	347.6	1155	1531.40 ± 1330.87

6MET – six-minute walking test; BSA – body surface area; ERO – effective regurgitant orifice; LVDD – left ventricular diastolic dimension; LVEDV – left ventricular end-diastolic volume; LVEF – left ventricular ejection fraction; LVSD – left ventricular systolic dimension; MC – MitraClip; MR – mitral regurgitation; NT-proBNP – N-terminal pro-B-type natriuretic peptide; PVR – pulmonary vascular resistance; RVD – right ventricular dimension; RVEe – echo-derived right ventricular ejection efficiency; RVSP – right ventricular systolic pressure; SD – standard deviation; sPAP – systolic pulmonary artery pressure; TAPSE – tricuspid annular plane systolic excursion; TR – tricuspid regurgitation; V_{max} – maximal velocity; WU – Wood Unit

Table 2. The follow-up echocardiographic assessment

	Patient 1	Patient 2	Patient 3	Patient 4	Mean ± SD
MR range	4+	2+	1+	1+	–
LVDD [mm]	68	81	71	66	71.5 ± 5.77
LVSD [mm]	41	59	57	43	50.0 ± 8.06
LVEDV [mL]	142	261	200	135	184.50 ± 50.87
LVEF [%]	40	27	20	35	30.50 ± 7.63
RVD [mm]	37	40	30	29	34.35 ± 5.06
TR range	1+	2+	1+	2+	–
TAPSE [mm]	13	16	19	17	16.25 ± 2.16
PVR [WU]	6.68	4.95	2.79	3.94	4.60 ± 1.43
RVSP [mm Hg]	31	52	31	38	38.0 ± 8.57
TAPSE/sPAP [mm/mm Hg]	0.41	0.31	0.61	0.44	0.45 ± 0.11
(TR dP/dt)/TR V_{max}	70.0	102.86	113.95	158.87	111.42 ± 31.81
RVEe [mm/WU]	1.94	3.21	7.18	4.31	4.16 ± 1.93

6MET – six-minute walking test; LVDD – left ventricular diastolic dimension; LVEDV – left ventricular end-diastolic volume; LVEF – left ventricular ejection fraction; LVSD – left ventricular systolic dimension; MR – mitral regurgitation; PVR – pulmonary vascular resistance; RVD – right ventricular dimension; RVEe – echo-derived right ventricular ejection efficiency; RVSP – right ventricular systolic pressure; SD – standard deviation; sPAP – systolic pulmonary artery pressure; TAPSE – tricuspid annular plane systolic excursion; TR – tricuspid regurgitation; V_{max} – maximal velocity; WU – Wood Unit

immediately after attaching the MitraClip to the valve leaflets. The iASD occlusion was performed regardless of the right heart geometry and function at baseline assessment. Right ventricular geometry and function were assessed based on transthoracic echocardiography performed the day before the MitraClip procedure. The following parameters were assessed: right ventricular dimension (RVD), right ventricular systolic pressure (RVSP), pulmonary vascular resistance (PVR), echo-derived right ventricular efficiency (RVEe), tricuspid annular plane systolic excursion (TAPSE) and tricuspid regurgitation (TR) range. The PVR was calculated using the TR peak velocity/right ventricular (RV) outflow tract velocity-time integral, and RVEe was defined as TAPSE/PVR. The follow-up data were collected at 12 months and included clinical and echocardiographic parameters.

Results

In the analysed cases where the iASD closure procedure was performed, all patients at baseline had severe functional mitral regurgitation. All of them had a reduction in MR grade by at least 1+, but after a one-year follow-up, one person had a regurgitation recurrence to grade 4+. Left ventricular remodelling, expressed as a reduction in left ventricular end-diastolic volume, was noticeable in 2 of the four reported cases and occurred only in cases where mitral regurgitation was significantly reduced.

Parameters evaluating the RV are presented in Table 2. In all cases, the RV dimension in distant observation was reduced. RVSP decreased in all cases where MitraClip treatment was effective. Pulmonary resistance increased > 6 Wood units only in a patient who had a recurrence of severe mitral regurgitation. No deterioration in the RV systolic function was observed. TAPSE before MitraClip and in distant observation were similar. At the same time, the parameters assessing RV performance considering the follow-up load (TAPSE/sPAP, [TR dP/dt]/TR V_{max}) improved or remained almost unchanged (PVEe) in patients with reduced mitral regurgitation. The RV-pulmonary artery coupling evaluated by TAPSE/sPAP ratio improved in all cases.

