Medicine

Changes in perfusion angiography after IVC filter placement and retrieval

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Abstract
Inferior vena cava (IVC) filters are posited to effect flow dynamics, causing turbulence, vascular remodeling and eventual thrombosis; however, minimal data exists evaluating hemodynamic effects of IVC filters in vivo. The purpose of this study was to determine differences in hemodynamic flow parameters acquired with two-dimension (2D)-perfusion angiography before and after IVC filter placement or retrieval. 2D-perfusion images were reconstructed retrospectively from digital subtraction angiography from a cohort of 37 patients (13F/24M) before and after filter placement (n = 18) or retrieval (n = 23). Average dwell time was 239.5 ± 132.1 days. Changes in the density per pixel per second within a region of interest (ROI) were used to calculate contrast arrival time (AT), time-to-peak (TTP), wash-in-rate (WIR), and mean transit time (MTT). Measurements were obtained superior to, inferior to, and within the filter. Differences in hemodynamic parameters before and after intervention were compared, as well as correlation between parameters versus filter dwell time. A P value with Bonferroni correction of <.004 was considered statistically significant. After placement, there was no difference in any 2D-perfusion variable. After retrieval, ROIs within and inferior to the filter showed a significantly shorter TTP (1.7 vs 1.4 s, P = .004; 1.5 vs 1.3 s, P = .001, respectively) and MTT (1.7 vs 1.4 s, P = .003; 1.5 vs 1.2 s, P = .002, respectively). Difference in variables showed no significant correlation when compared to dwell time. 2D-perfusion angiography is feasible to evaluate hemodynamic effects of IVC filters in vivo. TTP and MTT within and below the filter after retrieval were significantly changed, without apparent correlation to dwell time, suggesting a functional hemodynamic delay secondary to filter presence.

Abbreviations: 2D = two-dimension, AT = arrival time, DSA = digital subtraction angiography, DVT = deep venous thrombosis, IVC = inferior vena cava, MTT = mean transit time, PD = peak density, PE = pulmonary embolism, ROI = region of interest, TACE = transarterial chemoembolization, TIPS = transjugular intrahepatic portosystemic shunt, TTP = time-to-peak, VTE = venous thromboembolic, WIR = wash-in-rate.

Keywords: venous thromboembolism, inferior vena cava filter, perfusion angiography, deep venous thrombosis, pulmonary embolism, interventional radiology, hemodynamics

1. Introduction

Venous thromboembolic (VTE) disease such as deep venous thrombosis (DVT) and pulmonary embolism (PE) are amongst the most common life-threatening cardiovascular diseases, carrying a high rate of morbidity and mortality as well as a significant economic burden.[1–4] In patients who have failed or have contraindications to anticoagulation, retrievable inferior vena cava (IVC) filters are indicated for the treatment of acute venous VTE disease in order to mechanically prevent thrombus migration.[5,6]

While prospective and randomized controlled trials are limited, observational and cohort studies have demonstrated both beneficial effects and complications of IVC filters.[7–13] Early randomized controlled trials comparing filters to anticoagulation showed a reduction of PE initially, with an inversion of the risk/benefit ratio after 14 days and associated increased incidence of recurrent DVT at 2 and 8-year follow-ups. However, secondary trials did not report similar findings.[14–16] Currently, minimal data exists evaluating the hemodynamic changes caused by IVC filters and associated complications. Incidence of IVC stenosis and/or thrombosis is estimated at 2.8% of filter placements,

occasionally requiring extensive iliocaval reconstruction to treat the resulting lower extremity swelling, pain, exercise intolerance, or phlegmasia.[14,17,18]

IVC filters are hypothesized to induce changes in flow dynamics, with the creation of turbulent flow, recirculation zones, and high sheer force, leading to vascular remodeling and thrombus formation.[19,20] In vitro and computational studies have examined the hemodynamic properties of IVC filters to elucidate these effects, however, hemodynamic changes caused by IVC filters are not well documented in vivo.[19–22]

Technologic advancements in two-dimension (2D) perfusion angiography now allows for post-processing of digital subtraction angiography (DSA) to qualitatively evaluate flow in vivo. 2D-perfusion angiography outputs have been successfully correlated with changes in vascular flow dynamics and clinical scales in critical limb ischemia, transarterial chemoembolization (TACE), and transjugular intrahepatic portosystemic shunt (TIPS).[23–33] The purpose of this study was to determine the differences in hemodynamic flow parameters in vivo acquired with 2D-perfusion angiography before and after IVC filter placement or retrieval.

