Impact of Unilateral Common Iliac Vein Occlusion on Trapping Efficacy of the Greenfield Filter: An in Vitro Study

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Rationale and Objectives. The purpose of this study was to assess the effect of unilateral common iliac vein occlusion on the capturing efficacy of the Greenfield filter in vitro.

Materials and Methods. A stainless steel over-the-wire Greenfield filter was placed in the Silastic inferior vena cava module of a pulsatile circuit. Three 30-mm blood clots in sets of five were injected through the module’s right iliac limb with the circuit in four experimental conditions: vertical position, both iliac limbs patent (VP); vertical position, left iliac limb occluded (VOC); horizontal position, both iliac limbs patent (HP); and horizontal position, left iliac limb occluded (HOC). Each experiment was repeated 15 times, resulting in 75 clots per condition and a total of 300 clot introductions.

Results. Clot trapping efficacy was 36 of 75 (48%) for VP, 41 of 75 (55%) for VOC, 32 of 75 (43%) for HP, and 26 of 75 (35%) for HOC. Cross comparisons of the four conditions revealed a marginally significant difference ($P = .0138$ with a corrected test-wise $\alpha = .0125$) only between horizontal and vertical positions with unilateral common iliac limb occlusion.

Conclusion. Unilateral common iliac vein occlusion decreases the capturing efficacy of the Greenfield filter in the horizontal position in vitro. In patients with unilateral common iliac vein occlusion, use of inferior vena cava filters with higher capturing efficacy may be considered.

Key Words. Venae cavae filters, embolism, veins; iliac, vein; thrombosis, laboratory investigation.

Placement of an inferior vena cava (IVC) filter is an accepted therapeutic option for patients with pulmonary embolism when anticoagulation has failed or is contraindicated. Clot from the lower extremities is the most common source of pulmonary emboli (1). In a recent multicenter study, 71.8% of patients referred for temporary IVC filtration had pelvic vein thrombosis (2). Simon et al (3) suggest that the trapping efficacy of caval filters may be adversely affected in the presence of unilateral iliac vein occlusion. Since this could impact a relatively large percentage of patients referred for IVC filtration, we performed an in vitro study with the widely used Greenfield filter. We tested the hypothesis that unilateral common iliac vein occlusion adversely affects trapping efficacy.

MATERIALS AND METHODS

Inferior Vena Cava Model

A flow model was constructed from rigid polyvinyl chloride (PVC) tubing with an inner diameter of 26 mm. For an 18-cm-long IVC module insert, 21-mm inner diameter Silastic tubing was used to allow excursions of the softer material with the cardiac cycles of the flow circuit. A common iliac vein simulation was represented by a 50° Y-connector plastic tubing with an inner diameter of 13
mm and Tygon tubing (Saint-Gobain Performance Plastics, Akron, Ohio). Tygon is softer and more flexible than PVC but less flexible than the Silastic used for the IVC module (Fig 1).

A 12-F, stainless steel over-the-wire Greenfield filter (Boston Scientific/Medi-Tech, Watertown, Mass) was placed in the IVC module with its apex centered 15 cm from the common iliac vein confluence. A cardiovascular pump (model 1421; Harvard Apparatus, South Natick, Mass) provided pulsatile flow from a heated (37°C) reservoir at a flow rate of 2.0 L/min (30 mL stroke volume and 66 beats per minute). Glycerin solution (glycerin USP 44%; Humco, Texarkana, Tex) was chosen to circulate in the system because of the close resemblance of its viscosity and specific gravity with that of human blood (4).

A side port in the right common iliac limb allowed for introduction of blood clots. A wire mesh at the entry to the reservoir retained clots passing through the filter. The circuit was mounted on a stepladder system allowing for positioning of the IVC model in vertical and horizontal positions.

Simulation of Thrombi
Fresh sheep blood was allowed to clot in 1-mL plastic syringes at room temperature. The clot-containing syringes were refrigerated at 4°C for availability. Clots were extruded, cut to 30-mm-long segments, and immersed in 44%-glycerin solution for 30 minutes at room temperature prior to use. Resulting clots were 3 × 30 mm.

