stopped with significant artifact on a nonfocused and off-axis frame shown in the display. With routine clinical application of intracardiac echocardiography in more than 3,000 cases of left heart ablation, we noted that a right-to-left-flow shunting of rASD can be occasionally detected immediately following TC (**Figure 1**) when a patient has significantly increased pulmonary artery systolic pressure (PASP) (**Figures 1A to 1C**) or right heart dysfunction (**Figures 1D to 1F**). Schueler et al. (1) did not provide clear hemodynamic and cardiac functional evidence for worse clinical outcome and increased mortality related to persistent rASD with further increased PASP, severity of tricuspid regurgitation, or a right-to-left-flow shunt at their 6-month follow-up. Of note, Schueler et al. (1) provided discrepant baseline echocardiographic measurements between left ventricular diastolic volume (LVVd) and end-diastolic dimension (LVEDD) for the patients with rASD (191.6 ± 75.3 ml and 7.3 ± 0.7 cm, respectively) and no rASD (198.4 ± 80.2 ml and 6.1 ± 0.7 cm, respectively) in Table 3. The similar discrepancy is also noted between LV systolic volume and LV end-systolic dimension (LVESD) for these 2 patient groups. The LVEDD and LVESD are clinically reliable parameters, especially for patients with volume overload from MR, which have been used as rough surrogates for preload and afterload, respectively (4). These measurement discrepancies make it difficult to understand which parameter is more accurate. However, in Table 4, echocardiographic measurements of patients in follow-up only used the LVVd parameter, without including LVEDD measurements (1). Finally, in order to properly interpret the cause of increased mortality in these patients, the analysis should include all available data through the last available follow-up echocardiographic studies. Obviously, severe functional MR and significantly dilated LVEDD and LVESD at baseline are associated with increased mortality, not necessarily related to rASD with left-to-right shunt.

Iatrogenic rASD and its clinical effects, especially when using a large TC sheath, need further study. The investigators should be congratulated for reporting a high persistence of rASD at 6-month follow-up when using 21-F TC sheath for the MitraClip procedure. However, their data missed the opportunity for quantitative assessment over time on the size and flow features of rASD. Care is needed to identify hemodynamically significant changes and their impact on cardiac function and hemodynamics.

*Jian-Fang Ren, MD
David J. Callans, MD
Francis E. Marchlinski, MD

*Cardiac Electrophysiology Section
Division of Cardiovascular Medicine
University of Pennsylvania Health System
111 N 9th Street
Philadelphia, Pennsylvania 19107
E-mail: jianfren127@gmail.com

http://dx.doi.org/10.1016/j.jcin.2015.05.011

Please note: The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

REFERENCES

1. Schueler R, Ozturk C, Wedekind JA, et al. Persistence of iatrogenic atrial septal defect after interventional mitral valve repair with the MitraClip system: a note of caution. J Am Coll Cardiol Intv 2015;8:450–9.

2. Ren JF, Marchlinski FE, Callans DJ, Schwartzman D. Practical Intracardiac Echocardiography in Electrophysiology. Oxford, UK: Blackwell Publishing, 2006:64–5.

3. Singh SM, Douglas PS, Reddy VY. The incidence and long-term clinical outcome of iatrogenic atrial septal defects secondary to transseptal catheterization with a 12F transseptal sheath. Circ Arrhythm Electrophysiol 2011;4:166–71.

4. Grayburn PA, Foster E, Sangli C, et al. Relationship between the magnitude of reduction in mitral regurgitation severity and left ventricular and left atrial reverse remodeling after MitraClip therapy. Circulation 2013;128:1667–74.

REPLY: Quantitative Evaluation of Residual Atrial Septal Defect Following Transseptal Catheterization for Intracardiac Interventional Procedures

We thank Dr. Ren and colleagues for the comment on our paper (1).

Iatrogenic atrial septal defect (iASD) sizes were considerably smaller in our study than Ren et al. (2) found in previous analyses of procedures using smaller transseptal sheaths. They found that iASDs <4 mm had no clinical significance. In our opinion, the cited studies are not comparable to our results due to the fact that we treated mainly typical heart failure patients with a significant proportion of patients with severely reduced left ventricular ejection fraction (LVEF). Assuming that in our cohort, left atrial pressures are significantly higher than in a healthier cohort, the hemodynamic consequences and persistence rates may differ significantly due to markedly increased shunt volumes. In fact, the hemodynamic relevance of ASD must not be calculated based only on the sheer and may have overestimated shunt sizes. Hemodynamic consequences are directly related to the associated shunt volumes, and high-flow shunts with small diameters can lead to significant volume overload.