Discussion

According to the current recommendations, the MitraClip procedures should be avoided in patients with pulmonary hypertension exceeding 70 mm Hg and with severe RV dysfunction. Right ventricular volume overload resulting from left-to-right shunt causes an increase in pulmonary pressure, RV dilatation, and RV failure, and consequently is associated with increased mortality. Therefore, the qualification considering the recommendations reduces the deoxygenation risk described in the case of right-to-left leakage. However, the problem is the RV volume overload. There are no clear recommendations, mainly due to the difficulties in assessing the RV function.

So far, mainly iASD closures have been described in patients with persistent iASD. Proponents of this approach point out that in some cases, the iASD is spontaneously closed after a few months. Moreover, in the REDUCE LAP-HF study conducted on a population of patients with heart failure with preserved systolic function, the implantation of an interatrial shunt device reduced left atrium pressure. Also, 52% of patients showed a reduction in pulmonary capillary wedge pressure at rest, and in 34 cases (58%) presented lower pulmonary capillary wedge pressure during exertion, which resulted in increased exercise time [12]. These experiments, however, apply to a different patient population than those with heart failure with reduced ejection fraction and mitral regurgitation. So far, there is no data in that population to determine when iASD should be closed and when it is the optimal time for such a procedure. It is questionable whether it is rational to postpone the decision until a follow-up after a few months and expose the RV to volume overload for such a long period. Hence, an alternative approach may be to close the iASD immediately after its generation. This approach is also supported by the observations of Ussia et al. [1], who performed iASD closure in 3 patients who developed haemodynamic instability immediately after insertion of MitraClip. Two of these patients improved immediately [3].

The negative consequences of right heart overload due to iASD include increased tricuspid regurgitation, the rise of systolic pulmonary artery pressure, and worse NYHA functional class. Also, iASD was associated with poorer 6MWT results and higher NT-proBNP values [5].

The analysis of cases described in the present work shows that closing the iASD immediately after the MitraClip procedure is safe and prevents the development of right heart failure. In the cases described in this study, iASD closure was associated with a favourable reduction in the RV dimensions and the lack of progression of tricuspid regurgitation. In the GRASP registry comparing the results of MitraClip procedures in groups distinguished by the severity of tricuspid regurgitation, it was found that TR 4+/3+ deteriorates the patient prognosis. The composite endpoint of deaths and rehospitalizations for heart failure was significantly more frequent in the presence of 4+/3+ (67.7 vs. 88.8%; log-rank $p = 0.015$) [13]. Similarly, Meijerink et al. [14] found differences in the prognosis of patients undergoing MitraClip procedures depending on the coexisting tricuspid regurgitation. Survival of patients with severe TR after transcatheter mitral valve repair was 58% after two years compared to 82% for those with non, mild or moderate TR.

Closing the iASD immediately after the MitraClip also prevents an increase in RVSP. No patients had a higher RVSP on follow-up than in the baseline study in the reported cases. Preventing the rise of RVSP by closing the iASD may positively affect patients' prognoses. It was shown that the mortality rate of patients within a year from MitraClip was higher in the group of patients with elevated sPAP values. In the case of sPAP < 36 mm Hg, the mortality was 15.2%, for sPAP 37–50 mm Hg 24.4%, and in the group of patients with sPAP > 50 mm Hg, the annual mortality increased to 26.4% ($p < 0.01$) [15].

However, no studies assess the impact of pulmonary hypertension on the prognosis after MitraClip depending on the type of pulmonary hypertension: isolated post-capillary and combined pre-, and post-capillary pulmonary hypertension. Also, the COPAT study found that patients with PASP of ≥ 50 mm Hg had a higher both unadjusted (1.70; 95% CI: 1.34–2.14; $p < 0.0001$) and adjusted hazard ratio (1.52; 95% CI: 1.17–1.97; $p = 0.002$) risks of the 2-year composite endpoint of death or hospitalization for heart failure [16].

