Introduction

The Antiphospholipid Syndrome (APS) is an autoimmune multisystem disorder characterized by both arterial and venous thrombosis (1). The most common sites for thrombosis are in the deep veins of the lower limbs and the arteries that comprise the cerebral circulation (2). The disease is defined by a combination of at least one clinical feature characterized by vascular thrombosis or pregnancy morbidity and elevated titers of antiphospholipid antibodies (aPL), which include anti-Beta2 Glycoprotein-I antibodies, anticardiolipin antibodies, and lupus anticoagulant (3). Catastrophic APS (CAPS) is a severe subset of APS that mainly involves small vessels (microvascular thrombosis) affecting multiple organs such as the lungs, heart, brain, kidney, liver, or GI tract and in various combinations with a high mortality rate (4, 5).

Because of the high propensity to form further clots, long-term anticoagulation therapy is usually recommended. Inferior vena cava (IVC) filter placement may be considered to prevent propagation of a distal thrombus to the pulmonary system. However long-term benefits of filters remain controversial. In particular, in APS, recurrent pulmonary emboli and thrombus proximal and distal to the IVC filter have been described in patients with permanent filters (6). Experts recommend avoiding IVC filters in the acute APS setting, as these devices can be associated with a variety of adverse events, including IVC thrombosis and pulmonary embolus (PE) (7).

Retrievable filters are filters that can be placed in patients at high risk for pulmonary embolism and then removed later once the risk has decreased. Relative indications for IVC filter placement include high clot burden in the setting of low cardiopulmonary reserve and high risk patients. In 2010, the FDA announced a safety communication recommending removal of retrievable IVC filters due to reports of several adverse clinical outcomes associated with retained filters, including thrombus formation and recurrent PE. In 2014, FDA recommended removal of IVC filters within two months after filter placement if the patient’s risk of thrombosis had passed (8, 9). However, many of these IVC filters are not retrieved and become permanent devices with complications (10). Retrievable filters have the advantage that they can be placed and removed while the patient is anticoagulated.

Objective

Consideration for placement of an inferior cava filter arises in patients with APS where cessation of anticoagulation is necessary or thrombotic complications continue despite maximal anticoagulation. Permanent IVC filters are recommended to be avoided. We evaluated the safety of placement and removal of retrievable inferior vena cava filters in patients with APS.

Methods: Case series of 5 patients with APS and aPL antibodies who had placement and removal of retrievable IVC filter (because of contraindication to anticoagulation or ongoing thrombosis despite full anticoagulation) to assess for safety, presence of clots in the vena cava or on the filter while in the body, evidence of PE, or clot on the explanted filter.

Results: Insertion and removal, even while on anticoagulation, was safe. There was no evidence of clot in the vena cava, on the filter or pulmonary embolism in all cases.

Conclusion: Where necessary, retrievable IVC filters may be safer in APS patients but should not be left in for long periods of time.

Keywords: Antiphospholipid syndrome, filter, inferior vena cava, thrombosis, anticoagulant
Given the potentially devastating effect of lack of anticoagulation in patients with APS, and the complications and concerns about lack of efficacy with permanent filters, we evaluated the safety of retrievable IVC filters (placement and removal) in a small case series of patients with APS requiring cessation of anticoagulation because of massive gastrointestinal bleeding, those requiring surgical procedures or other clinical situations where placement of a filter is considered while the patient is anticoagulated (6).

Methods

We performed a retrospective chart review of a total of five patients with aPL and APS who had placement (five) and removal (four/five) of a retrievable IVC filter at a single health plan and institution (HealthPartners Medical Group and Regions Hospital) between 2012 and 2015. One patient has not had their filter removed due to ongoing medical issues and non-compliance. Demographic and underlying disease data, indications for IVC filter placement, length of time IVC filter in place before removal, clots in the vena cava or the filter, evidence of further pulmonary embolism while having IVC filter in place, and results of the vena cavaogram and inspection of filter were assessed.

The IVC filter was placed either through the right common femoral vein or the right internal jugular vein. If the patient was anticoagulated, the anticoagulation was not stopped or altered for the procedure. The filters were deployed in an infrarenal location and checked for position. Removal was via the right internal jugular vein. A diagnostic inferior vena cavaogram, at the time of removal, showed the previously placed IVC filter and whether there was caval or filter thrombus. Following removal, the filter was inspected for evidence of clot. Patient consent rules were followed as per the instructions of the HealthPartners Institutional Review Board.

