The Heart Surgery Forum

Heart Surg. Forum **2026**; 29(1): 49911
https://doi.org/10.31083/HSF49911

Article

Total Endoscopic Removal of Patent Foramen Ovale and Atrial Septal Defect Occluder Devices: A Retrospective Analysis

Hua Shen[1,†], Mingshi Ren[2,†], Dong Li[1], Shengli Jiang[1], Nan Cheng[1,*], Lin Zhang[1,*]

[1]Department of Cardiovascular Surgery, The First Medical Center of Chinese PLA General Hospital, 100853 Beijing, China
[2]Department of Thoracic Surgery, The Third Medical Center of Chinese PLA General Hospital, 100039 Beijing, China
*Correspondence: cn86919@163.com (Nan Cheng); drzhanglin@outlook.com (Lin Zhang)
[†]These authors contributed equally.

Academic Editor: Massimo Bonacchi
Submitted: 31 July 2025 Revised: 15 September 2025 Accepted: 27 October 2025 Published: 12 January 2026

Abstract

Background: This study aimed to evaluate the safety and efficacy of total endoscopic removal of patent foramen ovale (PFO) or atrial septal defect (ASD) occluder devices in managing nickel hypersensitivity complications. **Methods**: A retrospective analysis of 95 patients (2020–2025) undergoing total endoscopic occluder device removal via femoral cardiopulmonary bypass was performed using preoperative nickel allergy screening via patch testing. Outcomes included procedural success, symptom resolution, quality-of-life (QoL) trends, and complications. **Results**: All devices were removed successfully without thoracotomy. The median bypass time was 71.2 min; 96.8% of residual defects were directly sutured. Nickel hypersensitivity was confirmed in 89.5% of cases. QoL "good" ratings increased from 7.4% preoperatively to 95.8% at 6 months ($p < 0.001$). No major complications were observed; however, there were two cases of transient atrial fibrillation (2.1%). The median blood loss was 36.8 mL; no reoperations/mortality were noted. **Conclusions**: Total endoscopic removal is safe and effective for nickel allergy-related complications, with high symptom resolution and improvement in QoL. Preoperative nickel screening optimizes outcomes, while this minimally invasive approach reduces morbidity, thereby supporting the adoption of this approach for device explantation.

Keywords: patent foramen ovale; atrial septal defect; nickel allergy; endoscopic device removal; cardiac surgery; residual septal defects

1. Introduction

Patent foramen ovale (PFO) occluder devices are commonly used in clinical practice to prevent recurrent cryptogenic strokes and treat migraines [1,2]. These devices, which are often composed of nickel-containing alloys, have demonstrated long-term efficacy in reducing the risk of thromboembolic events [3]. However, complications related to device implantation, such as device migration, incomplete endothelialization, and nickel hypersensitivity, have been increasingly reported [4,5]. Nickel allergy, in particular, is a significant concern due to the widespread use of nickel in medical devices. The prevalence of nickel allergy in the general population is high, yet its incidence following PFO or atrial septal defect (ASD) occluder is not well documented [6]. Despite these challenges, the exact pathophysiology behind nickel hypersensitivity in intracardiac devices remains unclear, prompting further investigation into the role of nickel allergy in device-related complications [7,8].

Nickel hypersensitivity reactions can manifest with a broad range of symptoms, including chest pain, migraines, palpitations, and dyspnea, often appearing weeks to years after device implantation. In patients with pre-existing nickel sensitivity, the body's immune response can lead to chronic inflammation, which can result in persistent symptoms that do not resolve with conventional medical management [9]. Nickel ions (Ni^{2+}) leached from occluders act as haptens that bind to host proteins (e.g., toll-like receptor 4/TLR4), triggering innate immune activation via the NF-κB pathway [10]. This promotes dendritic cell maturation and antigen presentation, activating nickel-specific $CD4^+$/$CD8^+$ T-cells [11]. Sustained inflammation results in mast cell degranulation (histamine, tryptase release $\rightarrow$ chest pain, rash), macrophage recruitment (IL-1β, TNF-α release $\rightarrow$ endothelial dysfunction) [4], and impaired endothelialization due to matrix metalloproteinase (MMP)-mediated tissue remodeling. These processes establish a prothrombotic milieu, facilitating microthrombi formation on incompletely endothelialized struts [12]. Microemboli can then traverse residual shunts, potentially triggering migraines or systemic inflammation [9]. In such cases, device explantation has been shown to significantly improve patient outcomes, particularly in individuals who have not responded to pharmacological interventions such as corticosteroids and antiplatelet therapy. Several case reports and studies have documented the complete resolution of symptoms following device removal, reinforcing the importance of recognizing nickel hypersensitivity as a potential cause of device failure [13,14].

Despite the growing awareness of nickel hypersensitivity in patients with implanted PFO/ASD occluder devices, there are no standardized guidelines for preopera-

