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EDITORIAL COMMENT

Atrial Septal Defect Closure With the ReAces Device

Burning No Bridges*

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Fifty years ago, King and Mills performed the first percutaneous closure of atrial septal defect (ASD) using a double-umbrella device consisting of stainless-steel struts covered with Dacron. In the following decades, engineering refinements aimed to improve device deliverability, achieve complete closure, and minimize complications. Today, 2 Food and Drug Administration-approved and several CE-marked occluders with excellent performance profiles are used to close the majority of ASDs worldwide.[1] However, all these devices are permanent implants with a sizable footprint, making future access to the left atrium (LA) challenging and often unattainable. Although the feasibility of puncturing through currently available ASD occluders has been reported, the procedure is lengthy, often requires balloon dilation, and may impact the integrity and function of the device. With the growing number and complexity of transseptal procedures for structural defects, heart failure, and rhythm disorders, there is a renewed interest in closure devices that enable LA reaccess.

Historically, attempts to achieve this goal focused on assembling partially or completely bioabsorbable devices. However, up till today, the success of this approach has been limited. Albeit many bioabsorbable occluders have been introduced, only a few reached human testing.[1] The Immediate Release Patch (Custom Medical) did not attain wide acceptance due to its technically demanding implantation techniques and limited supportive data. The BioStar and BioTrek devices performed favorably but were discontinued in 2011 amid the insolvency of their manufacturer (NMT Medical). The newest biodegradable device (Carag Septal Occluder, CARAG) has shown promising results in a small proof-of-concept study.[2] However, its efficacy data remain limited pending the completion of its first early feasibility trial (Safety and Efficacy Study of reSept ASD Occluder for Treating Secundum ASD [ASCENT ASD]; NCT04591392). Furthermore, there are no data on the feasibility of LA reaccess after ASD closure with any of the bioabsorbable devices. Hence, efforts devoted to address this unmet need are welcome.

In this issue of *JACC: Basic to Translational Science*, Zhang et al[3] present preclinical and early clinical data on a completely different approach to LA-access preserving ASD closure: a "puncturable" ASD occluder. The novel ReAces device (Hanyu Medical) maintains the traditional 2 discs and middle-waist shape but features a unique central hole covered by polyethylene terephthalate (PET) membrane without a metal mesh. This membrane blocks blood flow between the atria but provides an easily puncturable platform for transseptal access. The waist's diameter ranges between 8 and 44 mm, and the puncturable area is slightly smaller than the waist. The occluder is delivered via a 12- to 16-F sheath according to its size. The investigators present their preliminary experience with the ReAces device in 14 swine and 10 humans. In the animal study, an iatrogenic ASD was created with a 20-mm balloon, and then closed in all animals with the ReAces occluder in the same setting. The diameter of the occluder was selected to be 6 mm

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The author attests he is in compliance with human studies committees and animal welfare regulations of the author's institution and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

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larger than the ASD diameter (as measured by echocardiography after the septostomy). The ReAces occluder was repunctured in 4 of 14 animals with a 14-F sheath at 60 days (n = 2) or at 180 days (n = 2), and this was successful in all 4 pigs with reaccess time ranging between 2.7 and 4.5 minutes. Gross examination of the septum in the 10 animals who did not undergo reaccess showed a well-seated device with evidence of endothelialization and no thrombus. The thickness of the central membrane was 2.2 ± 0.2 mm. Examination of the septum in the 4 animals where transseptal puncture was done through the device showed defects ~4 mm with no tears, thrombus, or device distortion. In the human study, 10 patients with septum secundum ASD (diameter 8 to 20 mm; 4/10 with a deficient aortic rim) were treated with a ReAces device (device diameter 14 to 30 mm). Procedural time was 22.8 ± 9.3 minutes, device success was 100%, and there were no complications. At a mean follow-up of 104.6 ± 9.5 days, echocardiographic examination showed complete closure, no residual shunt, and no thrombus in all patients. Five patients had a follow-up computed tomography examination that showed a considerably thinner middle portion of the device.

