# Lipomatous Atrial Septal Hypertrophy: A Review of Its Anatomy, Pathophysiology, Multimodality Imaging, and Relevance to Percutaneous Interventions



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Lipomatous atrial septal hypertrophy (LASH) is a histologically benign cardiac lesion characterized by excessive fat deposition in the region of the interatrial septum that spares the fossa ovalis. The etiology of LASH remains unclear, though it may be associated with advanced age and obesity. Because of the sparing of the fossa ovalis, LASH has a pathognomonic dumbbell shape. LASH may be mistaken for various tumors of the interatrial septum. Histologically, LASH is composed of both mature and brown (fetal) adipose tissue, but the role of brown adipose tissue remains unclear. In interventional procedures requiring access to the left atrium, LASH may interfere with transseptal puncture, as traversing the thickened area can reduce the maneuverability of catheters and devices. This may cause the needle to enter the epicardial space, causing dangerous pericardial effusions. LASH was once considered a contraindication to percutaneous device closure of atrial septal defects because of an associated increased risk for incorrect device deployment. However, careful attention to preprocedural imaging and procedural intracardiac echocardiography enable interventional cardiologists to perform procedures in patients with LASH without serious complications. In this review article, the authors describe anatomic and functional aspects of LASH, with emphasis on their roles in percutaneous interventions. (J Am Soc Echocardiogr 2016;29:717-23.)

Keywords: Lipomatous atrial septal hypertrophy, Transseptal puncture

Over the past several years, there has been a marked increase in the number of percutaneous cardiac procedures performed requiring a transseptal approach and echocardiographic guidance.<sup>1</sup> These include atrial arrhythmia ablation, left atrial appendage occlusion, mitral balloon valvuloplasty, mitral clipping, and closure of paravalvular leaks of mitral prostheses. Additional procedures are being developed, including percutaneous mitral valve replacement. Therefore, knowledge of the anatomy of interatrial septum, including lipomatous atrial septal hypertrophy (LASH), is crucial for echocardiographers.

LASH is a histologically benign lesion of the heart characterized by excessive fat deposition in the region of the interatrial septum.<sup>2</sup> The magnitude of fat accumulation is defined as >2.0 cm in thickness.<sup>3-</sup>

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0894-7317/\$36.00

Copyright 2016 by the American Society of Echocardiography. http://dx.doi.org/10.1016/j.echo.2016.04.014 <sup>5</sup> It was first described in 1964 in postmortem specimens.<sup>6</sup> LASH is encountered in a significant number of individuals, but its exact prevalence is not known. The reported prevalence ranges from 2.2% in patients undergoing multislice computed tomography (CT) to approximately 8% in patients referred for transesophageal echocardiography (TEE).<sup>3,7</sup> LASH is associated with advanced age and obesity<sup>3,7</sup> and may be associated with an increased risk for atrial arrhythmias.<sup>8</sup> Here we describe anatomic and functional aspects of LASH, emphasizing their roles in percutaneous interventions.

## ANATOMY: WHERE IS LASH LOCATED?

Although LASH is technically referred to as lipomatous hypertrophy of the interatrial septum, this is a misnomer.<sup>9</sup> Anatomically, the true interatrial septum is confined to the region of the fossa ovalis and the area just below the fossa near the orifice of the tricuspid valve (the septum primum). The muscular rim surrounding the fossa in the superior, anterior, and posterior margins (the embryologic septum secundum) is in fact an infolding of the atrial wall extending into the right atrial cavity with epicardial fat on the outside.<sup>1,10</sup> These infoldings are sometimes referred to as Søndergaard's groove or Waterston's groove.<sup>9</sup> The fat accumulation of so-called LASH does not actually occur within the true septal tissue but rather in infoldings of the atrial wall adjacent to the true interatrial septum.