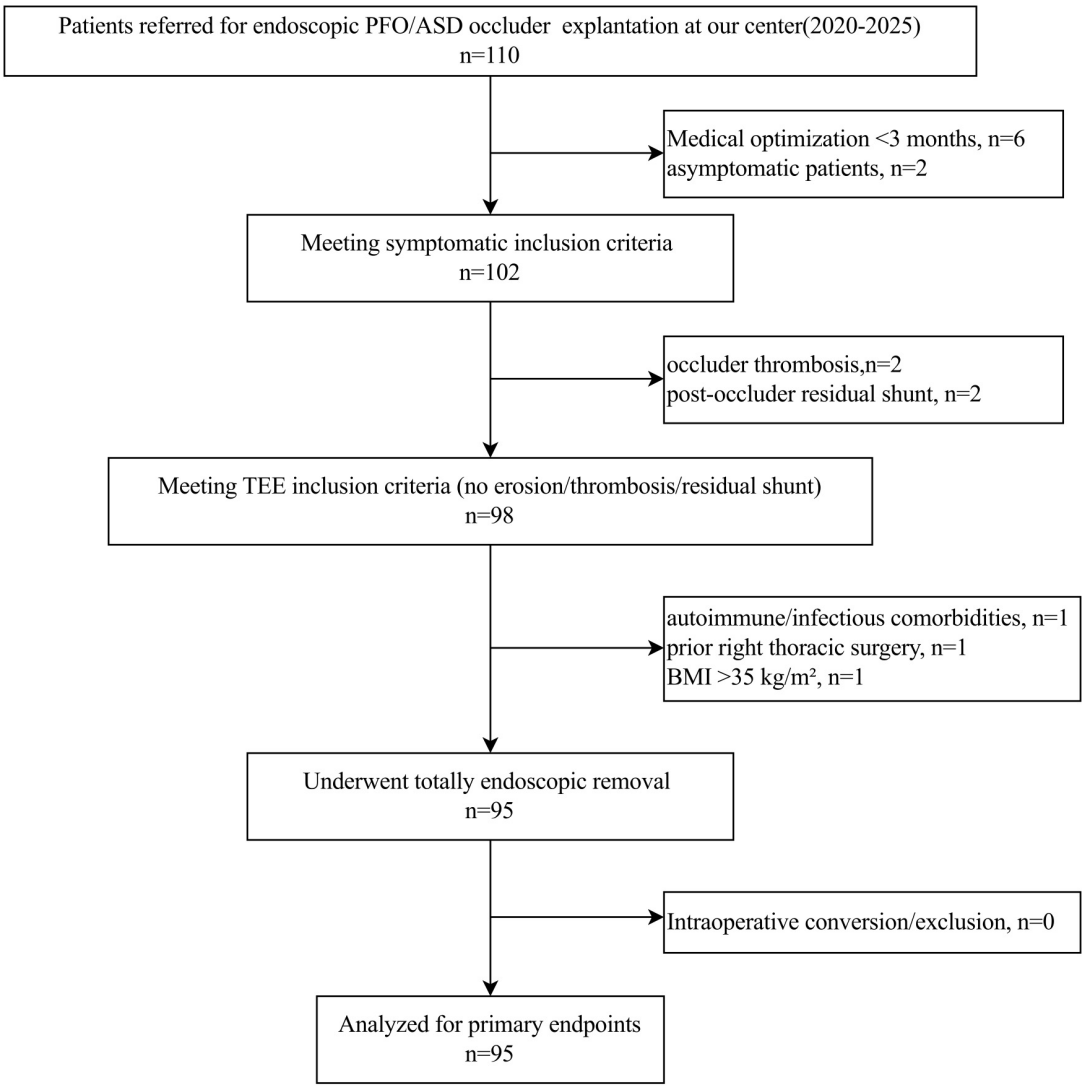


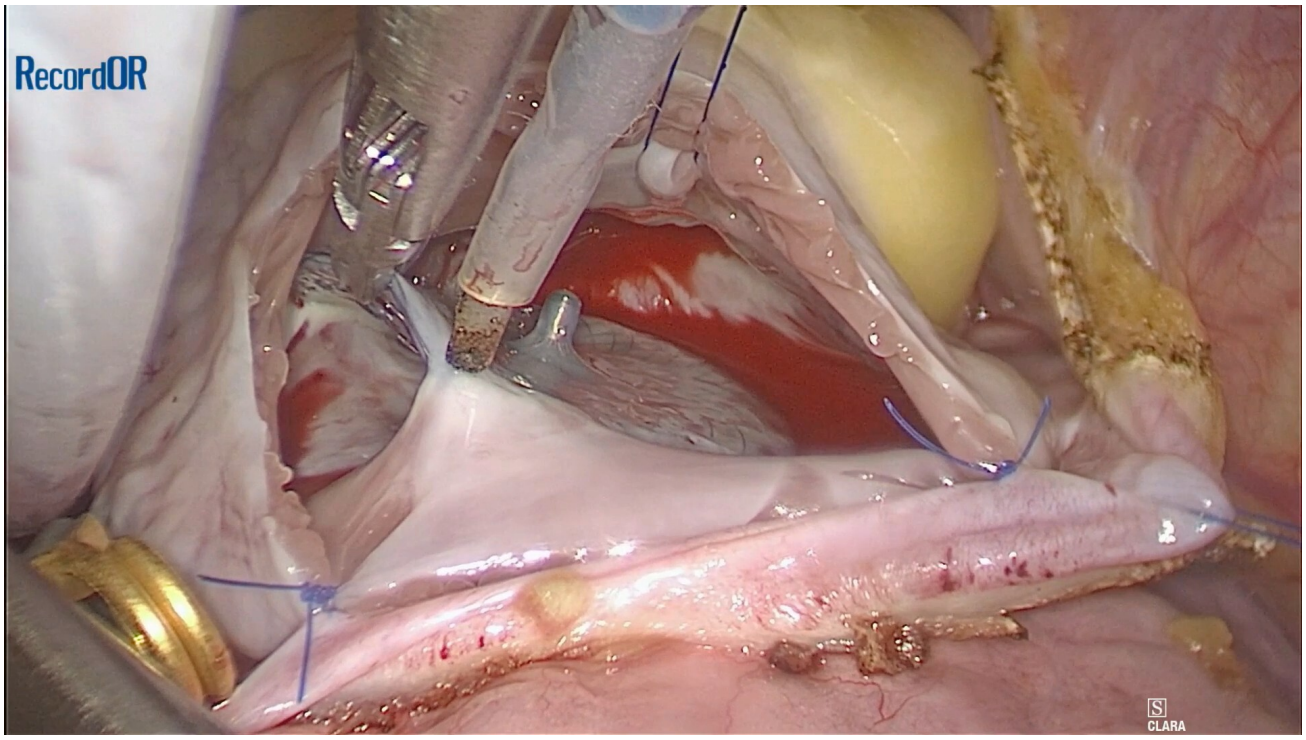
Fig. 1. Patient enrollment flow chart. This diagram illustrates the screening process for patients undergoing totally endoscopic PFO/ASD closure device removal (2020–2025). Of 110 initially assessed patients, 15 were excluded due to: insufficient medical optimization (n = 5), asymptomatic status (n = 3), device thrombosis (n = 2), significant residual shunt (n = 2), or contraindications to endoscopic surgery (n = 3). The final cohort consisted of 95 patients who underwent successful endoscopic explantation. TEE, transesophageal echocardiography.

tive allergy screening or the management of nickel-related complications. Current diagnostic approaches rely on skin patch testing, which can identify patients at risk of developing hypersensitivity reactions before or after device implantation [15]. Additionally, the decision to remove the device often depends on the severity of symptoms and the patient's overall quality of life (QoL) post-implantation. The present study aims to retrospectively analyze the outcomes of patients who underwent totally endoscopic removal of PFO/ASD occluder devices due to nickel hypersensitivity, focusing on symptom resolution and the safety of the minimally invasive surgical approach.

2. Methods

2.1 Patients

This retrospective study included 95 patients who underwent totally endoscopic removal of PFO/ASD occluder devices at our center between 2020 and 2025. Consecutive patients referred for endoscopic device explantation were evaluated. Device removal was considered only after documented failure of a standardized medical optimization protocol [16–18]. Inclusion required: (1) $\geq$2 refractory symptoms persisting >6 months despite medical therapy, including migraines, chest pain, palpitations, and dyspnea; (2) Transesophageal echo verifying device position without erosion/thrombosis or residual shunt. Exclusions:



Video 1. Intraoperative video of totally endoscopic intracardiac patent foramen ovale (PFO)/atrial septal defect (ASD) occluder device removal. Video associated with this article can be found, in the online version, at https://doi.org/10.31083/HSF49911.

severe valvular/coronary disease, autoimmune/infectious comorbidities, or contraindications to totally endoscopic surgery, such as severe pleural adhesions, prior right thoracic surgery, and BMI >35 kg/m^2 (limited working space). All patients were evaluated for nickel allergy through patch testing prior to surgery. Patient selection followed a rigorous multi-stage screening process as detailed in Fig. 1.

2.2 Echocardiographic Assessment Protocol

Comprehensive transthoracic echocardiography (TTE) and transesophageal echocardiography (TEE) were performed preoperatively and 48 h postoperatively following the guidelines of the American Society of Echocardiography (ASE). Key parameters included: (1) Septal morphology: Defect size, rim thickness (aortic/atrial/caval), septal aneurysm (excursion >10 mm); (2) Hemodynamic impact: right ventricular function assessed by tricuspid annular plane systolic excursion (TAPSE) and fractional area change (FAC); (3) Complications: Device erosion/thrombosis, residual shunt. Device erosion, thrombosis, or residual interatrial shunt. A significant residual shunt was defined as a color Doppler jet width of ≥2 mm measured by TEE, and/or the presence of >10 microbubbles in the left atrium within 3 cardiac cycles on saline contrast study (agitated saline bubble test) according to current guideline recommendations.