Experimental Sequence
Clots were introduced in sets of five. Clots were slowly delivered individually through the side port with a 60-mL catheter-tip syringe containing glycerin solution. Air was carefully expelled from the syringe to avoid flow disturbances caused by bubbles. A clot was considered captured if it was arrested by the filter for at least 1 minute (3,5). If a clot was captured by the filter for less than 1 minute or it immediately passed through, it was considered not captured. After the 1-minute period elapsed, a subsequent clot was released. After introduction of each set of five clots, the filter was cleaned of all clots.

We tested our hypothesis with the circuit in four conditions: vertical position, both iliac limbs patent (VP); vertical position, left iliac limb occluded (VOC); horizontal position, both iliac limbs patent (HP); and horizontal position, left iliac occluded (HOC) (Fig 2). Each set of five-clot deliveries was repeated 15 times for each of the four conditions, resulting in delivery of a total of 300 clots.

Statistical Analysis
The number of first-clot and subsequent-clot captures was recorded. Using a Pearson χ² test (6), we compared the total number of captures between the vertical versus horizontal position with unilateral patency, the vertical versus horizontal position with bilateral patency, unilateral patency versus bilateral patency in the horizontal position, and unilateral patency versus bilateral patency in the vertical position. In each case, the hypothesis being tested is that the experimental conditions differ with respect to clot capture. The test is whether the differences in proportions exceed those expected as random deviations from proportionality.

The alpha level for multiple tests was corrected by using the Bonferroni inequality; the test-wise alpha level was 0.05/(4 tests) = .0125. In making multiple tests using α = .05, the probability of making at least one type I error—that is, falsely rejecting the null hypothesis in a test—increases. There is a principle from probability theory that gives us an upper bound for the probability that one or more such tests will lead to a type I error. This Bonferroni inequality implies that we should divide α = .05 by the number of tests if we wish the probability to be no more than .05 that at least one type I error occurs (7).
Please note that this is a relatively conservative and statistically puristic approach toward data analysis, in particular when comparing the results of the various working groups referenced, who—as far as we can judge—did not use corrections for multiple testing. Inherently, use of the Bonferroni inequality makes it more difficult to show statistical differences among groups.

RESULTS

For all conditions, the first clot in each set of five was retained at a higher frequency than subsequent clots (Fig 3). Capturing efficacy of the first clot in each set was 73% in the horizontal position with both iliac limbs patent (HP) or the left limb occluded (HOC). In the vertical position the capturing capacity of the first clot in each set was 93% with the left iliac limb occluded (VOC) and 86% with both iliac limbs patent (VP).

Of 75 clots injected for each experimental condition, 26 (35%) were captured in the horizontal occluded position (HOC), 32 (43%) in the horizontal patent condition (HP), 41 (55%) in the vertical occluded position (VOC), and 36 (48%) in the vertical patent (VP) condition. No significant differences in the frequencies of capture were found between HOC and HP (Pearson $\chi^2 = 1.012, P = .3144$), VOC and VP (Pearson $\chi^2 = 0.667, P = .4141$), and HP and VP (Pearson $\chi^2 = 0.430, P = .5118$). Clot capture in the HOC condition was significantly poorer than that in the VOC condition (Pearson $\chi^2 = 6.069, P = .0138$). If we correct the alpha level for multiple tests with the Bonferroni inequality, the test-wise alpha level becomes 0.05/(4 tests) = .0125. The difference in clot capture between HOC and VOC would be marginally significant by this standard. Representative modes of clot capture are shown in Figures 4 and 5.