LASH has a pathognomonic "dumbbell" shape, as fat accumulation is cephalad and caudad to the fossa ovalis, with sparing of the fossa itself.<sup>11,12</sup> The cephalad thickening is usually more extensive than the caudad, and both masses project into the right atrial cavity. Furthermore, the cephalad component is contiguous with the rest

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| <b>ASD</b> = Atrial septal defect |
|-----------------------------------|
| <b>BAT</b> = Brown adipose tissue |
|                                   |

**CT** = Computed tomography

FDG = Fluorodeoxyglucose

**ICE** = Intracardiac echocardiography

**LASH** = Lipomatous atrial septal hypertrophy

**MRI** = Magnetic resonance imaging

**TEE** = Transesophageal echocardiography

**3D** = Three-dimensional

of the subepicardial fat, which is generally markedly increased in patients with LASH.<sup>13</sup>

Although LASH is typically confined to the atrial infoldings,<sup>14</sup> fat accumulation can be so extensive that it emulates a neoplasm. On very rare occasions, it may extend toward the superior vena cava, causing obstruction of right atrial inflow. Patients with vena cava obstruction may present with symptoms of congestive heart failure.<sup>15</sup>

## EMBRYOLOGY

The exact etiology of LASH is unclear. However, it has been postulated that fat accumulation is due to embryologic development of the interatrial septum.<sup>16</sup> In utero, the septum secundum and septum primum fuse, leaving the foramen ovale as the residual communication. Outgrowths of tissue from the walls of the primitive atria create infoldings that fuse with the region of fossa ovalis to form the apparent edges of the interatrial septum. During this fusion, mesenchymal cells become trapped within the atrial wall and later develop into mature adipocytes with appropriate stimuli.<sup>16</sup>

#### HISTOLOGY

As previously described, LASH is located outside the true interatrial septum (the fossa ovalis). Microscopically, the myocardial fibers of the septum secundum are infiltrated with mature adipose cells interspersed with a variable number of vacuolated fetal fat cells.<sup>17</sup> Myocardial cells are seen entrapped in the mass and show hypertrophic, degenerative, or atrophic changes.<sup>17</sup>

Many reports suggest that LASH consists predominantly of mature adipocytes (also known as white fat) and that there is a positive correlation between LASH and generalized obesity.<sup>3,11,14</sup> It is important to note that histologically, LASH does not represent a malignancy, because mitoses are absent.<sup>14</sup> Furthermore, because there is no capsule around the fat deposits, LASH is a distinct entity from lipoma.

Interestingly, studies have also suggested the presence of brown fat (also known as fetal fat) in LASH.<sup>12,18</sup> These cells are distinguishable from surrounding mature adipose tissue by their vacuolated cytoplasm and more centrally placed nuclei.<sup>14</sup> The exact role of this brown adipose tissue (BAT) is a subject of debate. Some investigators have shown that focally increased fluorodeoxyglucose (FDG) uptake occurs in LASH and postulated that the metabolic activity of the brown tissue is the reason for this finding.<sup>12</sup> However, more recent studies have questioned this theory, arguing that the mechanism of FDG uptake in LASH differs from that of brown fat elsewhere in the body.<sup>19</sup> These researchers instead suggest that the increased uptake may be secondary to an inflammatory process in LASH.

A recent case report of a patient with LASH and isolated mediastinal FDG uptake in the interatrial septum (mimicking metastasis) suggests the possibility that neither brown fat nor inflammation is the reason for uptake.<sup>20</sup> The investigators pointed out that activation of BAT is usually due to cold temperature, and external warming has been shown to deactivate BAT and reduce FDG uptake. They went on to explain that although inflammatory uptake in lesions is usually confirmed by washout of FDG on delayed imaging, there was no decrease in uptake on external warming or on delayed time point imaging in their patient. This suggests that uptake may not be due to metabolic activity of BAT or inflammation and thus that there must be an alternative explanation for FDG accumulation in this condition.

