

## First Case of Endoscopic Resection for Left Atrial Appendage Aneurysm with Suspected Viral Myocarditis: A Multimodal Approach

### Viral Miyokardit Şüphesiyle Sol Atriyal Apendiks Anevrizması İçin Endoskopik Rezeksiyon Uygulanan İlk Olgu: Multimodalite Yaklaşım

#### ABSTRACT

Left atrial appendage aneurysm (LAAA) is a rare cardiovascular anomaly, with fewer than 200 documented cases. It is often associated with severe complications, such as arrhythmias and thromboembolic events. Recent evidence suggests that viral infections, particularly viral myocarditis, might be an underlying cause of LAAA. We report the case of a 36-year-old woman with a history of asthma who presented with palpitations and atrial tachyarrhythmia two months after a severe upper respiratory infection. Transthoracic echocardiography revealed a large aneurysmal left atrial appendage (LAA) measuring 5.6 × 3.5 cm and a reduced left ventricular ejection fraction of 50%. Cardiac computed tomography confirmed the LAAA and revealed abnormal flow dynamics. Late gadolinium enhancement showed mid-subepicardial hyperenhancement in the posterolateral segments of the left ventricular wall, consistent with a previous myocarditis. The patient underwent a novel, minimally invasive endoscopic thoracoscopic resection of the aneurysm, guided by transesophageal echocardiography. No thrombus was present. The procedure was successfully completed with the aid of cardiopulmonary bypass. This case highlights a potential association between viral myocarditis and LAAA, while also acknowledging the possibility of a congenital and incidentally discovered aneurysm. It underscores the critical role of multimodal imaging in accurate diagnosis and management. The successful minimally invasive surgical resection and subsequent restoration of cardiac function demonstrate the effectiveness of this approach, offering a promising outlook for patients with LAAA. Clinicians should consider viral infections as potential contributors to LAAA development and advocate for early diagnosis and intervention to improve clinical outcomes.

**Keywords:** Arrhythmias, cardiac surgical procedures, left atrial appendage aneurysm, myocarditis

#### ÖZET

Sol atriyal apendiks anevrizması (LAAA), tıpta nadir görülen ve çoğunlukla tanı konulamayan bir kardiyovasküler anomalidir; literatürde bildirilen vaka sayısı 200'ün altındadır. Genellikle aritmi ve tromboembolik olaylar gibi ciddi komplikasyonlarla ilişkilidir. Son araştırmalar, özellikle viral miyokardit olmak üzere viral enfeksiyonların LAAA'nın altta yatan bir nedeni olabileceğini öne sürmektedir. Bu ilişki yeterince araştırılmamış olsa da, viral enfeksiyonlar sonrası açıklanamayan aritmiyle başvuran hastalarda dikkatli klinik değerlendirme yapılmasının önemini vurgulamaktadır. Bu yazıda, astım öyküsü olan ve ağır bir üst solunum yolu enfeksiyonundan iki ay sonra çarpıntı ve atriyal taşiaritmi şikayetleriyle başvuran 36 yaşındaki bir kadın olgu sunulmuştur. Transtorasik ekokardiyografi, 5,6 x 3,5 cm boyutlarında büyük bir anevrizmatik LAA ve sol ventrikül ejeksiyon fraksiyonunun %50 olduğu saptanmıştır. Kardiyak BT, LAAA'yı ve anormal akım dinamiklerini desteklemiştir. Gadoliniumla geç evre görüntülemesinde, sol ventrikül posterolateral duvar segmentlerinde orta-subepikardiyal hiperenhansman görülmüş, bu bulgular geçirilmiş miyokarditi düşündürmüştür. Hastaya, transözofageal ekokardiyografi rehberliğinde, minimal invaziv endoskopik torakoskopik anevrizma rezeksiyonu uygulanmıştır, trombüs izlenmemiştir. Cerrahi, kardiyopulmoner bypass desteğiyle başarılı şekilde gerçekleştirilmiştir. Bu olgu, viral miyokardit ile LAAA arasında potansiyel bir bağlantıyı tanımlayan ilk vaka olup, doğru tanı ve yönetimde multimodalite görüntülemenin görüntülemenin kritik rolünü ortaya koymaktadır. Minimal invaziv cerrahinin kalp fonksiyonunu yeniden kazandırmadaki başarısı, bu yaklaşımın etkinliğini göstermekte ve LAAA hastaları için umut verici bir seçenek sunmaktadır. Klinisyenler, viral enfeksiyonların LAAA gelişimindeki olası katkılarını göz önünde bulundurmalı ve daha iyi klinik sonuçlar için erken tanı ve müdahale sürecini benimsemelidir.

