Thrombus formation on an atrial septal defect closure device: A case report and review of the literature

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Thrombus formation; Transcatheter closure; Atrial septal defect; Transesophageal echocardiography

**Abstract** We report on a case of a mobile left atrial thrombus formation on an atrial septal defect occluder system (28 mm StarFLEX\textsuperscript{a}-Occluder) despite 6 months of postprocedural anticoagulation with phenprocoumon and platelet antiaggregation with aspirin in a 69-year-old woman. The closure was performed because of a significant left to right atrial shunt (Qp/Qs 1.8) with enlargement of the right atrial and ventricular cavities and impairment of right ventricular function in the presence of persistent atrial fibrillation and chronic heart failure (NYHA II–III). The 6-month follow up by transesophageal echocardiography (TEE) revealed the floating thrombus located at the left atrial side of the occluder.

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We are presenting this case in context with a review of the current literature focussing on predictors of thrombus formation on transcatheter ASD-closure devices.

**Case presentation**

A 69-year-old woman was admitted for transcatheter closure of an atrial septal defect (ASD).

The patient showed symptoms of chronic heart failure (NYHA II–III) and had a medical history of systemic hypertension for 19 years and received oral anticoagulation with phenprocoumon due to atrial fibrillation for 1 year. There were no episodes of systemic embolism or deep vein thrombosis in the past.

Echocardiography and cardiac catheterisation revealed an ASD leading to a significant left to right atrial shunt (Qp/Qs 1.8) with enlargement of the right atrial and ventricular cavities and impairment of right ventricular function. The patient underwent a TEE-guided transcatheter closure of the atrial septal defect under local anaesthesia using a 28 mm StarFLEX\textsuperscript{a}-Occluder without residual shunt. The medication with phenprocoumon had been stopped 5 days prior to closure device implantation and changed to anticoagulation with intravenous heparin before and in the first days after ASD closure. Phenprocoumon was started again with a target INR of 2.5 and aspirin 100 mg per day was added.

The patient came back for a scheduled follow-up after 6 months. She did not report any complications during the period after closure device implantation to follow-up except episodes of epistaxis. Therefore aspirin 100 mg per day had

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been stopped by her general physician after 5 months. There was a reduction of heart failure symptoms (NYHA I–II). According to the weekly blood samples, the anticoagulation with phenprocoumon was strictly managed during the 6 months with INR values ranging between 2.0 and 3.0.

TEE after 6 months showed a floating echogenic structure connected to the left atrial part of the well positioned StarFLEX®-Occluder without any additional atrial or ventricular thrombi and absence of spontaneous echo contrast (Fig. 1). There was no residual shunt on colour Doppler imaging. The patient was checked for a possible coagulation disorder although congenital or acquired hypercoagulation seemed rather improbable. The check up was performed without testing resistance to activated Protein C and Protein S deficiency because of ongoing therapy with phenprocoumon, and with heparin under continuing atrial fibrillation.

The patient was referred for surgery and underwent a successful explantation of the device together with the thrombotic apposition and a closure of the atrial septal defect using a pericardial patch (Fig. 2).

Comment on the current literature

Transcatheter closure of different congenital atrial septal defects leading to paradoxical embolism or intracardiac shunt has become an effective and less invasive alternative to surgery. Appropriate anticoagulation after transcatheter device placement is discussed controversially especially in cases without history of systemic embolism. Patients without thromboembolism or neurologic events typically receive antiplatelet therapy for several months until the endothelialisation of the blood exposed parts has been completed. For patients with a history of stroke or atrial fibrillation, there are no established guidelines for postprocedural anticoagulation. Most of the patients receive warfarin, antiplatelet therapy, or different combinations.

In our department, patients undergoing a transcatheter device placement with a StarFLEX®-Occluder due to an ASD with significant shunt or paradoxical embolism in cases of PFO receive anticoagulation with phenprocoumon (target INR 2.5) together with antiplatelet therapy with aspirin 100 mg per day for 6 months in order to avoid postprocedural device associated thrombus formation.