#### **CLINICAL SIGNIFICANCE**

Although LASH is considered a histologically benign entity and is usually clinically silent, it has on rare occasion been associated with atrial arrhythmias and even more rarely with sudden death.<sup>3,8</sup> As previously noted, the prevalence of LASH increases with age and obesity. Given that older age and obesity are risk factors for atrial fibrillation, more analyses are needed to determine if an independent relationship between LASH and arrhythmias exists.<sup>21</sup> Nonetheless, in an elderly and/or obese patient with an atrial arrhythmia in the absence of other causative factors (such as congenital or valvular heart disease, atriomegaly, or sick sinus syndrome), the arrhythmia may be due to LASH.<sup>13</sup>

A possible explanation for this association is the progressive disruption of myocardial fibers that result from fat accumulation and infiltration into pathways that ordinarily facilitate orderly atrial depolarization.<sup>13</sup> This disorganization of fibers ultimately leads to fibrosis, with consequent impairment of contractility and electrical conduction.<sup>12</sup>

Case reports have described the association of LASH with serious cardiac arrhythmias resulting in sudden death. In these patients, post-mortem examination revealed LASH and no other pathologic findings.<sup>22,23</sup> The authors of these reports have suggested that the location of LASH (i.e., in the area of the sinoatrial node) and its anatomic distribution within the septum may have contributed to the incidence of malignant arrhythmias. They also observed that the total volume of fat tissue may be a major factor in the development of arrhythmias,<sup>22,23</sup> especially given that the incidence of atrial arrhythmia appears to be related to septal thickness.<sup>22</sup>

#### **IMAGING OF LASH**

Multiple imaging modalities, including echocardiography, CT, and magnetic resonance imaging (MRI),<sup>11</sup> can be used to diagnose LASH. Irrespective of the imaging modality, LASH has a characteristic dumbbell appearance of the interatrial septum, with sparing of the fossa ovalis. This typical appearance is often sufficient to establish the diagnosis of LASH by echocardiography. In less typical cases, confirmation of its fatty composition may be obtained by either CT or MRI.<sup>12</sup>

On standard and contrast-enhanced CT (Figure 1), LASH appears as a homogenous, dumbbell-shaped mass of fat attenuation that is confined to the region of the interatrial septum; it has smooth margins and is nonenhancing.<sup>16</sup> Because CT identifies relative densities, it aids in differentiating LASH, which has the attenuation coefficient of adipose tissue, from neoplasms and other entities.<sup>13</sup>

MRI can provide additional information (Figure 2) about the extension of the process into the interventricular septum and



**Figure 1** LASH on CT. Axial computed tomographic images of lipomatous hypertrophy of the interatrial septum (*arrows*), shown on both unenhanced **(A)** and contrast-enhanced **(B)** images. The low attenuation (i.e., *dark* appearance) and lack of enhancement are characteristic of lipomatous hypertrophy on CT. *LA*, Left atrium; *LV*, left ventricle; *RA*, right atrium; *RV*, right ventricle.



**Figure 2** LASH on MRI. Cardiac magnetic resonance images of four-chamber views of lipomatous hypertrophy of the interatrial septum (*arrows*) on steady-state free precession (**A**) and T2-weighted images (**B**). The high signal (i.e., *bright* appearance) on T2-weighted images is characteristic of lipomatous hypertrophy on MRI. *LA*, Left atrium; *LV*, left ventricle; *RA*, right atrium; *RV*, right ventricle.

#### LASH MASQUERADERS

ventricular free wall and is useful in distinguishing fat from solid, fibrous, or cystic tissue.  $^{18}\,$ 

Two-dimensional transthoracic echocardiography and TEE are often the diagnostic modalities of choice for identifying LASH (Figure 3 and Video 1, available at www.onlinejase.com; Figures 4A and 4B and Videos 2 and 3, available at www.onlinejase.com).<sup>7,24</sup>

Intracardiac echocardiography (ICE) and three-dimensional TEE (Figure 4C and Video 4; available at www.onlinejase.com) may provide additional information to aid in making the correct diagnosis. For example, one case report illustrated the use of both two-dimensional and three-dimensional (3D) TEE in distinguishing between LASH and lymphoma, concluding that a combination of clinical scenario, multiple two-dimensional transesophageal echocardiographic views, and 3D reconstruction images can be helpful in differentiating these two entities.<sup>25</sup>

