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Original Article

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An animal study to evaluate the safety and efficacy of a novel superelastic sizing device

Abstract

Aim: Atrial septal defect measurement can be performed by stretching balloon diameter, two- and 3-dimensional transesophageal echocardiography (TEE). We evaluated a new superelastic sizing device (SSD) for deliniation of atrial septal defect margins and exact measurement without changing anatomy of the defect.
Material and Methods: An artificial ASD was created in 8 swines and defect sizing was done by TEE and SSSD in fluoroscopy and autopsy. Correlation analysis was done between 3 methods in defect size measurement. Any adverse events, such as mortality or heart perforation were assessed.
Results: There was a cardiac tamponade case in one animal because of the limited animal experience of the operator. Thrombus formation was observed in some animals due to prolongation of procedure time and low heparin dosage. SSD and TEE correlation ($r=0.97$, $p<0.0001$); TEE and autopsy correlation ($r=0.973$, $p<0.0001$); SSD and autopsy correlation ($r=0.993$; $p<0.0001$) all were statistically significant.
Conclusion: In our animal study superelastic sizing device precisely delineated atrial septal defect margins on TEE and fluoroscopy. SSD measurements showed good correlation with TEE and autopsy measurements. The right and left portions of the device were well formed and central indentation allowed exact sizing of the atrial septal defect margins.

Keywords: Atrial septal defect measurement, two- and three-dimensional transesophageal echocardiography, superelastic sizing device

INTRODUCTION

Developing medical technology allowed treatment of atrial septal defects (ASD), ventricular septal defects (VSD), patent foramen ovale, patent ductus arteriosus, mitral and aortic valve diseases in cardiac catheterization laboratory without open heart surgery. Percutaneous catheter-based methods have become a very successful standart approach for many of adult and childrens (1,2).

Exact sizing and relationship of ASD to neighboring structures is very important in percutaneous treatment of the defect. Stretch balloon diameter (SBD) sizing is accepted as gold standart for device selection in ASD closure but SBD could overestimate defect size in some patients (3-5). Two-dimensional transesophageal echocardiography (TEE) may give details about ASD anatomy, but one cross-sectional image may undestimate defect size (6-10). Two-dimensional TEE is also used to guide device deployment intraprocedurally (9,11-13). Three-dimensional TEE may demonstrate entire anatomy and post deployment procedure better than two-dimensional TEE (14). Intracardiac echocardiography (ICE) has recently been used instead of TEE (15), but lack of long-term data is not available for ICE use instead of balloon sizing.

Superelastic sizing device (SSD) has a base structure identical to all braided shape memory devices and is made of nitinol wires with an atraumatic soft tip design not to harm the surrounding tissue but to position the sizing device inside cavity to be measured to minimize the risk of mis measurement of defect location (Figure 1). A flexible delivery system is used with SSD which allows easy device advancing in difficult anatomies like angulation between catheter and the device shaft (Figure 2). The balloon-like shape memory braided structure is entirely new, and it is made by brand new molding technology which was patented with two different sizes and designs (Figure 3). The core wire for pushing and pulling is designed extra flexible to expand and straighten to fit into difficult anatomies. This forms an excellent structure for the formation of the sizing device in difficult locations and cavities to measure with other techniques. The device has a minimum radial strength in order not to stretch the surrounding tissue and netlike structure of SSD permits perfusion during procedure. Superleastic sizing device is intended for medical interventional measurement and imaging fields in all internal body cavities and holes with similar anatomies in a safe manner. Radiopaque markers on SSD provide measurement of distances in angiography and echocardiography. Thus, TEE, transthoracic echocardiography (TTE) and angiographic measurements can be integrated with proper hardware and software. SSD is a universal defect measurement and dimensioning device which can be used together with any imaging device or can be used alone for the intended purpose (Figure 3,4).