Results

Five patients (aged 32-83) had retrievable IVC filter placement because of ongoing thrombosis despite full dose anticoagulation, major surgical procedures requiring cessation of anticoagulation, or contraindications to anticoagulation, including massive gastrointestinal bleeding. Four/five patients had their filter removed from 7 days to 2 months post placement. One/five had ongoing medical complications and non-compliance, so her filter was not removed. No PE occurred in any of the patients. No evidence of clot formation was found with inspection of the retrieved filter or on vena cavaogram in the four/five patients. These results, along with demographic data, manifestations of APS, comorbid conditions, and indications, are summarized in Table 1.

Discussion

Patients with APS and thrombosis are often treated with long term anticoagulation since they carry a higher risk for recurrent thrombosis. Deep venous thrombosis is common and pulmonary embolism is a real concern. In clinical situations where anticoagulation is not possible or not advisable, consideration is often given for the placement of an IVC filter to prevent propagation of clots. Limited case reports on the use of permanent filters suggested that clot formation can still occur proximal and distal to the filter and recurrent pulmonary emboli may still be seen (6, 11). Cherian et al found clots on the proximal side of the filter (6). Zifman et al reported on 10 patients through 2007 who had IVC filter placement due to thromboembolic events. Four patients died within one year after the procedure and one after two years. Four patients did not experience a pulmonary embolus for more than five years after the procedure (11). Kasai et al have described this well in a patient with chronic thromboembolic pulmonary hypertension and primary APS. After placement of a Greenfield™ vena cava filter in 2003, a pulmonary endarterectomy was performed. By 2006, thrombi were visible by contrast CT in the IVC filter but no deep venous thrombosis or collateral circulation. In 2014, contrast CT showed complete obstruction of the inferior vena cava at the site of placement of the IVC filter. Further there was significant hyperplasia of collateral vessels. Blood flow below the occluded site of the IVC returned from the azygos vein to the superior vena cava via collateral circulation. The patient had transient dyspnea on exertion suggesting that this may have been related to pulmonary thromboemboli through collateral circulation (12). Lee et al reported on a 61-year-old patient with primary antiphospholipid syndrome who developed massive fatal pulmonary emboli despite placement of a bird’s nest filter seven months previously. At autopsy, both recent and organized thrombus was seen extending proximally from the filter (13).

Retrieval filters could possibly alleviate some of these problems. Montgomery and Ni et al have reviewed the types of retrievable IVC filters, indications, and complications that one must be aware of when contemplating their use in any patient. There are several available retrievable vena cava filters made of varying materials and design. Besides the immediate complications of access site pain, other complications may include filter penetration, filter embolization, filter movement/migration, filter tilt, and filter fracture. Since the best filter design remains elusive, further research on other filters, such as completely absorbable vena cava filters and drug eluting vena cava filters, is ongoing (14, 15).

Experts recommend avoiding permanent filters in the acute setting, as these devices can be associated with a variety of adverse events, including IVC thrombosis and PE. Also, IVC filter placement can exacerbate thrombotic complications in patients with heparin-induced thrombocytopenia (7). This review of five patients with APS and aPL suggests that retrievable IVC filters can be safely placed and removed. For the limited time they were in the body, there was no evidence of clot formation at the site of the filter or pulmonary embolus. One patient has not had the filter removed due to ongoing medical problems and non-compliance. The likelihood of successful removal of the filter after a longer period of time is reduced. This highlights one of the concerns even with retrievable filters as many are not retrieved and become permanent devices. It is unknown whether they are at higher risk for PE. In the short-term, retrievable IVC filters, may be safe and effective in patients with APS.

This series is limited by the small number of patients reported given that the clinical scenario where an IVC filter might be appropriate in an APS patient is uncommon.