**Anahtar Kelimeler:** Aritmiler, kardiyak cerrahi prosedürler, sol atriyal apendiks anevrizması, miyokardit

#### CASE REPORT OLGU SUNUMU

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During the fourth week of embryonic development, the left atrial appendage (LAA) forms along the left wall of the left atrium (LA) and extends anterolaterally as a finger-like projection.<sup>1,2</sup> Its structure differs from that of the LA itself.<sup>1</sup> The LAA plays a minor role in LA compliance, and therefore in LA pressure and left ventricular (LV) filling pressure.<sup>1,2</sup> When flow velocity in the LAA decreases, such as in atrial fibrillation, mitral stenosis, or elevated LV filling pressure, thrombus formation in LAA may occur.<sup>2</sup>

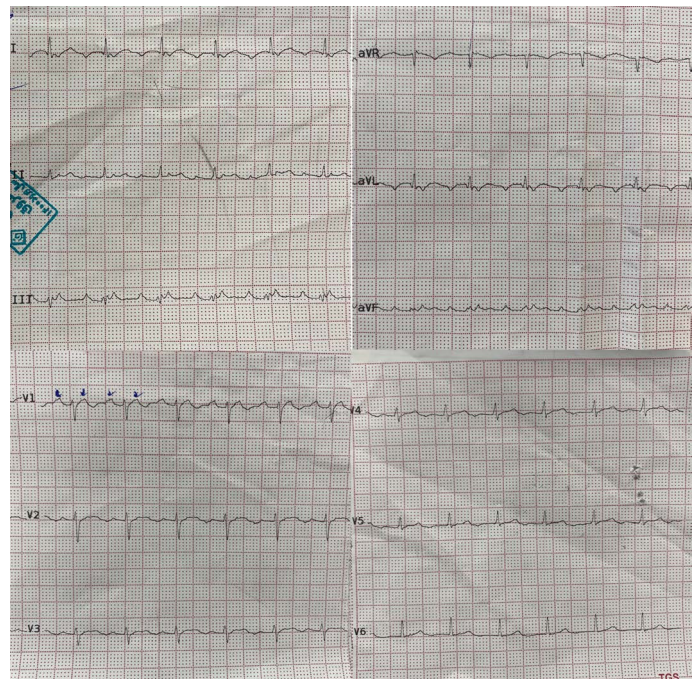
Left atrial appendage aneurysm (LAAA) is an extremely rare cardiovascular disorder, first described by Dimond et al. in 1960.<sup>3</sup> To date, over 180 cases have been reported.<sup>1</sup> Due to its rarity, diagnosis and the establishment of standardized treatment strategies remain challenging.<sup>4</sup> LAAA is typically discovered incidentally during surgery, autopsy, or through cardiovascular imaging techniques such as echocardiography, cardiac computed tomography angiography (CTA), or cardiac magnetic resonance imaging (MRI).<sup>4-6</sup> Clinical presentations of LAAA range from asymptomatic to severe complications, including cardiac arrhythmias, heart failure, thrombotic events, compression of adjacent structures, and even sudden cardiac death.<sup>4</sup> Etiologically, LAAA may be congenital, arising from dysplasia of the atrial pectinate muscles or pericardial defects, or acquired, secondary to conditions such as mitral valve disease, syphilitic myocarditis, or tuberculosis.<sup>7</sup> Literature reports that some aneurysms are intrapericardial, leading to wall weakness, while others are extrapericardial in nature.<sup>4,6,7</sup> Surgical resection, often in conjunction with medical treatment, is the recommended management strategy.<sup>4,5,8</sup> This report aims to highlight a rare presentation of LAAA and to review relevant literature to enhance understanding of its diagnostic and treatment strategies.

### Case Report

A 36-year-old woman, a recent smoker with a history of asthma, presented with palpitations and dyspnea that began two months after a severe upper respiratory infection. Apart from a heart rate of 150 beats per minute, her vital signs were within normal limits. Physical examination was unremarkable. An initial electrocardiogram (ECG) revealed atrial tachycardia with a 2:1 atrioventricular (AV) block, possibly originating in the LA (Figure 1). Transthoracic echocardiography (TTE) showed a normal LV size with mildly reduced systolic function (left ventricular ejection fraction (LVEF): 50% during tachycardia), abnormal motion of the interventricular septum, normal bi-atrial volumes (left atrial volume index: 21 cc/m<sup>2</sup>; right atrial volume index: 14 cc/m<sup>2</sup>), mild mitral regurgitation (MR), and a small pericardial effusion. The apical four-chamber view of the TTE revealed a large outpouching adjacent to the lateral aspect of the LA, extending toward the lateral side of the LV. It was connected to the LA via an ostium measuring 2.4 cm, consistent with a large aneurysmal LAA measuring 5.6 × 3.5 cm (Figure 2). Communication between the LA and LAA was confirmed by color Doppler imaging, which showed to-and-fro flow through the aneurysmal ostium. The patient underwent cardiac multidetector computed tomography (CT) with prospective ECG gating and a high-pitch non-ECG-gated delayed phase at 90 seconds using the Somatom Force system (Dual Source 192×2, Siemens, Forchheim, Erlangen, Germany). Computed