LASH has been mistaken for various intracardiac masses in the past, but echocardiography, CT, and MRI have made diagnosis possible without biopsy and histologic analysis. The differential diagnosis of LASH includes benign and malignant cardiac tumors involving the interatrial septum, such as metastases, myxomas, rhabdomyomas, fibroelastomas, and mesotheliomas.<sup>16</sup>

The most likely alternative diagnoses include myxomas and lipomas. However, myxomas arise from the interatrial septum near the fossa ovalis and typically have a stalk, whereas lipomas are encapsulated. Imaging techniques can thus differentiate these entities from LASH, which is noncapsulated and always spares the fossa ovalis.<sup>11</sup>

As previously mentioned, LASH can also be mistaken for lymphoma, although multiple two-dimensional transesophageal



**Figure 3** LASH on transthoracic echocardiography. Images of lipomatous hypertrophy of the interatrial septum (*asterisks*), with characteristic sparing of the fossa ovalis (*arrow*). **(A)** Apical four-chamber view. **(B)** Subcostal four-chamber view. *LA*, Left atrium; *LV*, left ventricle; *RA*, right atrium; *RV*, right ventricle.

echocardiographic views and 3D reconstruction can aid in the correct diagnosis.<sup>25,26</sup> One report discussing the differentiation of these two disease processes noted that in some views, involvement by lymphoma may resemble a coin lesion, in which multiple small echodensities lie within an echolucent area circumscribed by a rim of echogenic tissue. Conversely, in LASH, fat infiltration typically appears more diffuse, with significantly fewer echolucent areas.

As noted above, it has been shown that there is an increase in focal FDG uptake in LASH, which can contribute to false interpretation of malignancy.<sup>12</sup> Thus, it is important to correlate these findings with the appearance of LASH on CT or MRI to avoid misdiagnosis.

# RELEVANCE TO INTERVENTIONAL PROCEDURES

Any procedure requiring transseptal puncture through the hypertrophied area carries additional challenges and risks. In fact, LASH is



**Figure 4** LASH on TEE. The fossa ovalis has a thin floor (*arrow*); its rims (*asterisks*) are demarcated by fat accumulation. **(A,B)** Two-dimensional TEE, bicaval view. **(C)** Three-dimensional TEE, en face view of the interatrial septum from the right atrial perspective. *AV*, Aortic valve; *IVC*, inferior vena cava; *LA*, left atrium; *LV*, left ventricle; *RA*, right atrium; *RV*, right ventricle; *SVC*, superior vena cava.



**Figure 5** Transseptal puncture through LASH complicated by intracardiac shunt. An intracardiac shunt (*arrows*) between the right and left atrium is created after a transseptal puncture through the LASH (*asterisks*) seen in the midesophageal four-chamber view **(A)** and midesophageal short-axis view at the level of the aortic valve **(B)**. *AV*, Aortic valve; *LA*, left atrium; *LV*, left ventricle; *RA*, right atrium; *RV*, right ventricle.

typically included in the list of challenges for transseptal puncture alongside atrial septal aneurysm and previous atrial surgery. $^{27}$ 

Ideally, the septum should be crossed through the thin portion of the septum.<sup>1</sup> However, LASH may interfere with directing the needle to the fossa ovalis. Transseptal puncture attempted through the lipomatous area would require a higher degree of force than is normally required to cross into the left atrium. If excessive force is applied to the puncture apparatus, it is possible that the needle will pierce the roof or posterior wall of the atrium or an adjacent structure such as the aortic root.<sup>27</sup> Additionally, puncturing of the hypertrophied area can reduce maneuverability of the catheter after entering the left atrium.<sup>1</sup> This may lead to dangerous consequences, for example, needle puncture of the heart past the epicardium, resulting in pericardial effusion or an intracardiac shunt (Figure 5 and Video 5; available at www.onlinejase. com). Furthermore, delivery of intracardiac devices into the left atrium may also prove to be more problematic, such as passing a dilator and sheath assembly into the left atrium during a catheter ablation in a patient with atrial fibrillation.<sup>28</sup> However, successful percutaneous procedures can be performed even if transseptal puncture is done through the LASH (Figure 6).