DISCUSSION

In this in vitro study, the Greenfield filter trapped 35%–55% of clots depending on the flow condition: Uni-
lateral common iliac limb occlusion was associated with marginally significantly lower trapping efficacy in the horizontal position. The relatively low overall capture rates for similar-sized clots and the wide variation in capture rates dependent on the experimental condition agree with the findings of several other studies (3,5,8–12) (Table). One finds, however, less agreement when examining the impact of the specific flow conditions on the outcome: Simon et al (3) reported a significantly poorer clot trapping efficacy for the horizontal compared with the vertical position (40% vs 52% for the stainless steel Greenfield filter; 45% vs 58% for the titanium Greenfield filter) but not for Bird’s Nest, Simon Nitinol, or Vena Tech filters. Likewise, Hammer et al (5) observed differences between the horizontal and vertical positions in two filters (50% vs 70% for the stainless steel filter; 70% vs 83% for the titanium model) but not for the remaining seven filters tested in their study. Katsamouris et al (8) reported capture rates of 18% and 68% for the horizontal and vertical positions without a formal statistical evaluation. Qian et al (11) found nearly the same trapping efficacy for horizontal and vertical circuits with iliac bifurcations (43% vs 40%); likewise, we failed to show a difference. A marginally significant difference between horizontal and vertical positions emerged in our study only when one iliac limb was occluded (35% vs 55%).

The study that most closely assessed the impact of single-limb versus double-limb inflow was the work of Hammer et al (5). These authors measured trapping efficacy for a Greenfield filter in a vena cava model with and without an iliac bifurcation and found no difference (42% vs 45%; data estimated from figure 2 in reference 5). There are, however, methodological differences: The “single limb” of Hammer et al did not contain a bifurcation with one limb occluded but instead was a single straight length of tubing from the pump to the IVC module. A straight “uni-limb” arrangement is expected to have fewer flow disturbances than a model in which the iliac limbs join the caval module at an angle. In

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**Figure 3.** Graph of cumulatively trapped clots. The “ideal” line indicates a 100% trapping efficacy.
that case, passage of the total volume flow is through one patent limb, instead of two, resulting in higher linear velocities.

Our experimental model assumed that the flow rate through a single patent iliac limb equals the flow rate through both iliac limbs in the nonoccluded state. This may not necessarily reflect in vivo conditions, since not all flow from an occluded limb necessarily drains into a patent contralateral common iliac vein, and overall flow into and from the obstructed extremity may differ from flow in the healthy state. It is difficult, and perhaps impossible, to predict percentage reduction in flow in a generalizable fashion and thus simulate accurately the impact of unilateral common iliac vein occlusion on the flow profile in the IVC. This is an inherent limitation of our study and, in general, of all studies of this kind. Also, any kind of in vitro simulation typically lacks the complexities of the in vivo dynamics and the undulating curvatures of the iliac veins as they course through the pelvis.

Considering that in vitro testing is an integral component in evaluating the efficacy of caval filters, it is important to identify flow conditions that can be expected in the target population and, even more important, when these conditions compromise filter performance. As have others, we observed that clots encountering a Greenfield filter that is free of clot have a higher likelihood of capture (5,8). In our experiments, the majority of first clots injected became firmly wedged between the filter struts at the apex. Subsequent clots that entered the filter were less frequently wedged. Some halted, tended to follow the pulsations, and bounced against the wedged clot. In this unstable condition, small disturbances can easily cause this clot to pass through the filter struts (Fig 4). In the laboratory, we could easily disengage such clots from the filter by simply tapping the simulated IVC. Furthermore, transient changes of intracaval pressures may suffice to produce the same effect in vivo. Clots encountering a filter preloaded with clot had a greater

Figure 4. Vertical position. Three frames during (a) systole, (b) mid-diastole, and (c) diastole. In a, three clots appear well captured by the IVC filter as the forward direction of flow forces the clots against the filter’s apex. In b and c, however, clots are not firmly trapped at the apex; the inferiormost of the clots (arrow) will bounce against the apex and dislodge after a few pulsations. Findings were similar for circuits with patent and occluded iliac limbs.
tendency to pass laterally between the filter’s widespread struts, as was also observed by Robinson et al (10). The horizontal position favors gravitation of the clots to the dependent portion of the IVC and thus passage through the widespread struts. This has also been described in vivo (8). Inflow from both iliac veins tended to spiral the clot toward the apex of the filter in our experiments and thus increased the likelihood of capture (Fig 5a). With unilateral occlusion, the spiraling effect was less pronounced, and gravitational margination prevailed (Fig 5b). Thus, unilateral iliac vein occlusion may be expected to decrease trapping efficacy of the Greenfield filter also in the supine position in vivo. It is not clear how much additional tilting of the Greenfield filter would alter the results. (The filters in the experiment were deployed over a straight guide-wire from a right iliac approach and were centered, resulting in minimal tilt.) One may speculate that tilting associated with wider struts in the dependent position may allow even more clots to pass in the horizontal unilateral flow condition.