### ABBREVIATIONS

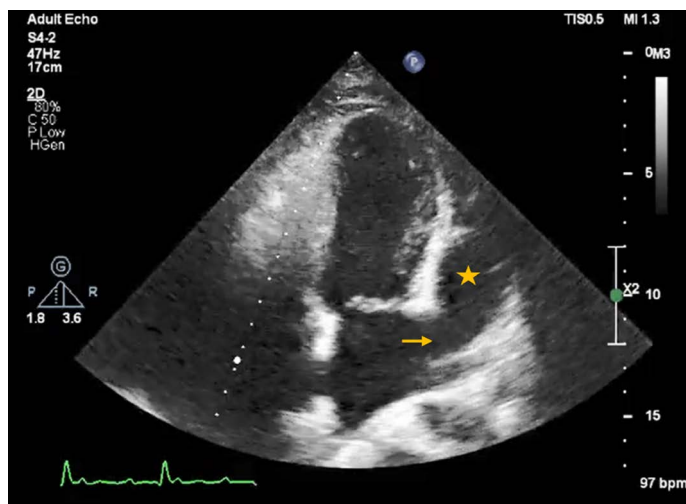
|      |                                    |
|------|------------------------------------|
| AF   | Atrial fibrillation                |
| AFL  | Atrial flutter                     |
| AV   | Atrioventricular                   |
| CPB  | Cardiopulmonary bypass             |
| CT   | Computed tomography                |
| CTA  | Computed tomography angiography    |
| ECG  | Electrocardiogram                  |
| EF   | Ejection fraction                  |
| LAAA | Left atrial appendage aneurysm     |
| LGE  | Late gadolinium enhancement        |
| LV   | Left ventricular                   |
| LVEF | Left ventricular ejection fraction |
| LVO  | Left ventricular opacification     |
| MR   | Mitral regurgitation               |
| MRI  | Magnetic resonance imaging         |
| SSFP | Steady-state free precession       |
| TEE  | Transesophageal echocardiography   |
| TTE  | Transthoracic echocardiography     |



**Figure 1. Electrocardiogram (ECG) showing atrial tachycardia with 2:1 atrioventricular (AV) block, characterized by a rapid atrial rhythm and alternate pulse transmission to the ventricles, originating from the left atrium.**

tomography angiography (CTA) confirmed the presence of a large aneurysmal LAA with a smoky appearance at its tip. No definite clot was detected on delayed imaging (Figure 3).

Due to the patient's decreased LVEF, she was referred to the imaging department for cardiac MRI to better evaluate the myocardium and accurately measure the ejection fraction (EF). The cardiac MRI was performed using the Magnetom SOLA system (Siemens, 48 gradient channels, Forchheim, Erlangen, Germany). Calculations were conducted using CVi42 software



**Figure 2. Off-axis apical four-chamber view on transthoracic echocardiography demonstrating a left atrial appendage (LAA) aneurysm measuring 5.6 cm × 3.5 cm (orange star), connected to the left atrium (LA) by a 2.4 cm ostium (orange arrow), during atrial tachyarrhythmia with 2:1 atrioventricular (AV) block.**

(Circle Cardiovascular Imaging Inc., Calgary, Canada). The MRI confirmed a large aneurysmal LAA with a smoky appearance and no obvious filling defects. The EF was calculated using a stack of short-axis steady-state free precession (SSFP) images, which demonstrated a reduced EF. A late gadolinium enhancement (LGE) sequence was performed following intravenous administration of DOTAREM (0.2 mmol/kg; Guerbet, Paris, France). The LGE images revealed mid-subepicardial hyperenhancement in the posterolateral segments of the left ventricular wall, suggestive of a prior episode of myocarditis (Figure 4).

Given the diagnosis of left atrial appendage aneurysm and the patient's symptomatic presentation, surgical intervention was planned. Intraoperative transesophageal echocardiography (TEE) was performed prior to surgery and confirmed the TTE findings. No smoke or clot was detected within the LAAA, and the LAAA emptying velocity was measured at 31 cm/second. Under general anesthesia, the procedure was carried out using a thoracoscopic approach through a minimal incision in the left hemithorax, with cardiopulmonary bypass (CPB) support. The total Cardiopulmonary bypass time was 73 minutes. Following pericardiotomy, thoracoscopic visualization confirmed the LAAA anatomy (Figure 5). The LAA orifice was carefully closed in three layers using a non-absorbable suturing technique, and the aneurysmal tissue was then resected. No intraoperative bleeding or suture line leakage was observed. Post-resection intraoperative TEE confirmed complete excision of the LAAA, with an emptying velocity of 24 cm/second in the small remaining portion of the LAA. No thrombus was observed, and surgical margins were satisfactory. The pericardium was subsequently closed. The remainder of the procedure was completed without complications.