There is a paucity of published data on technical issues and complications of transseptal puncture in patients with LASH. The available literature is summarized in Table 1. Three-dimensional transesophageal echocardiographic imaging modalities may improve safety and



**Figure 6** Lariat procedure in a patient with LASH. Successful transseptal puncture through LASH (*asterisks*) in a patient undergoing left atrial appendage (LAA) exclusion using the Lariat device is visualized by two-dimensional TEE (**A**) and 3D TEE (**B-D**). In (**A**), the *arrow* points to a very small residual left-toright shunt on color Doppler through LASH post-transseptal puncture. In (**B**), a transseptal catheter is seen passing through the superior edge of LASH from the right atrial perspective is seen. LAA orifice is visualized before (**C**) and after closure with the Lariat device (**D**). *AV*, Aortic valve; *LA*, left atrium; *PA*, pulmonary artery; *RA*, right atrium; *SVC*, superior vena cava.

prevent complications related to transseptal puncture in these patients. Identifying the exact location of septal tenting before actual puncture is key. Once proper location of tenting is confirmed by imaging, the Brockenbrough needle is advanced and transseptal puncture is performed. Biplane and 3D zoom imaging are two specific 3D transesophageal echocardiographic imaging modalities that are

| Table 1 Summary   | of published complications in pa                                | tients with LA        | SH undergoing transcatheter procedures  |  |
|-------------------|---|-----------------------|---|--|
| Procedure         | Publication   | Number<br>of patients | Device(s) used  | Results/complications  |
| ASD closure       | Lin <i>et al.</i> Catheter Cardiovasc<br>Interv 2011;78:102-107 | 2                     | Amplatzer muscular ventricular septal defect occluder (AGA Medical, Plymouth, MN)   | No residual right-to-left shunt at 1-mo follow-up.   |
| PFO closure       | Rigatelli <i>et al.</i> J Cardiovasc<br>Med 2010;11:91-95       | 0                     | 25-mm Amplatzer ASD cribriform occluder in<br>2 patients; Premere Closure System (St Jude<br>Medical, Minnetonka, MN) in 8 patients | On mean follow-up of $36.6 \pm 14.8$ mo, both patients<br>implanted with the Amplatzer device had small<br>residual shunts on TEE and residual moderate<br>shunts on transcranial Doppler. In 1 patient,<br>continued shunt was due to misalignment of the<br>device toward the septum, and in the second<br>patient, shunt was due to an excessive distance<br>between the 2 disks caused by device overelongation<br>by the rim hypertrophy.<br>No shunts were observed in the other 8 patients. |
| Closure of 2 ASDs | Paç e <i>t al.</i> Turk Kardiyol Dern<br>Ars 2010;38:366-368    | <del></del>           | 24-mm Amplatzer septal occluder   | No residual shunt after the procedure. During 3-y follow-up, no complications were observed.   |
| PFO closure       | Al-Faleh <i>et al.</i> Can J<br>Cardiol 2005;21:289-290         | 11                    | 28-mm Cardioseal device (Nitinol Medical<br>Technologies, Boston, MA)   | Continued shunt.   |
| ASD closure       | Moir <i>et al</i> . Circulation<br>2003;107:e217.               | -                     | 26-mm Amplatzer septal occluder device  | No residual left-to-right shunt.   |

Journal of the American Society of Echocardiography August 2016

particularly useful in guiding the transseptal puncture. Biplane 3D TEE ensures that transseptal puncture is confined to the true interatrial septum while preventing piercing of the aorta, superior vena cava, and the hypertrophied area in LASH.<sup>9</sup> Additionally, ICE has proved to be very useful both in the preprocedural evaluation of a hypertrophied interatrial septum and in the guidance of various interventional procedures.