Device associated atrial thrombi after transcatheter ASD- or PFO-closure are reported complications (Table 1), but the true incidence may be underestimated and there are no randomised trials assessing independent predictors of device associated thrombi. There are no investigations comparing patients receiving a transcatheter closure with similar pre- and postprocedural risk factors for thromboembolism or different closure devices under the same anticoagulation regimen.

In a study, La Rosée et al. analysed 102 consecutive patients treated for an ASD or PFO with the Amplatzer®, ASDOS® or PFO-Star® device. They saw 11 (11.2%) device associated thrombi in the early (2–3 days) TEE-follow-up (two ASDOS®-ASD, five ASDOS®-PFO, three PFO-STAR® and one Amplatzer®-ASD device). Phenprocoumon was used in the first 20 ASDOS®-treated patients and the other patients received a combination of aspirin together with either ticlopidine 500 mg or clopidogrel 75 mg per day for 6 months. The patients treated with the Amplatzer® device received aspirin 100 mg per day for 12 months and the PFO-Star® patients had a regimen with aspirin...
<table>
<thead>
<tr>
<th>Author</th>
<th>Treated disorder</th>
<th>No. and kind of closure device used</th>
<th>Antiaggregation and/or anticoagulation</th>
<th>Time of TEE follow up</th>
<th>No. of thrombus formed (%)</th>
<th>Outcome</th>
<th>Independent predictor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sievert et al.¹</td>
<td>ASD or PFO</td>
<td>139 ASDOSŹ</td>
<td>Warfarin or aspirin</td>
<td>1–4 weeks</td>
<td>9 (6)</td>
<td>1 surgically explanted, 7 resolved</td>
<td>Not known</td>
</tr>
<tr>
<td>La Rosée et al.²</td>
<td>ASD or PFO</td>
<td>22 ASDOSŹ</td>
<td>Warfarin</td>
<td>3 days to 4 weeks</td>
<td>6 (27)</td>
<td>All resolved</td>
<td>Not known</td>
</tr>
<tr>
<td>Franke et al.³</td>
<td>ASD or PFO</td>
<td>32 CardioSEAL®, 4 ASDOS®, 2 Amplatzer®</td>
<td>Warfarin or aspirin + clopidogrel</td>
<td>1–6 months</td>
<td>5 (13)</td>
<td>1 surgically explanted, 4 resolved</td>
<td>Not known</td>
</tr>
<tr>
<td>Sievert et al.⁴</td>
<td>PFO</td>
<td>98 PFO Star®, 57 Amplatzer®, 37 CardioSEAL®, 33 Helex®, 26 Sideris buttoned®, 19 Angel Wings®, 11ASDOS®</td>
<td>Aspirin or warfarin or aspirin + clopidogrel</td>
<td>2 weeks to 6 months</td>
<td>7 (2.5)</td>
<td>All resolved</td>
<td>Not known</td>
</tr>
<tr>
<td>Krumsdorf et al.⁵</td>
<td>ASD or PFO</td>
<td>26 Sideris buttoned®, 25 PFO-Star®, 16 Amplatzer®, 12 CardioSEAL®, 7 Helex®, 3 Angle Wings®</td>
<td>Aspirin + clopidogrel</td>
<td>4 weeks</td>
<td>3 (6)</td>
<td>All resolved</td>
<td>Not known</td>
</tr>
<tr>
<td>La Rosée et al.⁶</td>
<td>ASD or PFO</td>
<td>44 ASDOSŹ, 34 PFO-Star®, 25 Amplatzer®</td>
<td>Phenprocoumon or aspirin or aspirin + clopidogrel or aspirin + ticlopidin</td>
<td>3 days to 6 months to 1 year</td>
<td>11 (11.2)</td>
<td>All resolved</td>
<td>Not known</td>
</tr>
<tr>
<td>Krumsdorf et al.⁷</td>
<td>ASD or PFO</td>
<td>418 Amplatzer®, 161 Helex®, 142 StarFLEX®, 127 PFO Star®, 52 buttoned device, 42 ASDOS®, 30 Angle Wings®, 27 CardioSEAL®, 1 Rashkind®</td>
<td>Warfarin or aspirin + clopidogrel or aspirin</td>
<td>3 days to 4 weeks to 6 months to 1 year</td>
<td>20 (2)</td>
<td>17 resolved, 3 surgically explanted</td>
<td>CardioSEAL, StarFlex, atrial fibrillation, atrial septal aneurysm</td>
</tr>
<tr>
<td>Anzai et al.⁸</td>
<td>ASD or PFO</td>
<td>36 Amplatzer®, 30 CardioSEAL®</td>
<td>Aspirin + clopidogrel or additionally warfarin</td>
<td>1 month</td>
<td>5 (10)</td>
<td>3 resolved, 1 surgically explanted</td>
<td>CardioSEAL</td>
</tr>
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</table>
100 mg/day for 12 months together with clopidogrel 75 mg for 3 months. The majority of thrombi resolved after 6 months of anticoagulation and there was only one detectable thrombus after 1 year. There were no independent predictors of thrombus in this trial.