The patient experienced an uncomplicated recovery and was discharged in stable condition on postoperative day four. Follow-up TTE performed two weeks later demonstrated normal left ventricular function (LVEF: 55%), mild MR, and a small

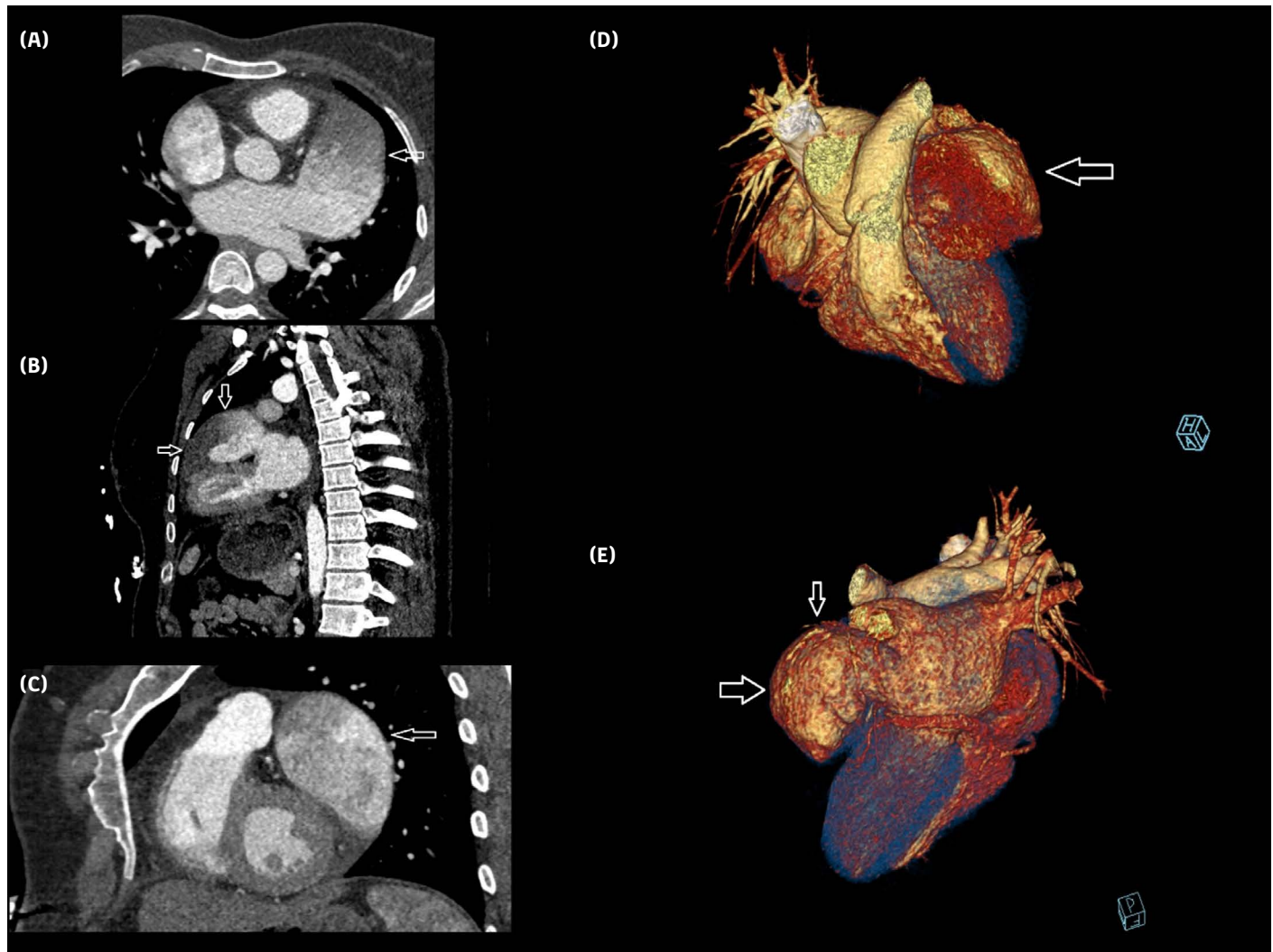
LAA remnant (Figure 6). Histopathological examination of the resected left atrial appendage was performed. Hematoxylin and eosin staining revealed endocardium and cardiac myocytes with mild hypertrophic changes and interstitial fibrosis (Figure 7). Serial clinical evaluations at one, three, and six months postoperatively revealed no recurrence of symptoms. The patient reported complete resolution of preoperative palpitations and maintained normal sinus rhythm on electrocardiograms throughout the follow-up period.