There is no general awareness that unilateral iliac vein occlusion can decrease capturing efficacy of Greenfield type filters. On the basis of our data, however, trapping efficacy may indeed be adversely affected in unilateral common iliac vein occlusion. Awareness of this possibility may stimulate the interventional community to explore the use of other filters with better trapping efficacy than the Greenfield filter (3,5) in this clinical situation, and to promote inclusion of this simulation in the in vitro testing of caval filters.

Figure 5. Horizontal position. (a) Bilateral inflow. Three sequential frames during the cardiac cycle (top to bottom) demonstrate the course of a clot with the circuit. Clots tend to flow toward the filter’s apex and become trapped. (b) Unilateral inflow. Three sequential frames (top to bottom) demonstrate the course of a clot with the circuit in the horizontal position and unilateral inflow. Occlusion of one limb of the IVC module combined with gravitational effect makes clots flow in the dependent portion of the IVC and escape through the struts.
Comparison of Reported Trapping Efficacies of the Greenfield Filter

<table>
<thead>
<tr>
<th>Study</th>
<th>Overall Trapping Efficacy (%)</th>
<th>Clot Type</th>
<th>Clot Size (mm)</th>
<th>Positional Differences</th>
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</thead>
<tbody>
<tr>
<td>Simon et al (3)</td>
<td>40–52</td>
<td>Human</td>
<td>2 × 30 and</td>
<td>GF: Horizontal, 40%; vertical, 52%</td>
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<td></td>
<td></td>
<td></td>
<td>4 × 30</td>
<td>TG: Horizontal, 45%; vertical, 58%</td>
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<tr>
<td>Hammer et al (5)</td>
<td>32–78</td>
<td>Human</td>
<td>2.5 × 30</td>
<td>KG: Horizontal, 50%; vertical, 70%</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>TG: Horizontal, 70%; vertical, 83%</td>
</tr>
<tr>
<td>Katsamouris et al (8)</td>
<td>18–68</td>
<td>Mixed blood with bovine thrombin</td>
<td>3 × 20</td>
<td>KG: Horizontal, 18%; vertical, 68%</td>
</tr>
<tr>
<td>Palestrant et al (9)</td>
<td>77</td>
<td>Canine</td>
<td>4 × 20 and</td>
<td>KG: 54% with filter tilt</td>
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<td></td>
<td></td>
<td></td>
<td>7 × 20</td>
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<tr>
<td>Robinson et al (10)</td>
<td>20, 23</td>
<td>Canine</td>
<td>6 × 30 and</td>
<td>Experiment done in horizontal position only</td>
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<td></td>
<td></td>
<td></td>
<td>9.2 × 30</td>
<td></td>
</tr>
<tr>
<td>Qian et al (11)</td>
<td>40–43</td>
<td>Canine</td>
<td>3 × 30</td>
<td>KG: Horizontal, 43%; vertical, 40%</td>
</tr>
<tr>
<td>Korbin et al (12)</td>
<td>15–98</td>
<td>Human</td>
<td>5 × 5, 5 × 10, 5 × 15</td>
<td>No interlocked legs, 95%–97.5%; one leg interlocking, 55%–97%; two legs interlocking, 15%–75% (TG with interlocking filter legs)</td>
</tr>
<tr>
<td>Kraimps et al (13)</td>
<td>34</td>
<td>Bovine</td>
<td>3 × 15</td>
<td>“Standard Greenfield”; experiment done in horizontal position only</td>
</tr>
<tr>
<td>Current study</td>
<td>35–55</td>
<td>Sheep</td>
<td>3 × 30</td>
<td>SS: Horizontal, 43% (patent iliacs) or 35% (unilateral occlusion); vertical, 48% (patent iliacs) or 55% (unilateral occlusion)</td>
</tr>
</tbody>
</table>

Note.—KG = Kimray-Greenfield filter, TG = titanium Greenfield filter, SS = 12-F over-the-wire Greenfield filter.

* Data from figure 3 of Katsamouris et al (8).

REFERENCES