Rubbio et al. [17] proposed to evaluate the ratio of TAPSE to RVSP as an indicator of the RV-pulmonary artery coupling. TAPSE/sPAP ≤ 0.36 remained a sustained predictor of mortality and hospitalization for heart failure one year after MitraClip (hazard ratio: 3.87; 95% CI: 1.83–8.22; $p \leq 0.001$). This parameter was improved in all patients in the described cases and remained lowered below the reference value in only one patient, proving that the closure of iASD prevents the deterioration of RV functioning after the MitraClip procedure.

Conclusions

Closing the iASD immediately after inserting the MitraClip prevents the RV volume overload. It promotes greater efficiency of RV performance, consequently reducing the risk of aggravation tricuspid regurgitation and pulmonary hypertension, which are recognized factors of worse prognosis after MitraClip. However, the impact of iASD closure on patient prognosis requires a randomized trial.

Conflict of interest

There is no conflict of interest to declare.

Funding

The study was conducted thanks to the funds obtained from the Medical University of Silesia for statutory research.

Streszczenie

Wstęp. Powstawanie jatrogennego ubytku przegrody (iASD) podczas zabiegu MitraClip może wiązać się z niekorzystnymi konsekwencjami, między innymi z przeciążeniem objętościowym prawej komory serca skutkującym nasileniem objawów niewydolności serca, hospitalizacjami i zwiększoną śmiertelnością.

Celem tej pracy jest ocena wpływu jednoczesnego zamykania iASD podczas zabiegów MitraClip na funkcję prawej komory serca (RV).

Materiał i metody. Przeanalizowano przypadki 4 pacjentów, którzy przeszli zabieg MitraClip, u których zamknięto powstały iASD za pomocą okludera Amplatzer podczas indeksowanej procedury. Pacjenci byli obserwowani przez 12 miesięcy.

Wyniki. Całkowite zamknięcie iASD osiągnięto u wszystkich pacjentów. Nie było zgonów podczas 12 miesięcy obserwacji. We wszystkich przypadkach wymiary RV zmniejszyły się średnio z 38 ± 5,35 mm do 34,35 ± 5,06 mm. U żadnego pacjenta nie wystąpiła progresja niedomykalności trójdzielnej do niedomykalności istotnej (TR ≥ 3+). Ciśnienie skurczowe prawej komory (RVSP) zmniejszyło się ze średnio 47,50 ± 7,82 mm Hg do 38 ± 8,57 mm Hg.

Wnioski. Wyniki wskazują na korzystny wpływ równoczesnego zamknięcia iASD podczas procedury MitraClip poprzez zmniejszanie ekspozycji RV na przeciążenie objętościowe i związane z tym nasilenie niedomykalności trójdzielnej i nadciśnienia płucnego.

Słowa kluczowe: MitraClip, jatrogenny ubytek przegrody międzyprzedsionkowej, zamknięcie ubytku przegrody międzyprzedsionkowej