2. Materials and methods

Institutional board review approval was obtained and consent was waived given the retrospective nature of the study. Clinical data were collected from all patients who underwent IVC filter placement or removal between June 2017 and June 2019 at a single academic center. Exclusion criteria were age <18 years old, venography not amenable to reconstruction with 2D-perfusion angiography, patients requiring additional post-retrieval intervention (balloon angioplasty or stenting), failure of filter placement or retrieval, lack of pre- or post- intervention venogram, adjustment of the patient table or C-arm during intervention, change in magnification between pre- and post-intervention venogram, or artifact in 2D-perfusion angiography reconstruction affecting data accuracy. Patient records were reviewed for demographic information, procedural dates, indication for IVC filter placement or removal, filter type, number of removal attempts, procedural technique, imaging findings, and additional interventions.

2.1. Procedural technique

Sedation was provided based on individual patient assessment per the American Society of Anesthesiologists guidelines or patient request. Percutaneous access of the right internal jugular or right common femoral vein was obtained under ultrasound guidance using a standard micropuncture set. Seldinger technique was used to place an introducer sheath in the neck followed by a flush catheter which was positioned immediately above the confluence of the iliac veins. Venography was performed for evaluation of the vena cava in preparation for placement or retrieval. Perfusion breath-hold DSA was performed at 3 frames per second following an injection 10 or 15 mL per second of contrast for a total volume of 30 mL, depending on patient characteristics. All parameters were identical for both pre- and post-intervention image acquisition including flow rates, catheter position, and angiography table position. The exact location of the flush catheter was noted based on imaging landmarks and radiopaque markers.

2.2. Filter placement

After initial imaging and identification of the level of the renal veins, the flush catheter was exchanged over a guidewire for the chosen filter delivery sheath after serial dilation. The IVC filter was placed in the infrarenal IVC. The flush catheter was subsequently reinserted over a guidewire and positioned in same location as initial venogram. Repeat venogram with identical parameters was obtained. The catheter was then removed, and hemostasis obtained via manual compression. Sterile dressings were applied.

2.3. Filter retrieval

After initial venography, if the filter was deemed appropriate for removal (e.g., no IVC thrombus), the flush catheter was exchanged over a guidewire for the chosen filter retrieval system after serial dilation of the tract. The retrieval system was placed superior to the filter hook. A snare retrieval device was initially attempted followed by endovascular forceps as appropriate. Once the filter was captured and collapsed within the retrieval sheath, the latter was removed, and the filter inspected. The introducer sheath and flush catheter were subsequently reinserted over a guidewire and positioned at the same location as the initial venogram. Repeat post-retrieval venography was performed using the same parameters. At the completion of the procedure, the catheter was removed, and hemostasis obtained via manual pressure. Sterile dressings were applied.

2.4. 2D-perfusion angiography post processing

2D-perfusion imaging and time-density curves were analyzed on a dedicated workstation (Philips Allura Xper FD20, Philips Medical Systems, Best, Netherlands). Pre- and post-intervention images were evaluated to ensure the minimal density of contrast was obtained and no artifact in 2D-perfusion angiography reconstruction was present which would affect data collection. Pre- and post- intervention images were linked, and a region of interest (ROI) was manually drawn to project on both images simultaneously. The ROI diameter was chosen individually for each subject based on the diameter of the IVC at the narrowest of the 3 locations of interest. The center of the ROI was placed in the center of the vena cava at each of the 3 locations of interest: approximately 1 cm above the hook of the filter, within the filter struts, and 1 cm below the struts (Fig. 1). Changes in contrast density per pixel per second within the ROI were calculated by the perfusion software to generate time-density curves and determine perfusion parameters, including: contrast arrival time (AT) (start of angiographic study to contrast media entering the ROI), time-to-peak (TTP) (time between AT and peak contrast of the time-density curve), wash-in-rate (WIR) (upward slope of the time density curve), and mean transit time (MTT) (width of time-density curve at half the maximum height). This data was calculated for each ROI at each location and exported from the dedicated workstation for statistical analysis.