2.3 Surgical Procedure

The patient was placed in a supine position with the right side elevated. Following the induction of general anesthesia and endotracheal intubation, invasive monitoring was established via left radial arterial and venous cannulation. Systemic heparinization was achieved. Cardiopulmonary bypass (CPB) was established through cannulation of the right femoral artery and vein. The femoral venous cannula was advanced to the orifice of the inferior vena cava (IVC), and the superior vena cava (SVC) was percutaneously cannulated via the right supraclavicular approach. The 3 cm main operating port was created in the 4th intercostal space just lateral to the right midclavicular line. The thoracoscope was introduced through a port in the 4th intercostal space at the right anterior axillary line. A transthoracic Chitwood clamp was introduced through 5th intercostal space at the midclavicular line to cross-clamp the ascending aorta and cardioplegic arrest was successfully induced. The SVC was temporarily occluded with an occlusion clamp and ensure satisfactory drainage with central venous pressure below 15 mmHg. The right atrium was incised and the previously implanted occluder was identified and meticulously dissected and completely removed. The iatrogenic atrial septal defect created by the occluder was repaired with no residual shunt confirmed by testing. After thorough de-airing, the aortic cross-clamp was released. The patient was weaned from CPB, heparin reversed, hemostasis achieved. A right thoracic drainage tube was placed and the thoracic incisions were closed in lay-

ers. Based on preoperative contrast echocardiography, intraoperative re-evaluation was performed to confirm the device condition, followed by complete removal and assessment of endothelialization status using a standardized visual scale: Complete (smooth tissue coverage, no visible metal), Partial (patchy coverage with $<$50% metal exposure), Incomplete ($>$50% metal struts exposed). The residual septal defects after device explantation were repaired either through direct suturing or with the bovine pericardium patch (Video 1). Postoperatively, patients were transferred to the intensive care unit (ICU) and managed with standardized analgesia protocols. Following extubation and chest tube removal, transthoracic echocardiography confirmed the absence of residual shunts. Patients were routinely discharged approximately 3–5 days after surgery.

2.4 Data Collection

Data on patient demographics, clinical symptoms, nickel allergy testing results, surgical details, and postoperative outcomes were collected from medical records. QoL was assessed preoperatively and at follow-up intervals (3 days, 1 month, and 6 months postoperatively). Preoperative nickel allergy screening via patch testing (TRUE Test™, 5% nickel sulfate) and the patch test contraindications included active dermatitis at test site, immunosuppressant use $>$10 mg/day prednisone. The patch is typically placed on the patient's back and left in place for 48 hours and monitored for allergic reaction. After 48 hours, the patch is removed, and the skin is evaluated for redness, swelling, itching, or blistering, which would indicate a positive reaction. The test site is then re-examined at 72 and 96 hours to observe any delayed allergic responses. All patients with positive/negative allergy results were closely monitored for symptom improvement after device removal. Postoperative complications were documented.

2.5 Follow-up

Patients assessments were performed at preoperative baseline and postoperatively (3-day, 1-month, 6-month). During each follow-up visit, clinical symptoms, QoL, and any potential complications were recorded. The primary endpoint was the complete resolution or significant improvement of symptoms, such as migraines, chest pain, and palpitations, as assessed through patient-reported outcomes and clinical evaluations. Secondary endpoints included the absence of major complications such as atrial fibrillation (AF), stroke, or the need for reoperation. QoL Scores were transformed to a 0–100 scale according to RAND Corporation protocols, with higher scores indicating better health status. QoL was categorized as: Poor: Score $<$50 (substantial limitations in $\geq$3 domains), Fair: Score 50–69 (moderate limitations), Good: Score $\geq$70 (minimal limitations, within 10% of population norms).

2.6 Statistical Analysis

Descriptive statistics were used to summarize patient demographics and clinical characteristics. Continuous variables were expressed as mean (SD) or median with interquartile range (IQR), as appropriate. Categorical variables were presented as counts and percentages. Patients' QoL was assessed using the 36-Item Short Form Survey (SF-36), administered at 3-day, 1-month, and 6-month postoperative intervals. Missing domain items were imputed using the domain mean if $\geq$50% of items were completed. Scoring followed RAND Corporation protocols, rated as Poor, Fair, or Good. The categorization thresholds align with established SF-36 population norms [19] and cardiac surgery validation studies [20,21]. To account for repeated ordinal measures within subjects over time, we employed generalized estimating equations (GEE) with a cumulative logit link (proportional odds model). An unstructured working correlation matrix was used to model within-subject dependence. The model included timepoint (categorical) as the main predictor, with pre-surgery as the reference. Random intercepts for each patient were included to account for individual variability. The following covariates were adjusted for in the model: Age, Sex, Indication for device placement (stroke/transient ischemic attack (TIA), migraine, ASD, asymptomatic), Device brand (AGA Amplatzer, Lepu Medical, LifeTech, Starway), Implant-to-explant interval (months) and Nickel allergy status (positive/negative). The proportional odds assumption was tested using score tests and graphical methods (parallel lines assumption). If violated, partial proportional odds models or alternative link functions were considered. Sensitivity analyses were conducted by: (1) Treating SF-36 domain scores as continuous and using linear mixed-effects models. (2) Using a binary logistic GEE model (Good vs. Not Good) to assess robustness. (3) Excluding patients with missing covariate data ($<$5%) to evaluate completeness. Model fit was assessed using QIC (Quasi-Likelihood under Independence Model Criterion). Pairwise comparisons between timepoints were adjusted using the Bonferroni method. A two-sided p-value $<$0.05 was considered statistically significant. All statistical analyses were performed using SAS version 9.4 (PROC GENMOD; SAS Institute Inc., Cary, NC, USA) and R version 4.2.0 (R Foundation for Statistical Computing, Vienna, Austria).

3. Results

Of 110 patients initially referred for endoscopic explantation evaluation, 95 (86.4%) comprised the final study cohort after application of exclusion criteria (Fig. 1). The screening process excluded 15 patients: 8 (7.3%) for insufficient medical optimization or asymptomatic status, 2 (1.8%) for device thrombosis, 2 (1.8%) for significant residual shunt, and 3 (2.7%) for contraindications to endoscopic approach (1 with autoimmune disease, 1 with prior right thoracic surgery, 1 with BMI $>$35 kg/m^2).

All 95 patients in the final cohort successfully underwent totally endoscopic device removal without conversion to open procedure (100% technical success rate). The cohort of 95 patients had a median age of 32.6 years, with a notable female predominance (89.5%). Among the patients, the most commonly used devices were from LifeTech Scientific Corporation accounting for 34.7%, while AGA Amplatzer devices were used in 10.5% of cases. Cardiovascular comorbidities, such as coronary artery disease (2.1%), hyperlipidemia (5.3%), and hypertension (5.3%), were relatively uncommon. Psychiatric conditions were also infrequent, with 7.4% of patients diagnosed with anxiety and 5.3% with depression. Autoimmune and thyroid conditions were rare. Notably, metal allergies were highly prevalent, with 47.4% of patients reporting allergies to common items like belt buckles or earring studs, indicating a potential link between metal sensitivity and device-related complications.

The primary indication for device placement was a history of stroke or TIA (47.4%), followed by refractory headaches or migraines (36.8%). ASD accounted for 10.5% of cases, and 5.3% of patients were asymptomatic. The high prevalence of neurological conditions, particularly migraines and stroke, reflects their established association with PFO. Importantly, patients with documented allergy histories, particularly metal allergies, may have experienced complications that led to the need for device removal, suggesting a possible influence of allergies on long-term device success (Table 1).

After device placement, 84.2% of the patients reported experiencing pain, with specific symptoms varying widely. Headaches or migraines were prevalent in 47.4% of patients, while chest pain affected 21.1%. Neurological symptoms were reported in 42.1% of the cohort, such as dizziness or vertigo (21.1%) and blurred vision (21.1%). Cardiovascular issues were common, such as palpitations (15.8%), breathlessness on exertion (21.1%), and arrhythmias or tachycardia (15.8%). Fatigue affected 31.6% of patients, and gastrointestinal symptoms, skin rash, and depression were reported by 10.5% of patients each. Notably, the majority of symptoms (84.2%) occurred immediately postoperatively, while 10.5% experienced symptoms within the first month, and 5.3% had symptoms that appeared more than one month after surgery (Table 2).