The paper by Zhang et al[3] in this issue of *JACC: Basic to Translational Science* represents an advance in the field, and elegantly illustrates the feasibility of ASD closure with a novel purpose-specific occluder designed to facilitate LA reaccess. However, there are several potential limitations with the study that warrant discussion. First, although the study was intended to demonstrate the feasibility of LA reaccess for various potential left-sided interventions after ASD closure, the investigators only tested reaccess with a single 14-F sheath, which represents the access needed for some, but not all, left-sided interventions. For instance, it remains unknown whether the ReAces occluders (especially small ones: 8-10 mm) would accommodate the larger bore (22- to 28-F) sheaths used for transcatheter mitral repair/replacement, or the double transseptal sheaths used for intracardiac echo-guided LA procedures. In addition, the feasibility of reaccess in this study was only assessed in the short term after ASD closure. It is plausible that further endothelization and hyperplasia could occur beyond the first 6 months, but whether that would impact the ease of LA reaccess through the occluder is uncertain. Second, although the investigators provide reassuring data about device healing after the index ASD closure in a limited number of cases, the healing of the central membrane after the second puncture was not evaluated. In clinical practice, the majority of small to medium-sized iatrogenic ASD spontaneously close, whereas a considerable proportion of large ASD (eg, 50% of ASD after mitral edge-to-edge repair) remain open at mid-term follow-up.[4] Although the clinical impact of persistent iatrogenic ASD is debatable, it would be important that future studies on the ReAces device consider the healing characteristics of the PET membrane after reaccess, as well as the feasibility of ASD reclosure with a similar or different occluder if needed. Third, the 10 patients who received the ReAces device in this study had single, small (8 to 20 mm) congenital ASDs. Further studies will be needed to evaluate the performance of the device in larger and more complex congenital ASD. The planned PASSER trial (Puncturable Atrial Septal Defect Occluder Trial; NCT05371366) will shed more light on this issue by enrolling patients with larger (up to 38 mm) ASD. Finally, the present study focused on the feasibility of closure of congenital ASD with the ReAces device. However, a large number of patients undergo transcatheter closure of patent foramen ovale. Will the ReAces occluder be also suitable for closure of these defects, or will its role be solely to treat congenital ASD? Can the ReAces occluder be used to effectively close iatrogenic ASD after large-bore left-sided interventions?

Forecasting the future needs of patient undergoing transcatheter interventions and identifying strategies to manage those needs is an emerging paradigm in structural heart interventions. Tailored implantation techniques and leaflet modification tools are now considered at the time of transcatheter aortic valve replacement to ensure the feasibility of future valve-in-valve therapy.[5] Electrosurgical laceration has also been performed to facilitate transcatheter valve replacement in patients with recurrent mitral regurgitation after edge-to-edge repair.[6] Coronary sinus shunts have emerged as a possible alternative to atrial septal shunting devices to preserve LA access.[7] In this realm, the ReAces device represent an important step forward in the lifetime management of patients with ASDs. Future studies such as the PASSER trial will hopefully address the open questions and build the evidence needed to validate the potential role of this innovative approach.

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REFERENCES

1. Kogure T, Qureshi SA. The future of paediatric heart interventions: where will we be in 2030? *Curr Cardiol Rep*. 2020;22:158.

2. Sievert K, Bertog S, Soderberg B, et al. Transcatheter closure of atrial septal defect and patent foramen ovale with Carag bioresorbable septal occluder: first-in-man experience with 24-month follow-up. *EuroIntervention*. 2022;17:1536–1537.

3. Zhang X, Chen S, Li W, et al. A novel puncturable atrial septal defect occluder: the results of preclinical experiment and first-in-human study. *J Am Coll Cardiol Basic Trans Science*. 2022;7:1200–1210.

4. Alkhouli M, Sarraf M, Zack CJ, Holmes DR, Rihal CS. Iatrogenic atrial septal defect following transseptal cardiac interventions. *Int J Cardiol*. 2016;209:142–148.

5. Rogers T, Greenspun BC, Weissman G, et al. Feasibility of coronary access and aortic valve reintervention in low-risk TAVR patients. *J Am Coll Cardiol Intv*. 2020;13:726–735.

6. Bartkowiak J, Reineke D, Tomii D, et al. Electrosurgical laceration and stabilization of MitraClip followed by valve implantation for iatrogenic mitral stenosis. *J Am Coll Cardiol Intv*. 2022;15:110–112.

7. Alkhouli M, Lurz P, Rodes-Cabau J, et al. Transcatheter coronary sinus interventions. *J Am Coll Cardiol Intv*. 2022;15:1397–1412.

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