2.5. Statistical analysis

Statistical analyses were performed with SPSS Statistical Software (Version 25, IBM, Armonk, NY). Shapiro–Wilk normality tests were performed on all data. Continuous parameters were analyzed using parametric 2-tailed paired t tests or non-parametric Wilcoxon signed rank tests as appropriate. Correlation analysis was performed by calculating the difference between variables post- versus pre-filter retrieval and comparing to filter dwell time using 2-tailed Pearson's correlation analysis. A conservative approach was taken, and a Bonferroni correction was applied to correct for the twelve comparisons between each intervention for a P value of <.004 for statistical significance.

3. Results

56 patients underwent successful IVC filter placement and/or retrieval using venography amendable to post-processing with 2D angiographic perfusion reconstruction. Four patients
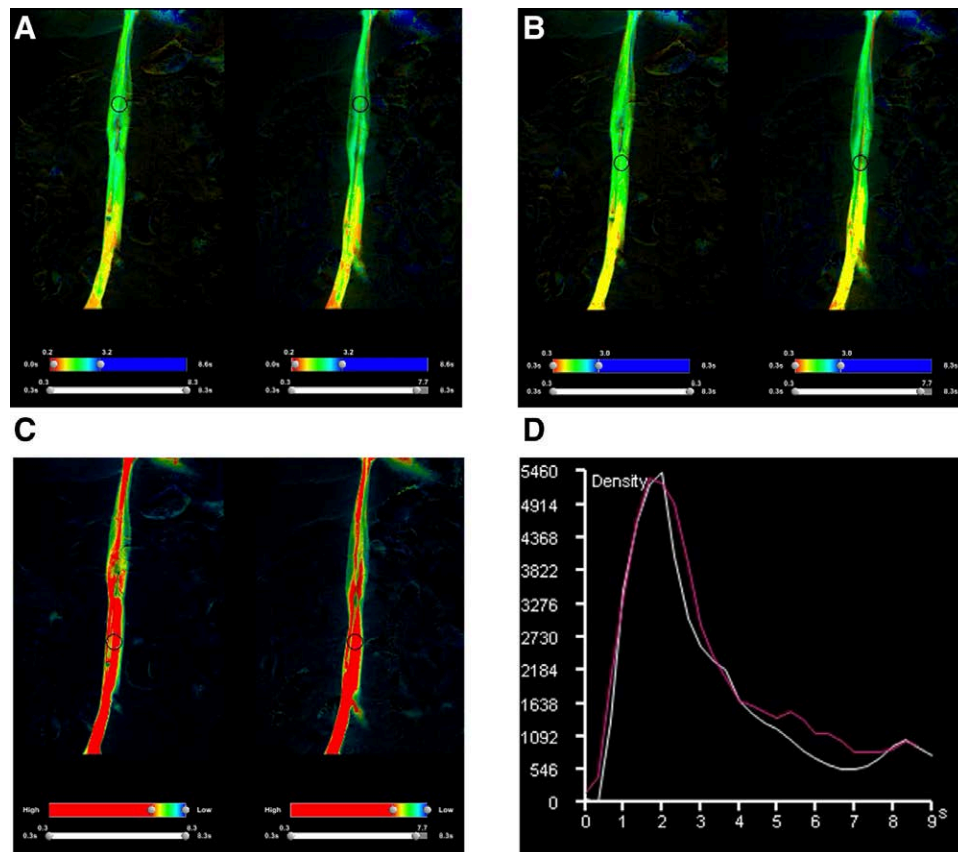
Figure 1. 2D-perfusion analysis before and after filter retrieval in a sample patient. Color flow maps depict examples of different perfusion variables and regions of interest (ROI): (A) mean transit time (MTT) for ROI above the filter, (B) time-to-peak (TTP) for ROI within the filter, (C) area under the curve (AUC) for ROI below the filter, and (D) time density curve produced for the ROI below the level of the filter.