## Discussion

The first reported case of LAAA was published by Dimond<sup>3</sup> in 1960 and involved surgical resection following angiographic confirmation. Initial intraoperative diagnoses, such as those by Parmley et al.<sup>9</sup> in 1962, were later complemented by advancements in imaging technology, including the use of I-131-labeled albumin by Godwin<sup>10</sup> in 19689, and further refined by echocardiographic techniques in the 1980s.<sup>9</sup> The advent of advanced diagnostic tools, including contrast-enhanced imaging and cardiac MRI, has led to increased detection of LAA. This, in turn, has improved our understanding of its natural history, as well as the associated morbidity and mortality.<sup>5</sup>

As demonstrated in case reports, LAAA can occur across a wide age range, from 28 weeks gestational age prenatally to 88 years old. However, most cases are diagnosed between the second and fourth decades of life, with approximately 25% occurring in the third decade<sup>4,8,11</sup> similar to the case presented in this report. This may suggest that LAA aneurysms gradually enlarge over time.<sup>7</sup> Some analyses also indicate a slight female predominance, with 53% of cases in women and 47% in men.<sup>5,11</sup>

As previously stated, LAA aneurysms are categorized into congenital and acquired types. The majority of LAAA cases (approximately 90%) are congenital anomalies, potentially resulting from dysplasia of the atrial pectinate muscles.<sup>12</sup> However, some authors have reported associations between LAAA and other congenital anomalies, including atrial septal defect, ventricular septal defect, anomalous pulmonary venous drainage, tricuspid atresia, Noonan syndrome, Hurler-Scheie syndrome, transposition of the great arteries, and, more rarely, mitral valve cleft.<sup>5,7,12</sup> Acquired LAA aneurysms may develop due to mitral valve disease, syphilitic myocarditis, or tuberculosis. Associations with viral infections, have also been reported.<sup>4,12</sup> In our case, evidence suggestive of prior myocarditis, such as LGE in the posterior basal segment of the LV in cardiac MRI, raises the possibility of a link to a preceding viral infection. Histopathological examination of the resected LAAA in our case revealed endocardium and cardiac myocytes with mild hypertrophic changes and interstitial fibrosis. Consistent with our findings, endocardial and myocardial fibrosis are commonly reported histopathologic features in both congenital and acquired LAAA.<sup>5</sup> Additionally, myocardial hypertrophy with interstitial fibrosis, similar to what we observed, has also been documented in several reported LAAA cases.<sup>1,12</sup> While fibrosis is a non-specific finding and can occur in various cardiac conditions, including both congenital and acquired LAAA, in the context of our patient's clinical presentation and MRI findings, it may represent a sequela of myocarditis or a pre-existing condition exacerbated by, or coincident with, the inflammatory process.



**Figure 3. Cardiac multi-detector computed tomography (CT) imaging: (A, B, C) Multiplanar reconstruction (MPR) images in axial, oblique, and sagittal views reveal a markedly enlarged left atrial appendage (LAA) (white arrows). (D, E) Volume-rendered technique (VRT) reconstructions further highlight the prominent LAA (white arrows).**

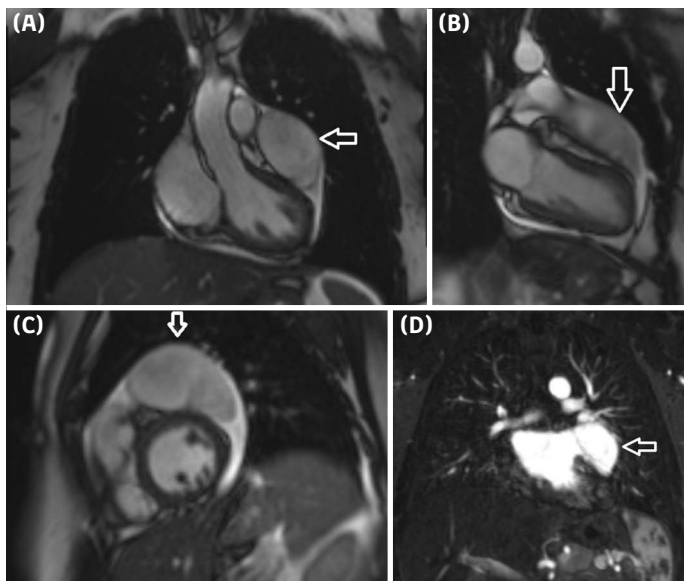
The literature describes a wide spectrum of clinical presentations for LAA aneurysms, ranging from asymptomatic cases discovered incidentally on chest X-ray or echocardiography to ruptured LAA aneurysms and sudden cardiac death.<sup>13</sup> Diagnosis can be challenging, as symptoms often result from compression of adjacent structures rather than direct cardiac dysfunction.<sup>14</sup> The most to least commonly reported symptoms associated with LAA aneurysms are palpitations (43%), dyspnea (22%), arrhythmias—primarily supraventricular tachyarrhythmias or atrial fibrillation (AF) (15%)—thromboembolic events such as cerebrovascular emboli (11%), chest pain (7%), and, very rarely, cough and hiccups.<sup>14</sup> A serious complication of LAAA is cerebrovascular embolism, which may occur due to blood stasis in the aneurysmal LAA, often as a result of AF, and sometimes is only diagnosed after a stroke.<sup>14,15</sup>