In situations where an IVC filter is considered in patients with APS (major bleeding or surgery where anticoagulation must be held, or ongoing thrombosis despite therapy), a retrievable IVC filter may be safe to use. Anticoagulation is not a contraindication to placement or removal; however, clinicians must be diligent about removal once the indication is resolved so these do not become permanent devices. Most importantly, even with placement of an IVC filter, development of arterial thrombosis can certainly continue to occur while the patient is off anticoagulants. Therefore, limiting the time that the patient is off anticoagulants is of utmost importance and placement of the IVC filter does not alleviate that concern.
Table 1. Clinical, radiological and filter results

<table>
<thead>
<tr>
<th>Age</th>
<th>Sex</th>
<th>Diagnosis</th>
<th>Indication for IVC Filter Placement</th>
<th>Filter Type</th>
<th>Manifestations of APS</th>
<th>APS Profile (present)</th>
<th>Comorbid Conditions</th>
<th>Use of Hydroxychloroquine</th>
<th>Duration of IVC Filter</th>
<th>Placed on Anticoagulation</th>
<th>PE with IVC Filter</th>
<th>Vena Cavagram &amp; Inspection of Filter at Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>61</td>
<td>M</td>
<td>APS</td>
<td>Meridian</td>
<td>1) DVT with bilateral PE on warfarin 2) Despite full anticoagulation with INR&gt;3.0 developed extensive DVT (common femoral, greater saphenous, deep femoral) with PE to vessels of all pulmonary lobes and right heart strain.</td>
<td>β2GP1 aCLa PTT*</td>
<td>DM Non-smoker</td>
<td>No</td>
<td>1 month</td>
<td>Yes</td>
<td>No</td>
<td>No clot</td>
</tr>
<tr>
<td>2</td>
<td>32</td>
<td>M</td>
<td>SLE, APS, CAPS, HIT</td>
<td>Denali</td>
<td>1) DVT                  2) Hepatic arterial thrombosis, ischemic bowel, hepatic vein thrombosis, skin necrosis despite supratherapeutic warfarin therapy.</td>
<td>β2GP1 aCLa LAC</td>
<td>Smoker: 1-2 cigarettes/day</td>
<td>No</td>
<td>7 days</td>
<td>Yes</td>
<td>No</td>
<td>No clot</td>
</tr>
<tr>
<td>3</td>
<td>42</td>
<td>F</td>
<td>SLE, APS</td>
<td>Denali</td>
<td>1) DVT                  2) Cerebral infarction involving multiple vascular territories bilaterally 3) Severe PAH</td>
<td>β2GP1 aCLa LAC</td>
<td>DM Hyperlipidemia Non-smoker</td>
<td>Yes</td>
<td>2 years - not removed</td>
<td>Yes</td>
<td>No</td>
<td>n/a</td>
</tr>
<tr>
<td>4</td>
<td>36</td>
<td>M</td>
<td>APS, SLE</td>
<td>Denali</td>
<td>1) Extensive new DVT in setting of nephrotic syndrome with renal insufficiency requiring renal biopsy</td>
<td>aCLa LAC</td>
<td>Nephrotic syndrome Non-smoker</td>
<td>Yes</td>
<td>1 month</td>
<td>No</td>
<td>No</td>
<td>No clot</td>
</tr>
<tr>
<td>5</td>
<td>83</td>
<td>F</td>
<td>APS</td>
<td>Meridian</td>
<td>1) Recurrent DVTs 2) PE</td>
<td>β2GP1 aCLa LAC</td>
<td>DM HTN Non-smoker</td>
<td>No</td>
<td>2 months</td>
<td>Yes</td>
<td>No</td>
<td>No clot</td>
</tr>
</tbody>
</table>

aCLa: anticardiolipin antibodies; APS = antiphospholipid syndrome; β2GP1: β2 glycoprotein 1 antibody; CAPS: catastrophic antiphospholipid antibody syndrome; DM: diabetes mellitus; DVT: deep venous thrombosis; GI: gastrointestinal; HIT: heparin induced thrombocytopenia; HTN: hypertension; LAC: lupus anticoagulant; PAH: pulmonary arterial hypertension; PE: pulmonary embolus; PTT: partial thromboplastin time; SLE: systemic lupus erythematosus.

*LAC result not retrievable from chart.
Ethics Committee Approval: Ethics committee approval was received for this study from the HealthPartners Institutional Review Board.

Informed Consent: Written informed consent was obtained as per the instructions of the HealthPartners Institutional Review Board.

Peer-review: Externally peer-reviewed.


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References