underwent both placement and retrieval of their IVC filter at this institution within the study dates for a total of 60 interventions. Within this cohort, 1 study was excluded for post-intervention IVC stenosis requiring stenting, 7 were excluded due to missing pre- or post-intervention venograms, 6 due to required adjustment in the patient table or C-arm during intervention, and 5 due to post-processing artifact preventing accurate data collection. All filters were infrarenal in positioning. No patients displayed renal vein anomalies on venography.

A total of 37 patients (13F/24M), age 53.8 ± 14.3 (average ± stdev) years, underwent 41 procedures, 18 IVC filter placements and 23 retrievals, which met criteria for final inclusion in the study. Seven patients were on therapeutic anticoagulation at the time of intervention. One patient undergoing filter retrieval had an additional TIPS revision performed at the time of the procedure for treatment of refractory hepatic encephalopathy. Indications for IVC filter placement included: DVT with or without PE, or PE with or without diagnosed DVT with a contraindication for anticoagulation (e.g., active bleeding, upcoming surgery) (n = 36), or prophylaxis in the setting of extensive trauma (n = 1). Indications for retrieval included resolution of DVT and/or the ability to be appropriately anticoagulated. Filter types included the Cook Celect (Cook Medical, Bloomington, IN) (n = 36) and Bard Denali (BD Bard, Murray Hill, New Providence, NJ) (n = 1).

For patients undergoing IVC filter retrieval, average (± stdev) time from placement to retrieval (filter dwelling time) was 239.5 ± 132.1 days (range: 24–627 days). Thirteen of the 23 filters retrieved in this study were placed at outside institutions. Five of the 23 filters had undergone previous attempts at removal. Anesthesia at retrieval consisted of general (n = 3), monitored anesthesia care (MAC) (n = 9), moderate sedation

(n = 10), and local/systemic analgesia only (n = 1). Retrieval devices included use of snares (n = 16) or endovascular forceps (n = 7). Two filter retrievals were complicated by filter leg fracture requiring retrieval, which were both successful. No significant thrombus was seen in the filter cone for any patient during initial venogram. Fluoroscopy time/ radiation dose ranged from 22.98 ± 39.56 minutes/ 451.09 ± 714.13 mGy (average ± stdev) for retrieval interventions. Time between pre- and post-intervention 2D-perfusion venograms was 16.03 ± 6.37 minutes for placement and 45.07 ± 67.48 minutes for retrieval.

During filter placement, there was no statistically significant difference in any 2D-perfusion variable at any location of interest, pre- versus post-filter placement (Table 1). After retrieval, there was no difference in 2D-perfusion variables at the ROI when located above the filter. At the ROI locations within and below the filter, TTP contrast density was statistically significantly shorter after filter removal (1.66 vs 1.40 s, P = .004; 1.53 vs 1.25 s, P = .001, respectively). Additionally, mean transit time of contrast was shorter within the filter (1.70 vs 1.40 s), and below the filter (1.50 vs 1.15 s) after retrieval (P = .003 and .002, respectively). There was no difference in AT or wash in rate when compared pre/post-retrieval within or below the level of the IVC filter (Table 1). When comparing the difference in 2D-perfusion variables and evaluating against filter dwell time, there was no significant correlation for any variables at any ROI (Table 2; Fig. 2).

4. Discussion

This study presents the application of 2D-perfusion angiography for the objective assessment of changes in flow dynamics secondary to IVC filters in vivo in humans. VTE disease such as

Table 1

Comparison of 2D-perfusion variables pre- versus post-filter intervention.