Despite the known predisposition of LAAA to thrombus formation, recent studies indicate that thrombus formation is not dependent on aneurysm size. Instead, it is more strongly associated with cardiac arrhythmias such as AF or flutter, neck size, and low flow

velocity within the aneurysm.<sup>4,7</sup> The case presented in this report involved palpitations, atrial tachyarrhythmia, and a 2:1 AV block (Figure 1) following a relatively severe viral respiratory infection, a clinical presentation not previously reported in the literature. The LAA measured by intraoperative TEE prior to surgery was 31 cm/s. Notably, no thrombus was detected within the aneurysm, and there was no history of thromboembolic events.

Various imaging modalities are used to diagnose LAAA, including chest X-ray, chest CT scan, CTA, cardiac MRI, TTE, and TEE.<sup>5,7</sup> Among these, chest X-ray is non-specific and typically shows signs such as cardiomegaly, a mass-like silhouette, or convexity of the left atrial contour.<sup>6,7,14</sup> A non-contrast chest CT can reveal a left atrial mass but cannot reliably distinguish among differential diagnoses such as a left atrial diverticulum, pulmonary artery dilation, pericardial cyst, or LAAA.<sup>5,7</sup>

An ECG-gated CTA can help resolve these ambiguities by providing better visualization to identify the aneurysmal sac and its connection with the LAA cavity, and it may also reveal



**Figure 4. Cardiac magnetic resonance imaging (MRI) findings: (A) Coronal steady-state free precession (SSFP) sequence showing the enlarged left atrial appendage (LAA) (white arrow). (B) Longitudinal SSFP view of the left ventricle (LV) depicting the extensive LAA (white arrow). (C) Short-axis SSFP view confirming the presence of the large LAA (white arrow). (D) Arterial phase of magnetic resonance (MR) angiography demonstrating filling of the enlarged LAA (white arrow).**

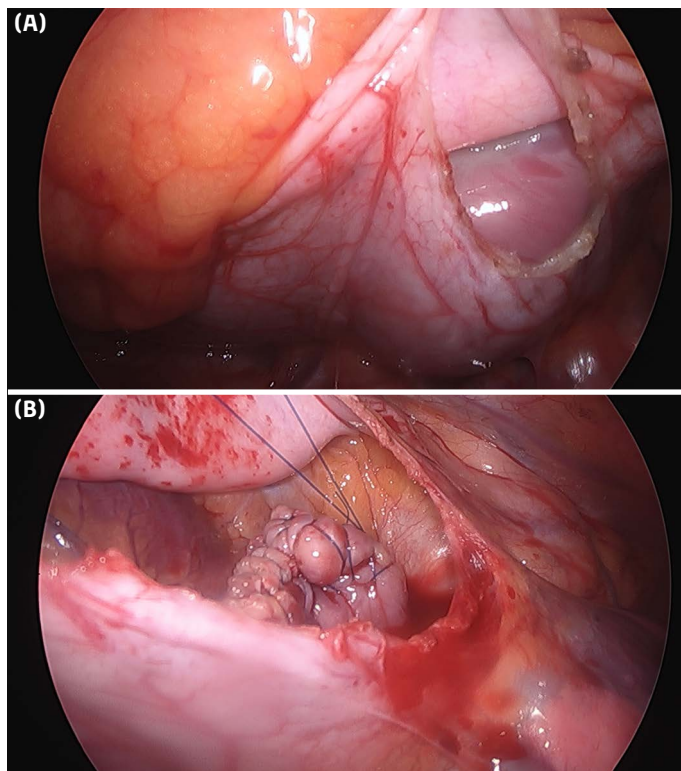
compression of adjacent structures.<sup>5</sup> Among all available modalities, cardiac MRI provides the highest diagnostic accuracy for LAAA, with an accuracy rate of 91%.<sup>5</sup> In our case, the diagnosis of LAAA was initially suggested by TTE and subsequently confirmed by both CTA and cardiac MRI (Figures 3 and 4).