Krumsfldorf et al.\textsuperscript{7} reported 1000 consecutive patients, 593 of them with PFO and 407 with an ASD. There were 20 device associated thrombi during the 4-week (n = 14) or 6-month (n = 6) follow up by TEE. Nine different closure devices were used. The thrombi occurred more often in patients with the CardioSEAL\textsuperscript{©} (7.1%) or the StarFLEX\textsuperscript{©} (5.7%) device compared to the Amplatzer\textsuperscript{©} device (p < 0.05). There was a trend toward device associated thrombi in patients with persisting or new onset atrial fibrillation after the procedure (n = 4; 6.2 vs. 20%; p < 0.05) as well as in patients with persisting atrial septal aneurysm (ASA) despite effective transcatheter closure (n = 4; 1.3 vs. 20%, p < 0.01). It should be mentioned that the patients underwent platelet antiaggregation with aspirin and clopidogrel and most of the thrombi (17/20) disappeared after anticoagulation with either heparin or warfarin alone or under their combined therapy. Three of the thrombi had to be surgically explanted together with the device after persistence under anticoagulation.

A similar trend towards the type of closure device used as a possible independent predictor of thrombus formation was revealed by Anzai et al.\textsuperscript{8} in a study with 66 consecutive patients treated for PFO or ASD with the Amplatzer\textsuperscript{©} or CardioSEAL\textsuperscript{©} closure system. Five thrombi were found on CardioSEAL\textsuperscript{®} devices (p = 0.02), none on the other system. Only one device was surgically removed, the other thrombi resolved under anticoagulation. ASA or atrial fibrillation were not identified as independent predictors of thrombus formation in this study.

In summary, there are only two studies trying to discriminate predictors of device associated thrombus formation after transcatheter closure. The trend towards persisting ASA as well as atrial fibrillation as possible independent risk factors or a preference for the CardioSEAL\textsuperscript{©} or the later developed StarFLEX\textsuperscript{©} occluder system in comparison with the Amplatzer device should be discussed very carefully; there are no randomised trials offering a randomly assigned patient collective with similar risk factors under the same or different anticoagulation regimens.

Cetta et al.\textsuperscript{9} focused on a patient after transcatheter closure of a PFO with the CardioSEAL\textsuperscript{©} closure device. A large left atrial thrombus formation occurred despite accurate warfarin therapy in the absence of arrhythmias or coagulation disorders.

In comparison, our case demonstrates an unexpected thrombus occurrence despite effective combined anticoagulation and platelet antiaggregation.

The optimal anticoagulation for transcatheter closure of atrial septal defects at increased thrombotic risk is not known. In the presence of atrial fibrillation and/or enlarged cavities, routine TEE follow up of the patients is suggested. TEE follow up should be performed after 6 months in cases without additional prothrombotic risk factors. An early TEE follow up after 4 weeks could be useful in the presence of increased thrombotic risk.

References