Variable	Pre-intervention	Post-intervention	P value
Filter placement (N = 18)			
ROI above filter			
AT (s)	0.650	0.789	.190
TTP (s)	1.789	1.761	.794
WIR	671.656	648.089	.698
MTT (s)	1.972	1.928	.733
ROI within filter			
AT (s)	0.622	0.667	.659
TTP (s)	1.611	1.611	1.000
WIR	681.650	709.661	.706
MTT (s)	1.733	1.767	.739
ROI below filter			
AT (s)	0.606	0.650	.475
TTP (s)	1.506	1.433	.428
WIR	676.744	662.256	.879
MTT (s)	1.507	1.561	.707
Filter retrieval (N = 23)			
ROI above filter			
AT (s)	0.570	0.539	.271
TTP (s)	1.765	1.591	.087
WIR	565.548	524.874	.322
MTT (s)	1.804	1.596	.015
ROI within filter			
AT (s)	0.522	0.535	.639
TTP (s)	1.657	1.396	.004*
WIR	679.004	545.283	.010
MTT (s)	1.696	1.400	.003*
ROI below filter			
AT (s)	0.578	0.596	.583
TTP (s)	1.530	1.248	.001*
WIR	574.291	566.561	.890
MTT (s)	1.504	1.147	.002*

AT = arrival time, MTT = mean transit time, ROI = region of interest, TTP = time to peak, WIR = wash in rate.
*Denotes statistical significance.

Table 2

Difference between 2D-perfusion variables after filter retrieval versus days indwelling (N = 23).

Variable	r	P value
ROI above filter		
AT (s)	0.095	.67
TTP (s)	−0.090	.68
WIR	0.172	.43
MTT (s)	−0.004	.98
ROI within filter		
AT (s)	0.016	.94
TTP (s)	−0.286	.19
WIR	0.040	.86
MTT (s)	−0.165	.453
ROI below filter		
AT (s)	−0.296	.17
TTP (s)	−0.123	.58
WIR	0.272	.21
MTT (s)	0.075	.73

AT = arrival time, MTT = mean transit time, ROI = region of interest, TTP = time to peak, WIR = wash in rate.
*Denotes statistical significance.

DVT and/or PE has been estimated at up to 600,000 cases annually in the United States alone and carries a high mortality at 30 days and 1 year after diagnosis.[1–4,34–36] IVC filters often play an essential role in the treatment of VTE disease, however, changes in flow dynamics secondary to IVC filters have been hypothesized to induce vascular remodeling and thrombus formation, potentially leading to IVC occlusion or recurrent DVT.[15] Large scale prospective studies evaluating the risks and benefits of several IVC filter types, most notably the PRESERVE registry, are currently underway, emphasizing the need to better understand real world IVC filter performance in order to approach available clinical data and improve future filter design.[9] While hemodynamic changes secondary to IVC filters have been studied in vitro and in animal and computational models, human in vivo studies remain limited.