Table 1. Patient demographic and characteristics.

Characteristic	Result (n = 95)
Age (y)	32.6 (12–52)
Female sex	85 (89.5)
Device type	
AGA Amplatzer	10 (10.5)
Lepu Medical	32 (33.7)
LifeTech Scientific Corporation	33 (34.7)
Starway Medical company	20 (21.1)
Cardiovascular	
Coronary artery disease	2 (2.1)
Hyperlipidemia	5 (5.3)
Hypertension	5 (5.3)
Psychiatric	
Anxiety	7 (7.4)
Depression	5 (5.3)
Autoimmune	
Rheumatoid arthritis	2 (2.1)
Hashimoto thyroiditis	2 (2.1)
Thyroid	
Hypothyroidism	2 (2.1)
Hyperthyroidism	2 (2.1)
Other	
Chronic kidney disease	0 (0)
Type 2 diabetes	2 (2.1)
Documented allergy histories	65 (68.4)
Metal allergy (Belt buckles/Earring stud/Intrauterine device)	45 (47.4)
Allergic rhinitis	5 (5.3)
Urticaria	5 (5.3)
Antibiotic allergy	5 (5.3)
Aspirin	5 (5.3)
Indications for PFO/ASD occluder device placement	
History of stroke/TIA	45 (47.4)
Refractory headaches/migraines	35 (36.8)
ASD	10 (10.5)
Asymptomatic	5 (5.3)

Values are presented as median (IQR) or n (%). PFO, Patent Foramen Ovale; ASD, Atrial Septal Defect; TIA, Transient Ischemic Attack.

3.1 Nickel Allergy Testing

Fig. 2 demonstrates the outcomes of nickel allergy patch testing in patients with implanted PFO/ASD occluder devices. In the left image, a clear positive reaction (indicated by the red arrow) is visible, showing localized inflammation at the nickel test site. The right image presents the testing process, where various allergens are applied on the patient's back using patches. Positive reactions to nickel were commonly observed in patients who experienced postoperative complications, reinforcing the connection between nickel hypersensitivity and the need for device explantation.

3.2 Intraoperative Findings and Surgical Procedure

Fig. 3 illustrates the critical steps in the totally endoscopic removal of a PFO occluder device, highlighting both the technical aspects and intraoperative findings. Upon exposure of the right atrium, the device is delicately separated from the septal tissue, after that, the residual septal defect is inspected for any structural abnormalities or incomplete healing. The procedure is completed with direct suturing of the septal defect or using tissue patch. The totally endoscopic approach, as demonstrated in these images, was

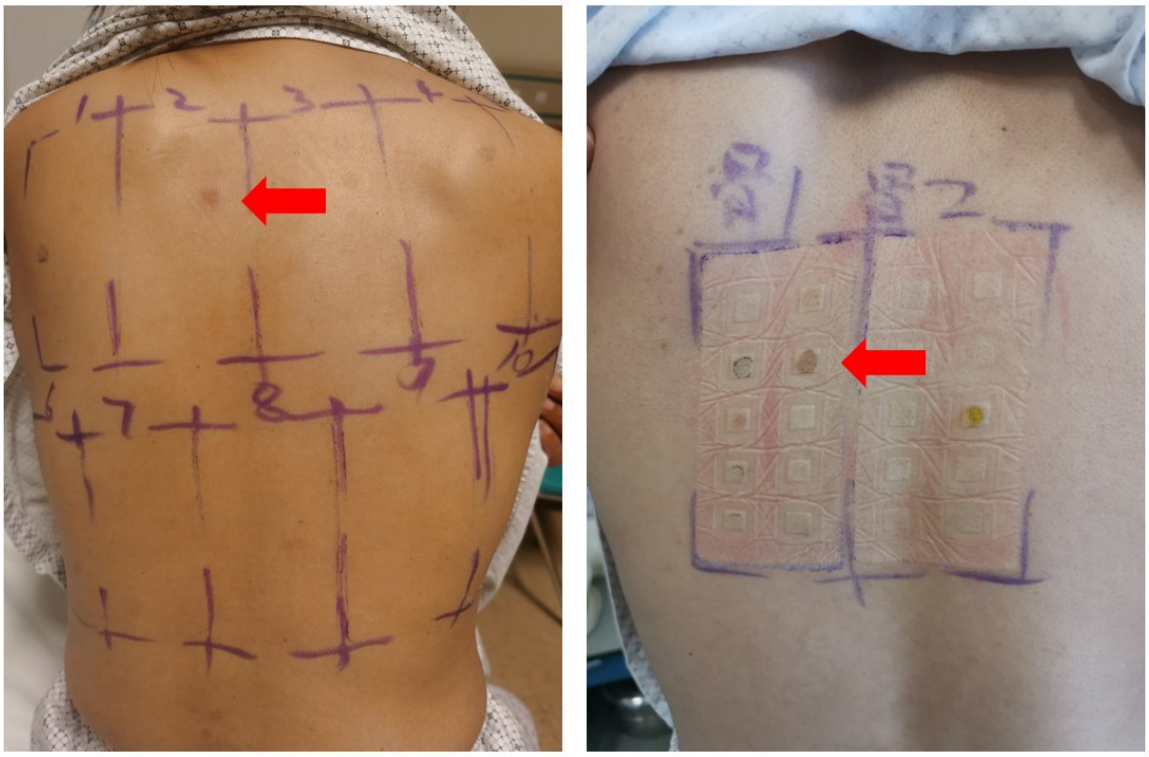


Fig. 2. Patch testing for nickel allergy in patients with PFO/ASD occluder devices. The images depict the results of patch testing, with positive reactions indicated by the red arrows. The left image shows a skin reaction with inflammation at the test site, while the right image displays the test setup, including various allergens applied via patches. The positive reaction suggests nickel hypersensitivity, a key factor in postoperative complications and device explantation decisions.

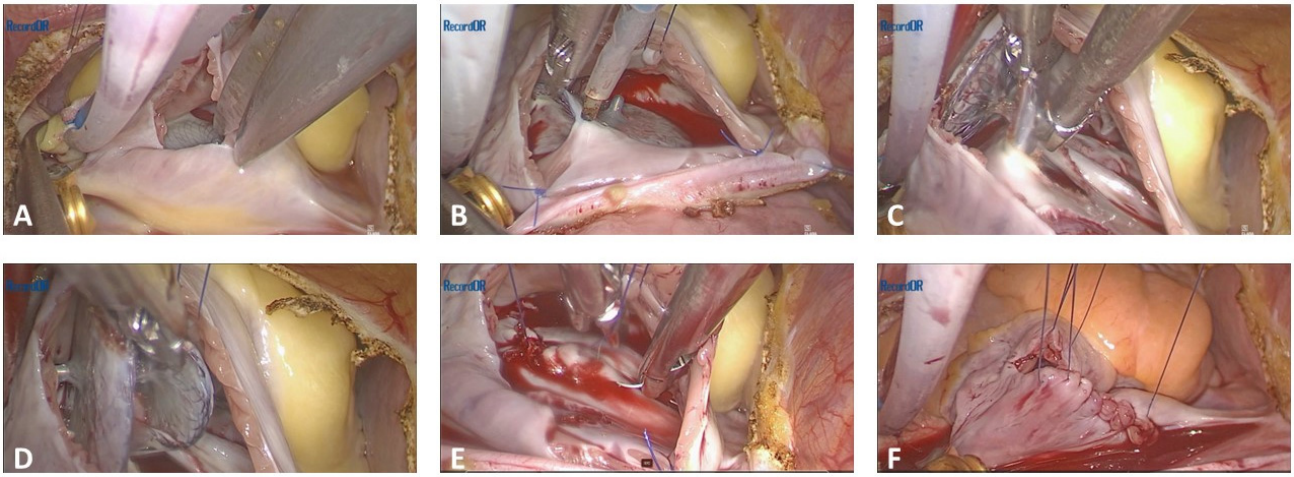


Fig. 3. Intraoperative images of totally endoscopic removal of a PFO occluder device. The sequence illustrates (A) initial exposure of the heart and surrounding structures, (B) identification and isolation of the PFO occluder device, (C) device removal and (D) inspection of the residual defect, (E) preparation for septal repair, and (F) completion of the repair with direct suturing.

efficient and resulted in a clear operative field, allowing for a successful and complication-free surgery.