LASH may interfere with transcatheter closure of atrial septal defects (ASDs) and patent foramen ovales, as most devices currently available in the United States, such as the Amplatzer family, have short waists that incompletely capture the septum secundum and cause incomplete apposition of the device resulting in persistent shunt or device embolization.<sup>21,29</sup> Indeed, it was previously thought that catheter-based closure of ASDs and patent foramen ovales was contraindicated in patients with LASH, as correct device deployment was deemed impossible.<sup>30</sup>

One report describes application of the Amplatzer muscular ventricular septal defect closure device in the successful closure of ASDs in two patients with LASH. The muscular ventricular septal defect device has a transverse waist 7 mm in length and is used in the muscular ventricular septum. This device was well suited to the atrial septum in these two patients because its thickness (1.5–2.5 cm) was comparable to that of a normal ventricular septum. The longer transverse waist length optimized apposition of the device to the hypertrophied rims of the septum secundum while still effectively grasping the smaller rims of the septum primum. These two patients had no complications following the procedures and had no residual shunts at 1-month follow-up.<sup>21</sup>

A retrospective analysis by Rigatelli et al.<sup>29</sup> examining transcatheter patent foramen ovale closure in patients with LASH concluded that the procedure may not be contraindicated as long as there is thorough evaluation of rim thickness with ICE and the devices used are stretchable transversally, enabling adaptation to very thick rims. In addition to measuring rim thickness, ICE can be used to measure the diameter of the fossa ovalis in patients with LASH. In this retrospective study, in which operators had used these findings to select the most suitable closure devices, two patients underwent closure via Amplatzer cribriform device and eight patients underwent closure using a Premere device (not available in the United States). Although none of the patients who received the Premere device had residual shunts, both patients who underwent closure using the Amplatzer devices continued to have residual shunts as a result of inadequate transverse waist length and malapposition. No patients had recurrence of stroke, aortic erosion, or device thrombosis on mean follow-up of  $36.6 \pm 14.8$  months.

This suggests that the Premere system may be preferable for thicker atrial septa, as the tethering system that connects the left and right atrial components is more adjustable than the standard Amplatzer device.<sup>29</sup> It is important to note that the reported mean thickness in this series, 14.8  $\pm$  3.6 mm, is at the smaller end of the LASH spectrum. It is unclear if these successful results would be seen in a septum >2.0 cm.<sup>21</sup>

#### CONCLUSIONS

<sup>2</sup>FO, Patent foramen ovale

LASH is characterized by nonencapsulated fat deposition in the septum secundum. Echocardiographically, LASH is identified by significant (>2 cm) fat infiltration in the area of the septum that spares the fossa ovalis. Histologically, LASH is composed of mature and

BAT; the role of BAT and FDG uptake is poorly understood. Although LASH is considered a histologically benign finding, there is a reported association with arrhythmias, sudden cardiac death, and congestive heart failure that appears to be related to the extent of infiltration and size of the lesion. LASH has also been mistaken for benign and malignant tumors of the interatrial septum, although several imaging modalities can now help distinguish this entity from its masqueraders.

Although LASH was once a contraindication to some catheterbased procedures, contemporary imaging modalities may now enable interventional cardiologists and electrophysiologists to perform these procedures more safely by avoiding puncture through the hypertrophied area. Interventionalists should therefore approach these patients with thorough preprocedural imaging and appropriate intraprocedural imaging that may include 3D TEE and ICE when necessary. With respect to transcatheter closure of septal defects in these patients, the most commonly used devices have minimal elongation capability, which make them unsuitable in LASH. However, novel devices with a more adjustable waist or innovative uses of ventricular septal defect closure devices in conjunction with the aforementioned imaging techniques, may facilitate successful defect closure.

Although the general anatomy and appearance of LASH are well described, the clinical significance of LASH separate from its importance during transseptal puncture is poorly understood. Welldesigned clinical studies of LASH associations with, for example, arrhythmia and truncal obesity, as well as ASD closure in the setting of LASH, are needed.

#### SUPPLEMENTARY DATA

Supplementary data related to this article can be found at http://dx. doi.org/10.1016/j.echo.2016.04.014.

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