2D-perfusion angiography has been used to evaluate treatment changes before and after TIPS revision, TACE, pulmonary angioplasty, and for the treatment of critical limb ischemia, with changes in 2D-perfusion variables correlating to clinical targets such as the porto-systemic gradients or ankle-brachial index.[23,24,26,27] Prior chronic limb ischemia, TACE, and pulmonary angioplasty studies have shown significant changes in TTP, AT, peak density, WIR, and area under the curve after interventional treatment.[24–27,32] In this study, there were no differences in 2D-perfusion variables after filter placement. This is consistent with clinical findings and literature. Randomized controlled trials demonstrated a clinical benefit in the short term associated with filters without an increased incidence of DVT.[15] Therefore, lack of hemodynamic changes immediately after filter placement corroborates these clinical observations. At the time of retrieval, TTP and MTT were both found to be significantly shorter after filter removal, compared to times with the filter in place. This hints to a change in flow dynamics secondary to the presence of the filter, leading to prolonged transit times localized to the filter itself and just below it, but not above the filter. Whether these flow dynamic changes and prolongation of transit times correlate to a filter's potential thrombogenic effects is uncertain. While pre-retrieval venography did not identify any significant
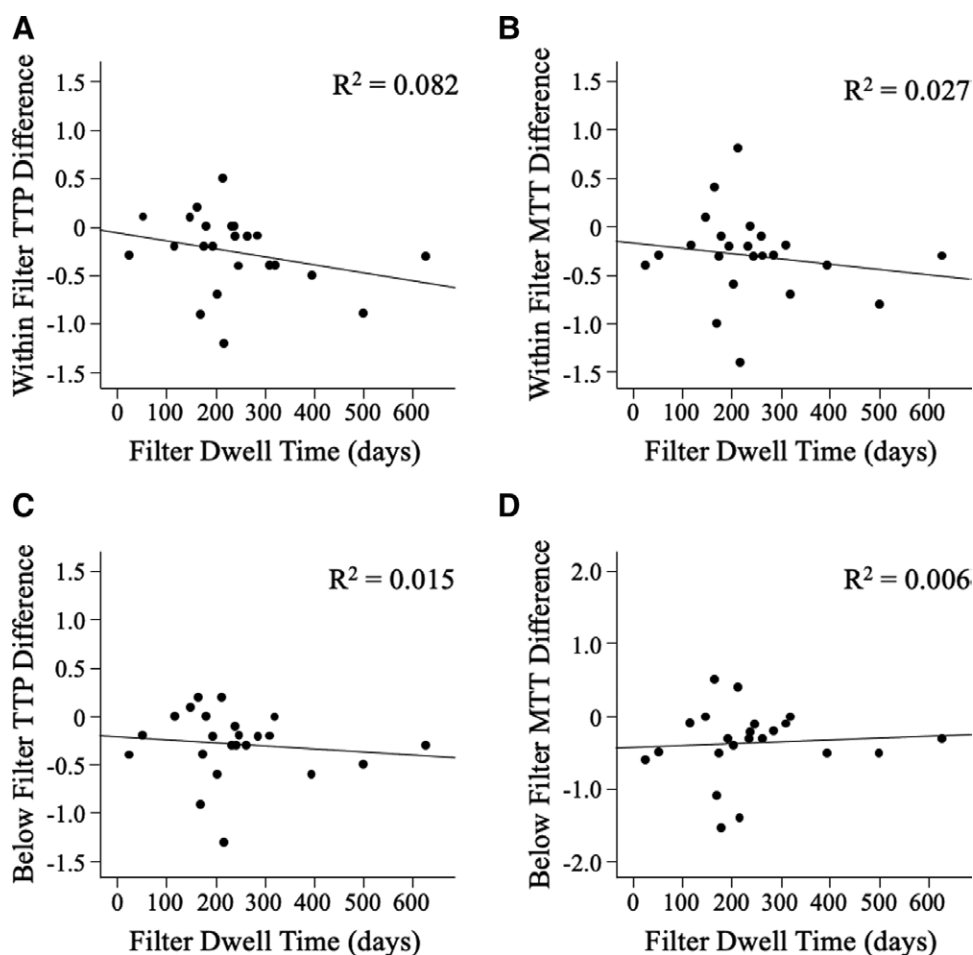
Figure 2. Scatter plots displaying filter dwell time versus difference in 2D-perfusion variables: (A) time-to-peak (TTP) for ROI within the filter; (B) mean transit time (MTT) for ROI within the filter; (C) time-to-peak (TTP) for ROI below the filter; (D) mean transit time for ROI below the filter.

clot within the IVC filter cone, smaller caliber clot or fibrin sheath development may be responsible for some component of the results shown. Even if fibrin sheath development on the filter was solely responsible for the hemodynamic changes noted in this study, this is nonetheless a consequence of the filter's presence. Additionally, prior computation models evaluating clot capture in the filter have noted increased recirculation zones downstream of the filter with filter occlusion, rather than below or within the filter struts.[22] If clot was responsible for the hemodynamic changes seen here, it would reason that hemodynamic changes would similarly be seen above the level of the filter, which was not seen in this study. An important point is that the changes occur immediately after filter removal, indicating that the prolonged flow is due to the filter presence or material adhered to the filter and appears reversible with filter retrieval.