All 95 patients undergoing PFO or ASD occluder removal were treated with a totally endoscopic surgical approach, without the need for thoracotomy or sternotomy. Residual septal defects after devices removal were sutured directly in 96.8% patients, and only 3 patients (3.2%) requiring a tissue patch. Nickel allergy testing was performed in all patients, with a majority (89.5%) testing positive, suggesting a strong correlation between nickel sensitivity and device-related complications. The mean CPB time was 71.2 minutes, while cross-clamp time averaged

Table 2. Symptoms after device placement and the time of symptom onset.

Symptoms	n = 95
Time of symptom onset	
Post-operative immediate	80 (84.2)
Within 1 month post-operatively	10 (10.5)
Over 1 month post-operatively	5 (5.3)
Pain	
Chest pain	20 (21.1)
Headaches/migraines	45 (47.4)
Muscle/body aches	15 (15.8)
Neurologic	
Dizziness/vertigo	20 (21.1)
Blurred vision	20 (21.1)
Cardiovascular	
Palpitations	15 (15.8)
Breathlessness on exertion	20 (21.1)
Arrhythmia/Tachycardia	15 (15.8)
Fainting	10 (10.5)
Fatigue	30 (31.6)
Depression	10 (10.5)
Gastrointestinal	10 (10.5)
Cough	10 (10.5)
Skin rash/Itching	10 (10.5)

Values are presented as median (IQR) or n (%).

Table 3. Perioperative data of patients received PFO/ASD occluder removal.

Characteristic	Result
Surgical approach	
Totally endoscopic	95 (100)
Thoracotomy/sternotomy	0
Residual septal defects	
Directly repair	92 (96.8)
Tissue Patch	3 (3.2)
Nickel allergy testing	
Patch positive	85 (89.5)
Patch negative	10 (10.5)
CPB time, median (IQR), min	71.2 (50–128)
Cross Clamp time, median (IQR), min	34.6 (14–76)
Blood loss, mean (SD), mL	36.8 (21.6)
Ventilation time, mean (SD), h	4.7 (1.8)
Reoperation for bleeding, n (%)	0
In hospital death (%)	0
Chest drainage volume, mean (SD), mL	17.5 (19.3)
Chest drainage weaning time, mean (SD), h	10.9 (1.8)
Postoperative AF, n (%)	2 (2.1)

Values are presented as median (range) or n (%). PFO, Patent Foramen Ovale; ASD, Atrial Septal Defect; CPB, Cardiopulmonary Bypass; SD, Standard Deviation; AF, Atrial Fibrillation.

34.6 minutes. Intraoperative blood loss was minimal, averaging 36.8 mL, and ventilation time postoperatively averaged 4.7 hours. There were no cases of reoperation for bleeding or in-hospital deaths, reflecting a favorable safety profile. The tricuspid valve was inspected intraoperatively and found to be functionally normal, thus requiring no repair. There was no iatrogenic damage to the valve. Chest drainage volume was low, averaging 17.5 mL, with an average chest drainage weaning time of 10.9 hours. Only 2 patients (2.1%) developed postoperative AF, further indicating a low complication rate (Table 3). Fig. 4 depicts the explanted PFO occluder device in multiple orientations. The images clearly show the device's structural integrity post-explantation, with visible tissue remnants and signs of complete endothelialization.

3.3 Postoperative Findings and Surgical Scarring

Fig. 5 shows the postoperative incisions following a totally endoscopic PFO occluder device removal. The red arrows indicate small thoracoscopic entry sites used during the surgery, while the white arrow highlights the primary incision through which the occluder device was removed. The image reveals minimal scarring and localized bruising, demonstrating the effectiveness of the endoscopic approach.

QoL ratings among the 95 patients markedly improved following PFO/ASD occluder removal (Table 4). Preoperatively, most patients reported poor QoL (55.8%, n = 53), with only 7.4% (n = 7) rating it as good. By 3 days post-surgery, a substantial improvement was observed: 52.6% (n = 50) reported good QoL, and poor ratings decreased sharply to 5.3% (n = 5). At 1-month follow-up, good QoL further increased to 76.8% (n = 73), while poor ratings persisted in only 2 patients (2.1%). The most dramatic improvement occurred at 6 months post-surgery, with 95.8% (n = 91) reporting good QoL, and only 2 patients each categorized as fair (2.1%) or poor (2.1%) (Fig. 6). Sensitivity analyses confirmed the robustness of these findings. Linear mixed models of continuous SF-36 scores showed a significant time effect ($p < 0.001$). A binary model for achieving "Good" QoL yielded similarly increasing odds over time (6-month OR = 42.10, 95% CI: 19.21–92.28). A complete-case analysis (n = 91) produced nearly identical results, indicating that missing data did not influence the conclusions.

4. Discussion

The present study demonstrates that totally endoscopic removal of PFO/ASD occluder devices is a safe and effective treatment for patients with severe, device-related complications, particularly those associated with nickel hypersensitivity. The primary findings indicate that device explantation significantly improves clinical symptoms, with 95.8% of patients reporting good QoL at six months post-operatively. Additionally, the totally endoscopic approach was associated with minimal perioperative complications, no conversions to thoracotomy, and excellent cosmetic out-

Fig. 4. Explanted PFO occluder device, displaying post-removal condition. The figure shows multiple views of the device, including top-down and side perspectives.

Table 4. Quality of life ratings over time with adjusted odds ratios from GEE ordinal regression (n = 95).

Follow-up timepoint	Quality of life rating, n (%)			Adjusted OR* (95% CI)	*p*-value†
	Poor	Fair	Good		
Pre-surgery	53 (55.8)	35 (36.8)	7 (7.4)	1.00 (Ref)	
3-day post-surgery	5 (5.3)	40 (42.1)	50 (52.6)	8.21 (4.12–16.35)	<0.0001*
1-month post-surgery	2 (2.1)	20 (21.1)	73 (76.8)	15.47 (7.89–30.35)	<0.0001*
6-month post-surgery	2 (2.1)	2 (2.1)	91 (95.8)	35.92 (16.84–76.61)	<0.0001*

GEE, generalized estimating equations; OR, Odds Ratio; CI, Confidence Interval, *Adjusted for age, sex, indication, device brand, implant-to-explant interval, and nickel allergy status. †*p*-values adjusted for multiple comparisons (Bonferroni correction; $\alpha = 0.0167$). Proportional Odds Assumption: Score test $p = 0.12$, assumption upheld. Sensitivity Analyses: Linear mixed model for continuous SF-36 scores showed consistent improvement over time ($p < 0.001$). Binary logistic GEE (Good vs. Not Good) yielded similar ORs and significance. Complete-case analysis (n = 91) did not alter conclusions.

comes, reinforcing its safety and efficacy. The findings underscore the need for careful patient selection and monitoring for nickel hypersensitivity in individuals undergoing PFO/ASD device implantation.