Figure 1. Open superelastic sizer device

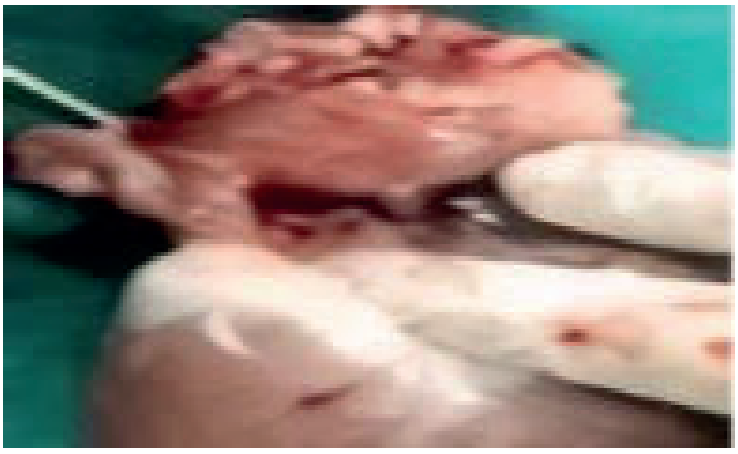

Figure 2. Autopsy image of created ASD

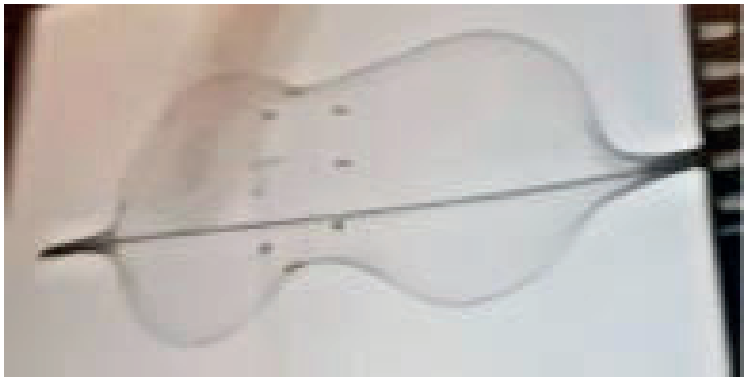

Figure 3. Fluoroscopic image of a deployed SSD in ASD

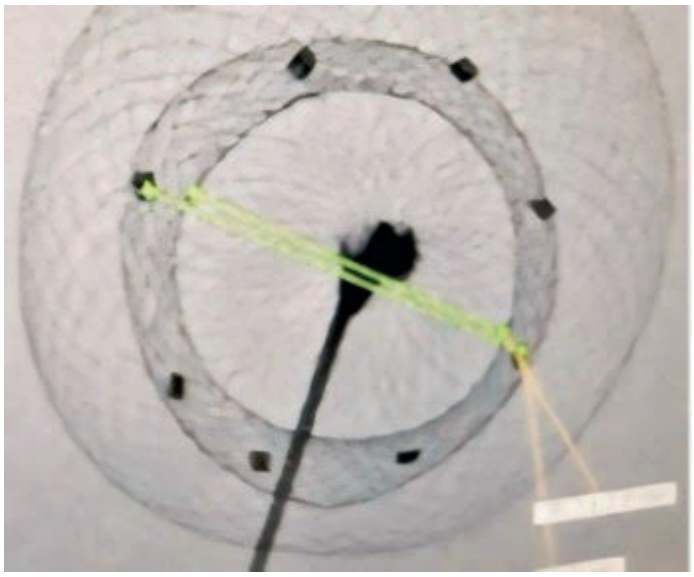

Figure 4. Enface view of diameter measurements in a SSD in atrial septal defect

The purpose of this study was an animal study to evaluate the safety and effectiveness of a novel superelastic sizing device designed by the research team.

MATERIAL AND METHODS

8 young adult swines weighing between 35-45 kg were enrolled into the study. Power analysis was performed, and the optimum number of animals was determined. The present study was approved by the İstanbul Mehmet Akif Ersoy Experimental Research, Development and Training Center, approval numbers [2018/18]. An atrial septal defect was created in animals by operators in animal catheterization laboratory under fluoroscopy. TEE was used to detect the location of the device and compare the measured ASD lengths with SSD device measured lengths under fluoroscopy. Created defect size was also measured at autopsy (Figure 2). Any adverse events, such as mortality or heart perforation were assessed. The correlation between 3 different measurement methods was examined by the Pearson correlation coefficient using the SPSS software (version 19, SPSS Inc., Chicago, IL, USA). There was a significant difference at the level of $P<0.05$.

Measurement Procedures

All animals received aspirin (300 mg) per os 1 day before the planned device intervention. Before the device procedure animals received 10000 IU unfractionated heparin, supplemented with additional 2000 IU heparin every hour during the implantation procedure, or as needed if a thrombus was seen in the animal's circulation. All animals were intubated, and the procedure was performed under general anesthesia.