We cannot follow the comment of Dr. Ren and colleagues We showed clearly a right-to-left shunting. In our opinion, it is not suitable to compare

periprocedural intracardiac echocardiography with transesophageal echocardiography performed 6 months after transseptal puncture. We agree with Ren et al. that it is not clear whether iASD persistence accounts for adverse outcomes after MitraClip procedures or whether the persistence of an ASD just reflects adverse conditions, which lead to higher mortality and impaired functional outcomes.

The cited "discrepancies" between left ventricular end-diastolic and end-systolic volumes in patients with or without iASD were not statistically significant, and therefore, it is highly hypothetical to draw any conclusion from this finding, which might be due to play of chance in a small patient cohort. LVEF, derived from left ventricular end-diastolic and end-systolic volumes, was entered into regression analysis and failed to show significance for the prediction of 6-month mortality rates.

Most of all, the aim of our study was to assess the persistence rate of iASDs after MitraClip procedure and to report a possible influence on functional outcome. We did not aim to measure development of ASD sizes and echocardiographic flow features. We doubt the reliability of 2-dimensional echocardiography for sizing small iASDs occurring in mobile anatomical structures and echocardiography can only give us a rough estimate of the true ASD sizes. The hemodynamic consequences of ASDs should be determined with invasive measures as depicted by current guidelines (3,4).

We feel that our work contributes to a more careful evaluation of patients with persistent iASD after transseptal procedures, which might help lead to a better understanding and, in addition, to increased watchfulness regarding the clinical consequences of interatrial shunting in such patients.

Robert Schueler, MD
***Christoph Hammerstingl, MD**
*Medizinische Klinik und Poliklinik II
Universitätsklinikum Bonn
Sigmund-Freud-Strasse 25
53105 Bonn
Germany
E-mail: christoph.hammerstingl@ukb.uni-bonn.de

http://dx.doi.org/10.1016/j.jcin.2015.07.001

Please note: The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

REFERENCES

1. Schueler R, Ozturk C, Wedekind JA, et al. Persistence of iatrogenic atrial septal defect after interventional mitral valve repair with the MitraClip system: a note of caution. J Am Coll Cardiol Intv 2015;8:450–9.

2. Ren JF, Marchlinski FE, Callans DJ, Schwartzman D. Practical Intracardiac Echocardiography in Electrophysiology. Oxford, UK: Blackwell Publishing, 2006:64–5.

3. Warnes CA, Williams RG, Bashore TM, et al. ACC/AHA 2008 guidelines for the management of adults with congenital heart disease: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Develop Guidelines on the Management of Adults With Congenital Heart Disease). J Am Coll Cardiol 2008;52:e143–263.

4. Baumgartner H, Bonhoeffer P, De Groot NM, et al. ESC guidelines for the management of grown-up congenital heart disease (new version 2010). Eur Heart J 2010;31:2915–57.

Iatrogenic Atrial Septal Defect After MitraClip Therapy

After reading the recent paper in *JACC: Cardiovascular Interventions* by Schueler et al. (1) describing the persistence of iatrogenic atrial septal defects (iASDs) after MitraClip therapy, we wish to point out an important omission. The authors stated that "persistence rates of iASDs after MitraClip procedures [are] unknown," and "this is the first study investigating the persistence rates of iASD after interventional edge-to-edge repair." In fact, our group published the first investigation on this topic in 2012, and we were surprised to see that our paper was not referenced in the paper or accompanying editorial (2). We reported on the incidence of iASD in 30 subjects undergoing MitraClip repair during the roll-in phase of the EVEREST II (Pivotal Study of a Percutaneous Mitral Valve Repair System) randomized trial, who had interpretable baseline, 30-day, and 6- and 12-month transthoracic echocardiograms (TTE). We found that iASDs were detectable in 27% of patients at 12 months by TTE. Although this is lower than the 50% prevalence of iASD detected at 6 months by Schueler et al. (1), their group used transesophageal echocardiography, which is more sensitive for iASD detection. Similar to Schueler et al. (1), we found that there was less regression in left ventricular size in patients with iASD. Importantly, we found that subjects with iASD at 12 months had more residual mitral regurgitation (MR), increased tricuspid regurgitation, and a trend toward larger LA volumes than non-iASD patients. Eighty-three percent of non-ASD patients were free from MR >2+ at 12 months versus 38% of those with iASD ($p = 0.016$). We did not note any adverse clinical events related to the presence of iASD. It is probably fair to say that the true significance of iASD remains unknown and may be related to other procedural or patient-level factors not well understood. Consideration for transcatheter closure of iASD should be