Our findings are consistent with previous studies that have highlighted the positive outcomes of device removal in patients experiencing complications associated with nickel hypersensitivity. Similar to the results reported by Sharma *et al.* [9] who found significant symptom relief in 58 patients following the removal of atrial septal occluders, our study showed a high rate of symptom resolution. Likewise, Fernandes *et al.* [22] reported complete migraine resolution in a 16-year-old patient following device explantation due to nickel allergy, a result that aligns with the improvements observed in our cohort. However, our study differs from prior research in terms of the surgical approach. While previous studies have primarily focused on open thoracotomy for device removal, such as in the case series by Verma and Tobis [23], we employed a totally endoscopic approach, which resulted in minimal scarring and faster recovery times. This minimally invasive method demonstrated similar efficacy in symptom resolution without the need for more invasive surgical techniques. Furthermore, our study highlights the importance of preoperative nickel allergy testing, as 89.5% of patients with positive tests showed substantial improvement post-explantation, which

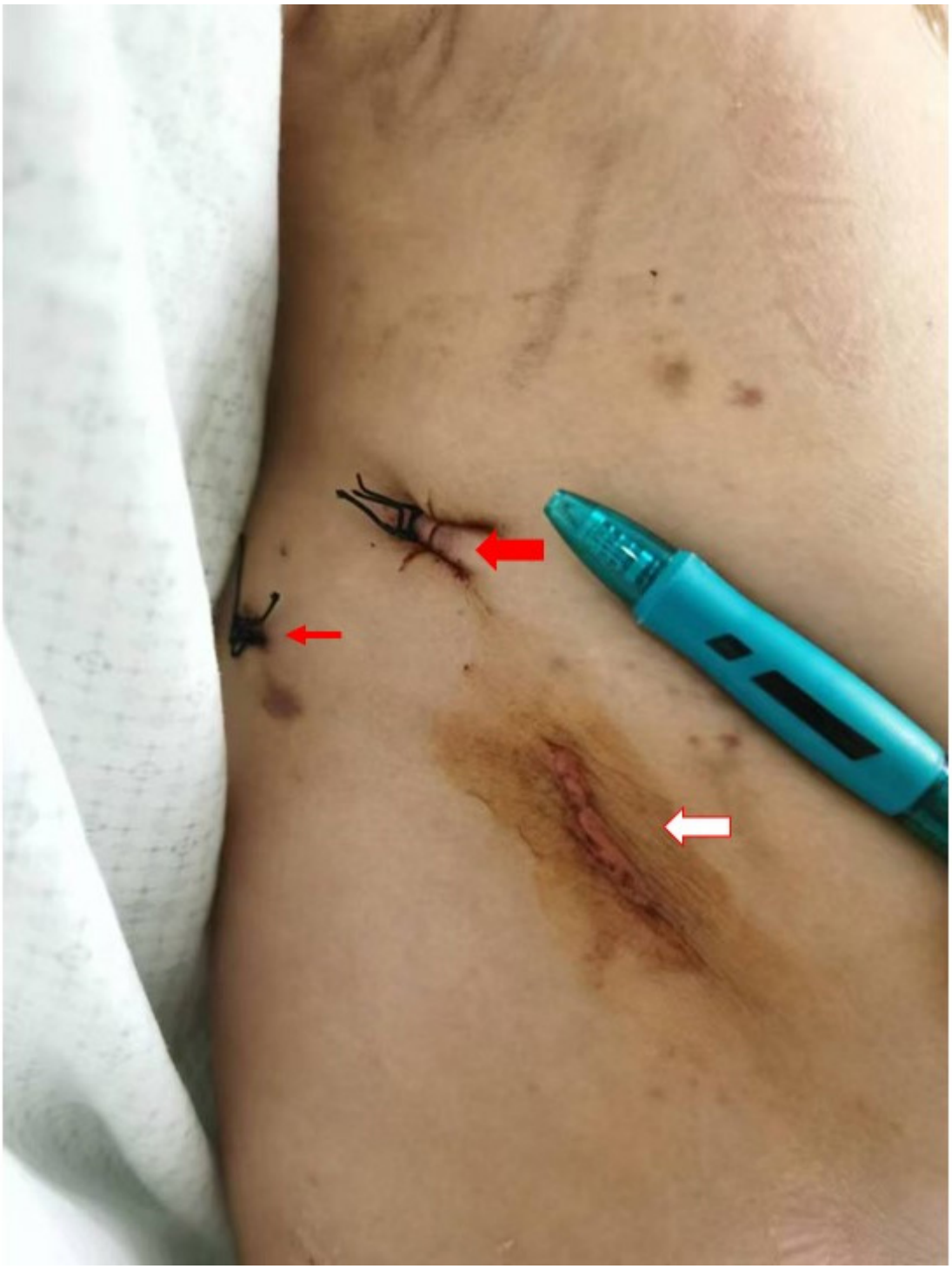


Fig. 5. Postoperative thoracoscopic incisions following totally endoscopic removal of a PFO occluder device. The red arrows highlight small thoracoscopic entry points, while the white arrow indicates the primary incision for device removal. Minimal scarring is visible, demonstrating the less invasive nature of the procedure. The image illustrates the favorable cosmetic outcome and limited surgical trauma associated with the endoscopic approach.

reinforces the findings of Apostolos *et al*. [6] on the role of nickel allergy in device-related complications. Besides, the 10.5% nickel-negative patients also exhibited improvement post-explantation, which may attributed to removal of endothelial dysfunction profiles, confirming device removal as a universal solution for refractory complications. The combination of our surgical approach and focus on allergy testing makes our study unique compared to prior literature.

The finding that a substantial majority of patients in this cohort presenting for occluder removal had a docu-