The right femoral vein and left femoral artery were catheterized under ultrasonography with an introducer. A 6 Fr right coronary diagnostic catheter was introduced into the right atrium to inject contrast media to visualize the right atrium and the septum. Transseptal needle catheter was then advanced to perform septostomy with several attempts. A 0.035-inch guidewire was placed to the left atrium either through septostomy or patent foramen ovale (PFO) to guide the Mullin's sheath to left atrium where the sizing device was to be placed to measure the defect created on atrial septum or orifice of PFO. Using the angiographic right superior oblique position the femoral vein sheath was replaced via a specific long sheath, which was detected by TEE guidance. A 5 Fr pigtail catheter was inserted into the left atrium in order to inject contrast media after positioning of the long sheath transseptally. The size of the SSD was chosen according to created defect diameter. The SSD was loaded into the 12 Fr. Mullin's sheath and was pushed out of the the sheath across the septal defect to create an hour-glass shape. Hour-glass shape was obtained by pulling the core wire of the device until obtaining the best location and visual image on the fluoroscopy screen and core wire was pulled back safely until enough resistance was met to ensure device safety and measure precise defect diameter. The proximal and the distal part of the SSSD created a larger diameter than the device to show the exact location of the defect (Figure 3,4). Three-dimensional TEE images of the deployed devices were obtained in some of the animals (Figure 5) and fluoroscopic images were obtained in all animals (Figure 6).

Prior to euthanasia, TEE with color doppler was performed, macroscopic photographic documentation of the explanted hearts was performed on some of the animals and ex vivo native radiology acquisition was performed in all animals. The explanted tissue was evaluated macroscopically during the autopsy and fixated in formalin according to the evaluation protocol.

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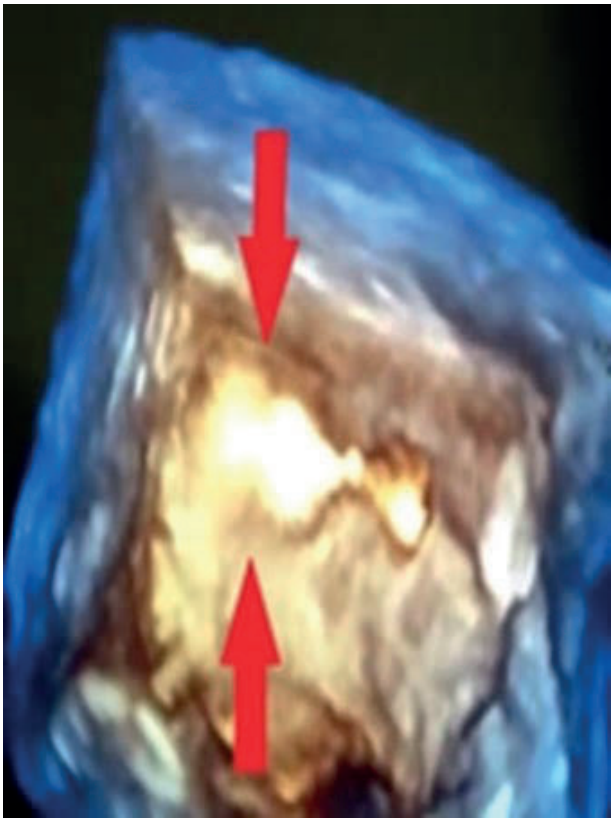

Figure 5. Three dimensional echocardiographic image of an SSD in an atrial septal defect

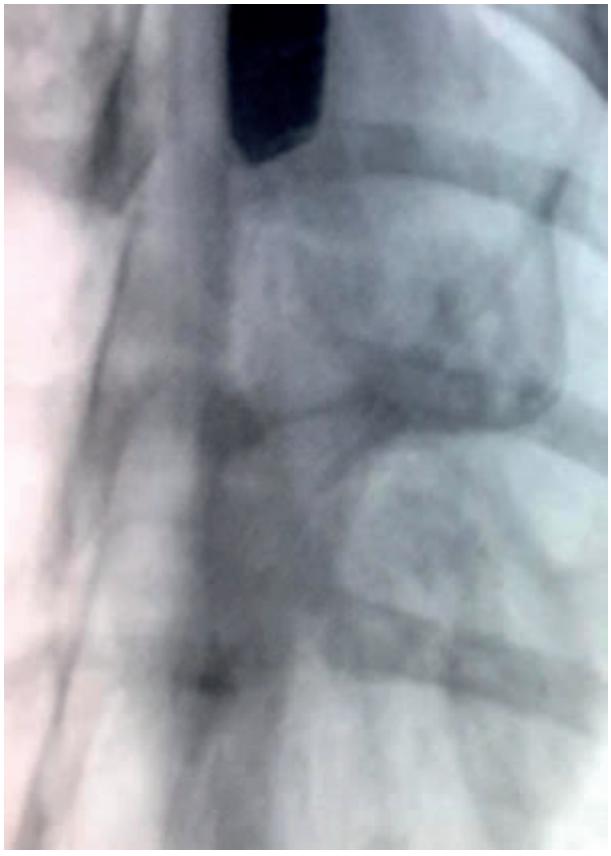

Figure 6. Fluoroscopic image of deployed SSD in swine

RESULTS

There was a cardiac tamponade and death in first animal because anatomy is slightly different from humans and physicians had limited experience with septostomy in pigs. We were not able to make measurements in that animal and it was excluded from analysis. Thrombus formation was observed in 2 animals due to prolongation of procedure time and low heparin dosage. Activated clotting time measurement was not available in animal laboratory.