Folia Cardiologica 2022; 17, 3: 157–162

References

1. Ussia GP, Cammalleri V, Marchei M, et al. Hemodynamic patterns of residual interatrial communication after transcatheter MitraClip repair. J Cardiovasc Med (Hagerstown). 2014; 15(4): 343–349, doi: 10.2459/JCM.0000000000000006, indexed in Pubmed: 24699012.
2. Saitoh T, Izumo M, Furugen A, et al. Echocardiographic evaluation of iatrogenic atrial septal defect after catheter-based mitral valve clip insertion. Am J Cardiol. 2012; 109(12): 1787–1791, doi: 10.1016/j.amjcard.2012.02.023, indexed in Pubmed: 22475361.
3. Smith T, McGinty P, Bommer W, et al. Prevalence and echocardiographic features of iatrogenic atrial septal defect after catheter-based mitral valve repair with the MitraClip system. Catheter Cardiovasc Interv. 2012; 80(4): 678–685, doi: 10.1002/ccd.23485, indexed in Pubmed: 22422577.
4. Ikenaga H, Hayashi A, Nagaura T, et al. Left atrial pressure is associated with iatrogenic atrial septal defect after mitral valve clip. Heart. 2019; 105(11): 864–872, doi: 10.1136/heartjnl-2018-313839, indexed in Pubmed: 30482796.
5. Schueler R, Öztürk C, Wedekind JA, et al. Persistence of iatrogenic atrial septal defect after interventional mitral valve repair with the MitraClip system: a note of caution. JACC Cardiovasc Interv. 2015; 8(3): 450–459, doi: 10.1016/j.jcin.2014.10.024, indexed in Pubmed: 25703879.
6. Toyama K, Rader F, Kar S, et al. Iatrogenic atrial septal defect after percutaneous mitral valve repair with the MitraClip system. Am J Cardiol. 2018; 121(4): 475–479, doi: 10.1016/j.amjcard.2017.11.006, indexed in Pubmed: 29268934.
7. Huntgeburth M, Müller-Ehmsen J, Baldus S, et al. Postinterventional iatrogenic atrial septal defect with hemodynamically relevant left-to-right and right-to-left shunt as a complication of successful percutaneous mitral valve repair with the MitraClip. Int J Cardiol. 2013; 168(1): e3–e5, doi: 10.1016/j.ijcard.2013.05.018, indexed in Pubmed: 23711441.
8. Chandraprakasam S, Satpathy R. When to close iatrogenic atrial septal defect after percutaneous edge to edge repair of mitral valve regurgitation. Cardiovasc Revasc Med. 2016; 17(6): 421–423, doi: 10.1016/j.carrev.2016.04.005, indexed in Pubmed: 27162141.
9. Blazek S, Unterhuber M, Rommel KP, et al. Biventricular physiology of iatrogenic atrial septal defects following transcatheter mitral valve edge-to-edge repair. JACC Cardiovasc Interv. 2021; 14(1): 54–66, doi: 10.1016/j.jcin.2020.10.032, indexed in Pubmed: 33413865.
10. Lurz P, Unterhuber M, Rommel KP, et al. Iatrogenic atrial septal defects following transcatheter mitral valve repair and implications of interventional closure. JACC Cardiovasc Interv. 2021; 14(24): 2685–2694, doi: 10.1016/j.jcin.2021.09.023, indexed in Pubmed: 34949392.
11. Lurz P, Unterhuber M, Rommel KP, et al. Closure of iatrogenic atrial septal defect after transcatheter mitral valve repair: the randomized MITHRAS trial. Circulation. 2021; 143(3): 292–294, doi: 10.1161/CIRCULATIONAHA.120.051989, indexed in Pubmed: 33054368.
12. Hasenfuß G, Hayward C, Burkhoff D, et al. REDUCE LAP-HF study investigators. A transcatheter intracardiac shunt device for heart failure with preserved ejection fraction (REDUCE LAP-HF): a multicentre, open-label, single-arm, phase 1 trial. Lancet. 2016; 387(10025): 1298–1304, doi: 10.1016/S0140-6736(16)00704-2, indexed in Pubmed: 27025436.

13. Ohno Y, Attizzani GF, Capodanno D, et al. Association of tricuspid regurgitation with clinical and echocardiographic outcomes after percutaneous mitral valve repair with the MitraClip System: 30-day and 12-month follow-up from the GRASP Registry. Eur Heart J Cardiovasc Imaging. 2014; 15(11): 1246–1255, doi: 10.1093/ehjci/jeu114, indexed in Pubmed: 24939944.
14. Meijerink F, Koch KT, de Winter RJ, et al. Tricuspid regurgitation after transcatheter mitral valve repair: clinical course and impact on outcome. Catheter Cardiovasc Interv. 2021; 98(3): E427–E435, doi: 10.1002/ccd.29464, indexed in Pubmed: 33458911.
15. Tigges E, Blankenberg S, von Bardeleben RS, et al. Implication of pulmonary hypertension in patients undergoing MitraClip therapy: results from the German transcatheter mitral valve interventions (TRAMI) registry. Eur J Heart Fail. 2018; 20(3): 585–594, doi: 10.1002/ejhf.864, indexed in Pubmed: 29575435.
16. Ben-Yehuda O, Shahim B, Chen S, et al. Pulmonary hypertension in transcatheter mitral valve repair for secondary mitral regurgitation: the COAPT trial. J Am Coll Cardiol. 2020; 76(22): 2595–2606, doi: 10.1016/j.jacc.2020.09.609, indexed in Pubmed: 33243380.
17. Popolo Rubbio A, Testa L, Granata G, et al. Prognostic significance of right ventricle to pulmonary artery coupling in patients with mitral regurgitation treated with the MitraClip system. Catheter Cardiovasc Interv. 2022; 99(4): 1277–1286, doi: 10.1002/ccd.30044, indexed in Pubmed: 34939726.