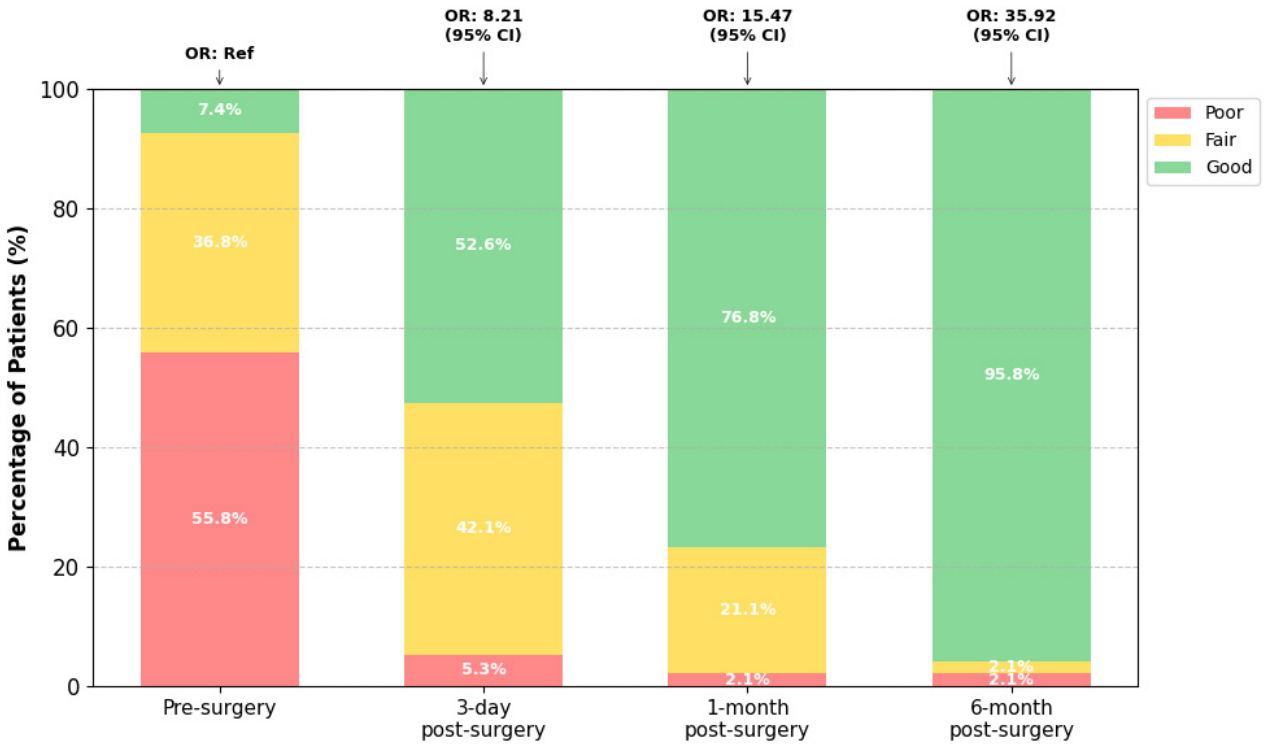


Fig. 6. Longitudinal quality of life improvement following endoscopic PFO/ASD occluder removal. Stacked percentage bar chart showing the distribution of Quality of Life ratings (Poor, Fair, Good) at four time points among 95 patients. Percentages are labeled within each segment. Adjusted odds ratios (OR) from GEE ordinal regression model are displayed above each bar, demonstrating significant improvement over time (all $p < 0.0001$). The proportion of patients reporting "Good" QoL increased from 7.4% preoperatively to 95.8% at 6 months post-surgery.

mented allergy—most commonly metal hypersensitivity—is striking but consistent with a growing body of evidence. This high prevalence is not representative of the general population receiving cardiac occluders but is instead a profound example of selection bias. This cohort does not consist of random post-operative patients; it is a highly specific group whose devices have failed, often due to intolerable adverse symptoms that prompted surgical intervention. Therefore, the 80%+ figure likely reflects the key etiological role of hypersensitivity reactions in driving device failure and explantation, rather than the incidence of allergy in all implanted patients.

Supplementary Table 1 highlight various cases and studies concerning patients who underwent device explantation due to complications related to PFO or ASD occlusion devices. A recurrent theme across several studies is the resolution of symptoms, such as migraines, chest pain, and systemic hypersensitivity, following the removal of the devices. In the case of Fernandes *et al.* [22], a 16-year-old male experienced complete relief from migraines post-explantation after six years, with incomplete endothelialization identified as a contributing factor [22]. Other studies, such as Spina *et al.* [24] and Wertman *et al.* [4], also underscore the link between nickel hypersensitivity and adverse outcomes, recommending preoperative allergy screening. Studies like Rodés-Cabau *et al.* [1] showed that dual antiplatelet therapy could reduce migraines in patients with ASD occlusion devices. Finally, Sadasivan Nair *et al.* [14] and Verma and Tobis [23] highlight that nickel allergies are a significant reason for explantation, with complete symptom resolution post-device removal in most cases. These findings underscore the importance of preoperative assessments and monitoring for nickel allergies to avoid long-term complications.

The endoscopic method used in our cohort resulted in shorter recovery times, minimal postoperative complications, and excellent cosmetic outcomes. Unlike traditional open thoracotomy, which has been the standard in cases requiring PFO or ASD device explantation [23]. Furthermore, the high success rate of direct septal repair (96.8%) without the need for extensive patch repair emphasizes the effectiveness of the endoscopic technique in managing residual septal defects, a finding that has not been as prominently addressed in prior studies. The minimal blood loss (36.8 mL) and low incidence of postoperative AF (2.1%) in our study further highlight the safety profile of this technique compared to previous reports where complications such as arrhythmia were more prevalent following device

explantation using traditional methods [9]. Additionally, the emphasis on preoperative nickel allergy testing, with 89.5% of patients showing positive results, supports the growing recognition of the importance of allergy screening in device-related procedures [6]. This comprehensive combination of a minimally invasive approach and targeted preoperative assessments makes our study unique and highlights the potential for improving patient outcomes in future cases.

One limitation of our study is its retrospective design, which may introduce selection bias and limit the generalizability of the results. While our retrospective design precludes definitive causal attribution, the temporal association between device implantation and symptom onset provides compelling evidence: 84.2% (80/95) of patients developed symptoms within 24 hours post-procedure (Table 2), corresponding precisely to the 12–72 hour activation window of Type IV nickel hypersensitivity reactions. This acute manifestation pattern—distinct from endothelialization failure (typically >4 weeks)—strongly implicates immune-mediated mechanisms rather than mechanical complications. Additionally, the relatively small sample size of 95 patients may not fully capture the broader population of individuals with PFO/ASD occluder devices, especially those with nickel hypersensitivity. While our cohort represents the largest reported series of totally endoscopic PFO/ASD device explantations, we acknowledge that rare indications inherently limit sample size. The lack of a control group for comparison with non-allergic patients further limits the strength of our conclusions. Moreover, long-term follow-up data beyond six months were not available, preventing an assessment of the durability of symptom relief and long-term complications. While our study confirmed nickel allergy via patch testing, we lacked micro-level analysis of explanted devices (e.g., SEM quantification of corrosion or microthrombi). Future work will include these analyses to quantify surface degradation and its clinical correlations. Lastly, while nickel hypersensitivity was identified in the majority of patients, the specific pathophysiological mechanisms linking nickel allergy to device-related symptoms remain unclear, requiring further research.

5. Conclusions

In conclusion, the totally endoscopic removal of PFO/ASD occluder devices offers a promising, minimally invasive option for patients experiencing complications related to nickel hypersensitivity or device intolerance. This approach is not only associated with favorable cosmetic outcomes and reduced surgical trauma but also provides significant symptom relief. However, the current understanding of nickel hypersensitivity and its long-term impact on intracardiac devices remains limited. Future studies should focus on developing standardized screening protocols for nickel allergy prior to device implantation and exploring the long-term safety and effectiveness of endoscopic explantation procedures. Additionally, more extensive research is needed to elucidate the pathophysiological mechanisms linking nickel exposure to device-related complications, which could inform both preoperative assessments and post-implantation monitoring strategies. Multicenter, prospective trials with larger, more diverse populations will be crucial to improving the management and treatment outcomes for patients requiring PFO/ASD occluder.

Availability of Data and Materials

The datasets generated and analyzed during the current study are not publicly available due to privacy and confidentiality concerns but are available from the corresponding author on reasonable request. Access to the data may be granted for research purposes following approval by the institutional review board and adherence to applicable data protection regulations.

Author Contributions

HS contributed to the conception and design of the work; acquired, analyzed, and interpreted the patient data; and drafted the manuscript. MR Contributed to the design of the work; acquired data (surgical procedures); analyzed and interpreted the intraoperative and outcomes data; and critically revised the manuscript for important intellectual content. DL contributed to the acquisition and analysis of the data, including statistical analysis; and critically revised the manuscript. SJ contributed to the design of the work, supervised the surgical procedures and data acquisition, and critically revised the manuscript. NC contributed to the conception of the work, the analysis and interpretation of follow-up data, and the revision of the manuscript. LZ contributed to the conception and design of the work; coordinated the study and supervised data acquisition; interpreted the results; critically revised the manuscript for important intellectual content; served as the corresponding author and finalized the manuscript; and ensured adherence to ethical standards. All authors provided final approval of the version to be published and agree to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

This study was conducted in accordance with the Declaration of Helsinki and was approved by the institutional review board of The First Medical Center of Chinese PLA General Hospital (No. S2025-492-01). Given the retrospective nature of the study, the requirement for informed consent was waived. All patient data were anonymized to ensure privacy and confidentiality. The ethical guidelines of the hospital were strictly followed throughout the research process.

Acknowledgment

Not applicable.

Funding

This research received no external funding.

Conflict of Interest

The authors declare no conflict of interest.