Due to the difficulty of fixing the distance between the probe and the animals heart (the beating heart and ventilation changes the length between the probe and the atrial septum dramatically), the cases were performed with TEE guidance on all animals but 3D TEE was performed on only 1 animal.

SSD and TEE measurement correlation was statistically significant (r=0.97, p<0.0001). TEE and autopsy measurement correlation was statistically significant (r=0.973, p<0.0001). SSD and autopsy measurements correlation was also significant in correlation analysis (r=0.993; p<0.0001) (Table 1).

Table 1. Correlation between atrial defect size measured in autopsy, TEE and superelastic sizer device

	ASD size in TEE, mm	ASD superelastic sizer measure in fluoroscopy, mm	ASD size in autopsy, mm
ASD size in TEE (Pearson correlation, r/p value)	1	r=0.97 p<0.0001	r=0.973 p<0.0001
ASD superelastic sizer measure in fluoroscopy (Pearson correlation, r/p value)	r=0.97 p<0.0001	1	r=0.993 p<0.0001
ASD size in autopsy (Pearson correlation, r/p value)	r=0.973 p<0.0001	r=0.993 p<0.0001	1

DISCUSSION

In ASD catheter closure balloon sizing is very effective but overestimating ASD size by balloon overstretching of the defect which may lead to device erosion. There is no randomized study comparing ICE vs balloon sizing, but ICE alone can be precise and safe during ASD closures. One drawback of ICE is investment in devices and expensive catheters which inflates procedure costs. Three-dimensional (3D) TEE can be used instead of balloon sizing occlusion device diameter selection, but 3D TEE is not available in every catheterization laboratory (11).

In our animal study SSD precisely delineated atrial septal defect margins. Right and left portions of the device were well formed and central indentation allowed exact sizing of the atrial septal defect. TEE, X-ray and autopsy measurements were well correlated in our study. Superelastic texture of the device allows real sizing of the defects by easily conforming to anatomy and avoids modification of real anatomy. Operator gets an idea about defect rims while slowly pushing and pulling the device to form double disc configuration of the device. Left disc of the device preliminarily shows definite aortic position of the real device beforehand when used in atrial septal defect closure. SSD device also does not need 3D TEE expertise and can be used by an average interventional cardiologist. Blood flow in interatrial septum and and right and left atrium is not disturbed during SSD formation in septum. SSD device can be very helpful in small children and hemodynamically unstable patients because it is not obstructing blood flow. There was a cardiac tamponade case in one animal because of the limited animal experience of the operator. Perforation of cardiac structure was not related to device but wrong puncture site. Thrombus formation was observed in some of the animals due to prolongation of procedure time, low heparin dosage and probably lack of measurement of ACT during prolonged procedure times.

Individualization according to the needs of a patient, physician experience, familiarity with each method, and common sense should be used during ASD or other orifice sizings. When in doubt SSD sizing provides additional information without a need for expertise and additional hardware or software in precisely defining the size of the ASD.

CONCLUSION

In conclusion, the superelastic sizing device demonstrated excellent precision in delineating atrial septal defect (ASD) margins, as observed on transesophageal echocardiography (TEE) and fluoroscopy during animal studies. Measurements obtained with the device correlated well with those from TEE and autopsy, confirming its accuracy and reliability. The well-formed right and left portions, along with a central indentation, facilitated exact sizing of the ASD margins. These findings highlight the device's potential as a valuable tool in accurately assessing ASD dimensions, paving the way for improved procedural planning and outcomes in clinical settings.

Conflict of Interests: Mehmet Hakan Akpinar is inventor and producer of superleastic sizing device.

Financial Disclosure: The authors declare that there is no financial support.

Ethics Committee Approval: The present study was approved by the İstanbul Mehmet Akif Ersoy Experimental Research, Development and Training Center, approval numbers [2018/18].

Patient Informed Consent: The patients included in the study were informed in detail about the operative and postoperative process and their written consent was obtained.

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