Although the most accessible and cost-effective imaging modality is TTE, TEE also offers high diagnostic accuracy for LAAA (83.3%).<sup>4,5,7</sup> These techniques are favored for their practical utility and relatively low cost, especially when a high level of diagnostic precision is required.

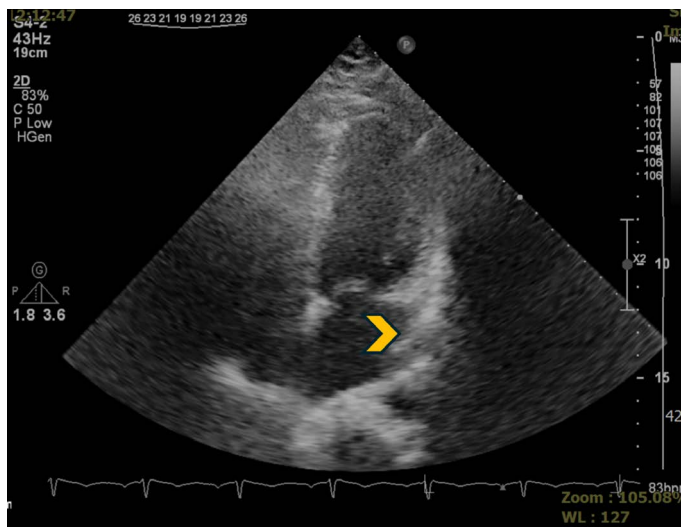
The typical echocardiographic finding in LAAA is an outpouching structure originating from the LAA, with preserved continuity to the LA cavity.<sup>5</sup> This characteristic helps distinguish LAAA from other anomalies, as the connection between the appendage and the atrium is usually intact, even when the aneurysmal sac is significantly dilated.

Aryal et al. defined the echocardiographic dimensions of LAAA, reporting a mean orifice diameter greater than 2.7 mm, a mean length of  $7.08 \pm 3.03$  cm, and a mean width of  $9.5 \pm 5.75$  cm.<sup>4</sup> These measurements are important for diagnosing LAAA, as they help define the abnormal size and shape of the LAA. The presence of such abnormal dimensions, especially if the orifice and appendage exceed certain size thresholds, raises suspicion for an aneurysmal condition.

In terms of visualization, left ventricular opacification (LVO) is considered one of the most effective methods for assessing blood flow in the left-sided heart chambers and is especially useful for detecting thrombi. This technique improves the accuracy of

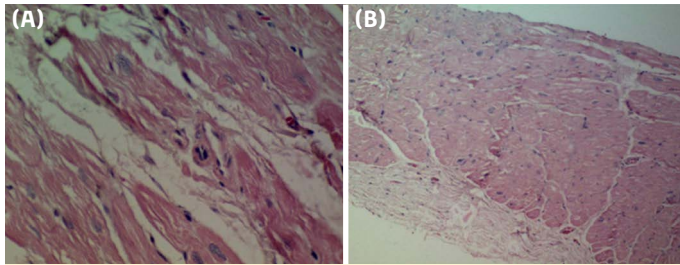


**Figure 5. Endoscopic views highlighting the precise surgical technique: (A) Identification of the left atrial appendage aneurysm (LAAA) with clear anatomical delineation. (B) Post-resection image demonstrating successful removal of the aneurysm while preserving surrounding tissue integrity and ensuring optimal patient outcomes.**



**Figure 6. Off-axis apical four-chamber transthoracic echocardiography view post-surgery, showing a significant reduction in left atrial appendage (LAA) size (yellow arrowhead) in sinus rhythm.**

detecting thrombotic formations, which is particularly important since LAAA is prone to thrombus development due to blood stasis in the aneurysmal sac, especially in the presence of atrial



**Figure 7. Microscopic findings of resected left atrial appendage tissue: Panels (A) and (B) show hematoxylin and eosin-stained sections of the resected left atrial appendage aneurysm. Histopathological analysis reveals endocardium and cardiac myocytes with mild hypertrophic changes and evidence of interstitial fibrosis.**

fibrillation.<sup>7</sup> Contrast-enhanced echocardiography has also proven useful not only for detecting thrombi but also for guiding therapeutic decisions, such as initiating anticoagulation therapy or planning surgical intervention.<sup>7</sup>