Supplementary Material

Supplementary material associated with this article can be found, in the online version, at https://doi.org/10.31083/HSF49911.

References

[1] Rodés-Cabau J, Horlick E, Ibrahim R, Cheema AN, Labinaz M, Nadeem N, *et al*. Effect of Clopidogrel and Aspirin vs Aspirin Alone on Migraine Headaches After Transcatheter Atrial Septal Defect Closure: The CANOA Randomized Clinical Trial. JAMA. 2015; 314: 2147–2154. https://doi.org/10.1001/jama.2015.13919.

[2] Chen Z, Liu Y, Song Q, Zou H. Re-conceptualization of the "Chinese Expert Guidelines for the Prevention of Stroke Associated with Patent Foramen Ovale" for the management of perioperative stroke in patients with lung cancer. Cardiovascular Innovations and Applications. 2023; 8: 980.

[3] Braun MU, Fassbender D, Schoen SP, Haass M, Schraeder R, Scholtz W, *et al*. Transcatheter closure of patent foramen ovale in patients with cerebral ischemia. Journal of the American College of Cardiology. 2002; 39: 2019–2025. https://doi.org/10.1016/s0735-1097(02)01904-6.

[4] Wertman B, Azarbal B, Riedl M, Tobis J. Adverse events associated with nickel allergy in patients undergoing percutaneous atrial septal defect or patent foramen ovale closure. Journal of the American College of Cardiology. 2006; 47: 1226–1227. https://doi.org/10.1016/j.jacc.2005.12.017.

[5] Zeng H, Lan B, Liu X, Xie H, Li B, Xue X, *et al*. Clinical Implications and Procedural Complications in Patients with Patent Foramen Ovale Concomitant with Atrial Septal Aneurysm. Cardiovascular Innovations and Applications. 2024; 9: 943.

[6] Apostolos A, Drakopoulou M, Gregoriou S, Synetos A, Trantalis G, Tsivgoulis G, *et al*. Nickel Hypersensitivity to Atrial Septal Occluders: Smoke Without Fire? Clinical Reviews in Allergy & Immunology. 2022; 62: 476–483. https://doi.org/10.1007/s12016-021-08867-0.

[7] Dickison P, Harris V, Smith SD. Nickel hypersensitivity following closure of atrial septal defect: A case report and review of the literature. The Australasian Journal of Dermatology. 2018; 59: 220–222. https://doi.org/10.1111/ajd.12787.

[8] Tjen VH, Yang PZ. Nickel-related hypersensitivity reactions following endovascular interventions: A review of current evidence. Science Progress. 2023; 106: 368504231200626. https://doi.org/10.1177/00368504231200626.

[9] Sharma V, DeShazo RA, Skidmore CR, Glotzbach JP, Koliopoulou A, Javan H, *et al*. Surgical explantation of atrial septal closure devices for refractory nickel allergy symptoms. The Journal of Thoracic and Cardiovascular Surgery. 2020; 160: 502–509.e1. https://doi.org/10.1016/j.jtcvs.2019.10.177.

[10] Schmidt M, Raghavan B, Müller V, Vogl T, Fejer G, Tchaptchet S, *et al*. Crucial role for human Toll-like receptor 4 in the development of contact allergy to nickel. Nature Immunology. 2010; 11: 814–819. https://doi.org/10.1038/ni.1919.

[11] Martin SF. Immunological mechanisms in allergic contact dermatitis. Current Opinion in Allergy and Clinical Immunology. 2015; 15: 124–130. https://doi.org/10.1097/ACI.0000000000000142.

[12] Wang S, Qiao W, Dong N. Residual shunt and microthrombosis associated with new-onset migraine after transcatheter atrial septal defect closure. European Heart Journal. 2023; 44: 4605. https://doi.org/10.1093/eurheartj/ehad645.

[13] Resor CD, Goldminz AM, Shekar P, Padera R, O'Gara PT, Shah PB. Systemic Allergic Contact Dermatitis Due to a GORE CARDIOFORM Septal Occluder Device: A Case Report and Literature Review. JACC. Case Reports. 2020; 2: 1867–1871. https://doi.org/10.1016/j.jaccas.2020.05.091.

[14] Sadasivan Nair P, Jaya JS, Comella A, Smith JA, Harper R, Joshi PP. Migraine-like headaches associated with nickel allergy requiring removal of atrial septal defect closure device. Indian Journal of Thoracic and Cardiovascular Surgery. 2021; 37: 299–302. https://doi.org/10.1007/s12055-021-01155-8.

[15] Rabkin DG, Whitehead KJ, Michaels AD, Powell DL, Karwande SV. Unusual presentation of nickel allergy requiring explantation of an Amplatzer atrial septal occluder device. Clinical Cardiology. 2009; 32: E55–E57. https://doi.org/10.1002/clc.20427.

[16] Silberstein SD, Holland S, Freitag F, Dodick DW, Argoff C, Ashman E, *et al*. Evidence-based guideline update: pharmacologic treatment for episodic migraine prevention in adults: report of the Quality Standards Subcommittee of the American Academy of Neurology and the American Headache Society. Neurology. 2012; 78: 1337–1345. https://doi.org/10.1212/WNL.0b013e3182535d20.

[17] Wintzer-Wehekind J, Horlick E, Ibrahim R, Cheema AN, Labinaz M, Nadeem N, *et al*. Effect of Clopidogrel and Aspirin vs Aspirin Alone on Migraine Headaches After Transcatheter Atrial Septal Defect Closure: One-Year Results of the CANOA Randomized Clinical Trial. JAMA Cardiology. 2021; 6: 209–213. https://doi.org/10.1001/jamacardio.2020.4297.

[18] Sposato LA, Albin CSW, Elkind MSV, Kamel H, Saver JL. Patent Foramen Ovale Management for Secondary Stroke Prevention: State-of-the-Art Appraisal of Current Evidence. Stroke. 2024; 55: 236–247. https://doi.org/10.1161/STROKEAHA.123.040546.

[19] McHorney CA, Ware JE, Jr, Raczek AE. The MOS 36-Item Short-Form Health Survey (SF-36): II. Psychometric and clinical tests of validity in measuring physical and mental health constructs. Medical Care. 1993; 31: 247–263. https://doi.org/10.1097/00005650-199303000-00006.

[20] Spertus JA, Winder JA, Dewhurst TA, Deyo RA, Fihn SD. Monitoring the quality of life in patients with coronary artery disease. The American Journal of Cardiology. 1994; 74: 1240–1244. https://doi.org/10.1016/0002-9149(94)90555-x.

[21] Belardinelli R, Georgiou D, Cianci G, Purcaro A. Randomized, controlled trial of long-term moderate exercise training in chronic heart failure: effects on functional capacity, quality of life, and clinical outcome. Circulation. 1999; 99: 1173–1182. https://doi.org/10.1161/01.cir.99.9.1173.

[22] Fernandes P, Sharma SR, Magee A, Michielon G, Fraisse A. Severe Migraine Associated With Nickel Allergy Requiring Surgical Removal of Atrial Septal Device. The Annals of Thoracic Surgery. 2019; 108: e183–e184. https://doi.org/10.1016/j.athoracsur.2019.01.034.

[23] Verma SK, Tobis JM. Explantation of patent foramen ovale closure devices: a multicenter survey. JACC. Cardiovascular Interventions. 2011; 4: 579–585. https://doi.org/10.1016/j.jcin.2011.01.009.

[24] Spina R, Muller DWM, Jansz P, Gunalingam B. Nickel hypersensitivity reaction following Amplatzer atrial septal defect occluder device deployment successfully treated by explantation of the device. International Journal of Cardiology. 2016; 223: 242–243. https://doi.org/10.1016/j.ijcard.2016.08.112.