As previously noted, the aneurysmal size in our reported case was 5.6 cm × 3.5 cm, with an ostial diameter of 2.4 cm. These dimensions are significant and suggest a relatively large aneurysm, potentially increasing the risk of complications such as thrombus formation, embolism, or rupture. In this case, both CT and intraoperative TEE confirmed the absence of thrombus within the LAAA prior to surgery. Monitoring the aneurysm's size and characteristics is critical, and contrast-enhanced echocardiography may offer valuable insights into both thrombus detection and flow dynamics within the aneurysmal sac.<sup>7</sup>

As reported in the literature, aside from symptomatic treatment, including antiarrhythmic agents and anticoagulants, there is currently no targeted medical therapy available for LAAA.<sup>13</sup> Most authors recommend surgical intervention, specifically aneurysmectomy, as the preferred therapeutic approach, regardless of whether the LAAA is symptomatic or asymptomatic.<sup>5,11</sup> A median sternotomy, with or without CPB, is the standard surgical approach commonly used for aneurysmectomy or excision of the LAA.<sup>13</sup> This method is particularly suitable for large aneurysms.<sup>5</sup>

We previously had a successful experience with median sternotomy and aneurysmectomy in a patient with a very large LAAA measuring 5.8 cm × 4.8 cm, with an orifice of 0.6 cm, at our tertiary care center.<sup>11</sup> However, for smaller LAA aneurysms, alternative surgical approaches may be considered, including minimally invasive endoscopic resection (Figure 5), percutaneous septal occlusion of LAAA using an occluder device, left thoracotomy with or without CPB, and the off-pump tourniquet snare technique, often performed under TEE guidance.<sup>11</sup>

Upon reviewing the literature, we did not find any specific size thresholds to guide the selection of a surgical method for LAAA. Therefore, based on the relatively smaller size of the LAAA in our case (5.6 cm × 3.5 cm with an ostial size of 2.4 cm), as shown in Figures 2 and 5, we opted for a minimally invasive endoscopic thoracoscopy with CPB for aneurysm resection (Figures 2 and 5). We believed that the minimally invasive thoracoscopic approach

offered significant advantages for our patient, including a smaller surgical scar, potentially faster recovery, and a shorter cardiopulmonary bypass time, all contributing to greater patient comfort and potentially reduced morbidity. Beyond these advantages, it is important to emphasize that in our symptomatic patient, who presented with atrial tachyarrhythmia and a large LAAA, surgical resection was considered the most appropriate and definitive treatment. In the absence of clear guidelines on size thresholds, careful consideration of individual patient anatomy and clinical presentation is paramount in surgical planning. For symptomatic LAAA, surgical resection is frequently recommended as the definitive management strategy, as supported by the literature. Our choice of a minimally invasive approach is further supported by recent studies highlighting its benefits in appropriately selected patients, including reduced recovery times and fewer postoperative complications.<sup>1,7</sup>

Atrial arrhythmias such as AF, atrial flutter (AFL), and atrial tachyarrhythmias are typically managed promptly following LAAA resection. In some cases, ablation procedures are required to treat persistent arrhythmias.<sup>16</sup> In our case, sinus rhythm was restored after surgical resection of the LAAA, and no ablation procedure was necessary during the six-month follow-up period.

Overall, postoperative complications associated with surgical management of LAAA are low, and the prognosis is generally favorable.<sup>12</sup> According to published studies, 5.3% of patients who underwent surgical treatment experienced postoperative thromboembolic events, and 4% developed cardiac arrhythmias during follow-up, leading to the need for cardiac ablation. However, in one reported case, an adult patient passed away during follow-up due to carcinoma.<sup>11</sup>

## Conclusion

Left atrial appendage aneurysm is a rare cardiovascular anomaly that presents both diagnostic and therapeutic challenges. This case of a young woman following a respiratory infection highlights the potential for atypical presentations and the effectiveness of surgical resection in managing this condition. Surgical intervention offers excellent outcomes and reinforces its role as the standard of care. Continued accumulation of case reports and further research are essential to refine diagnostic criteria and optimize management strategies for patients with LAAA.

**Ethics Committee Approval:** This is a single case report, and therefore ethics committee approval was not required in accordance with institutional policies.

**Informed Consent:** Informed consent was obtained from all individual participants included in the study. Participants were informed about the purpose of the study, and their consent was obtained in accordance with ethical guidelines.

**Conflict of Interest:** The authors declare that they have no known competing financial interests or personal relationships that could have influenced the work reported in this paper.

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**Author Contributions:** Concept – S.H., Z.E.; Design – R.K., S.S.E.; Supervision – R.K., Z.E.; Resource – H.N.Z., H.F.A.; Materials – H.P.; Data Collection and/or Processing – E.T., S.M.H.; Analysis and/or Interpretation – H.P., H.N.Z.; Literature Review – S.S.E., S.M.H.; Writing – R.K., S.S.E.; Critical Review – R.K., Z.E.

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