Metanalysis of filter studies have indicated that prolonged filter use >30 days is associated with higher risk of unanticipated complications.[14] 2D-perfusion analysis in this study showed no change in flow dynamics immediately post placement of the filter. The patient population of this study had retrieval at approximately 7.9 months after placement with only 2 patients undergoing retrieval prior to 2 months of indwelling time. Based on this analysis, one could hypothesize that changes in hemodynamic flow would increase with increasing dwell time, however, this was not seen in any correlation analysis, including in the variables (MTT and TTP). This may indicate that hemodynamic changes (in the absence of significant clot) are not progressive or additive, but an "all-or-nothing" type effect after a particular threshold of dwell time (i.e., 30 days). In

addition, the Cook Celect filter which comprised the majority of the filters evaluated in this study has been found to have lower rates of IVC thrombosis or occlusion which may limit both the degree of hemodynamic changes and evaluation of progressive effects.

Comparisons of multiple filter types have shown that filter geometry plays a significant role in determining the flow dynamics, complications of a filter, and rates of filter thrombosis.[21,37] The study presented here primarily assessed the Cook Celect filter (N = 40/41), as this is the filter used at our particular institution at the time of data collection. Both the Cook Celect and Bard Denali from this study utilize a conical shape, which have a lower rate of IVC stenosis and thrombosis.[37] In contrast, filters of cylindrical design or with umbrella components (i.e., Vena Tech LGM [B. Braun, Melsungen, Germany] or Optease [Cordis, Hialeah, FL], etc) have shown higher rates of IVC occlusion compared to other filter designs.[37] In fact, a systematic review stated that complications appear to be device dependent although the lack of prospective comparison precludes affirmation of the superiority of one design.[14] Of note, 5 of the 8 filter designs in the PRESERVE filter registry utilize a conical shape, emphasizing the importance in investigating this filter geometry. If changes in flow dynamics are responsible for the thrombosis caused by filters, the Cook Celect may display comparatively low levels of hemodynamic changes, which may account for the lack of change in other 2D-perfusion variables. Future studies or multicenter trials with additional filter designs will be necessary in order to better understand these hemodynamic changes in comparison to filters of other geometries in vivo.

In vitro studies and computational analysis have noted the majority of flow disturbances and recirculation or stagnation zones to be downstream of the filter which does not reconcile with the clinical concerns of increased thrombus in the lower extremities.[19,21,22] Only 1 study utilizing the 2-tiered umbrella filter design showed changes in flow from the start of the central strut to the filter tip.[20] In contrast to in vitro evaluations, this in vivo analysis only noted significant changes in the hemodynamic flow at or below the level of the filter which would be expected if the hemodynamic changes were the cause of increased DVT. While superior variable control, in vitro computational studies lack the ability to assess changes induced within a patient, such as intimal hyperplasia, fibrin sheath formation, or low volume adherent clot. For example, the lack of downstream flow changes in our study may be explained physiologically by the fact that the renal vein inflow was sufficient to alter the effects caused by the filter.

This study was limited secondary to retrospectively collected data. Relatively small sample size may have limited detection of significance in other 2D-perfusion variables. The data analyzed was that of primarily 1 filter shape, limiting generalizability to other filter geometries (i.e., cylindrical, umbrella, helical). Due to procedural requirements, the flush catheter required removal and replacement pre- and post-filter intervention. While the pre-intervention location of the flush catheter was carefully assessed with imaging landmarks and radiopaque markers, slight differences in catheter placements may exist between the comparative runs. Additionally, the 2D-perfusion analysis utilized for this study links pre- and post-intervention DSA runs to ensure that the chosen ROI location is identical between images, however, the software does not provide measuring tools to ensure that ROI placement can be perfectly standardized across different subjects' images. While the filter was used as a standard landmark across subjects, future analysis with updated software will hopefully provide additional tools for greater ability to standardize across subjects. Finally, 2D-perfusion analysis may be limited by DSA frame rate, or affected by flow diversion (e.g., from the renal veins), patient's underlying cardiopulmonary status, or movement artifact, including overlying bowel, catheter movement on injection, or if the patient was unable comply fully with breath hold instructions.

5. Conclusions

2D-perfusion angiography is a viable and potentially valuable tool for the evaluation of hemodynamic effects of IVC filters in vivo. Over time, IVC filters are hypothesized to induce changes in hemodynamic flow below and at the level of the filter which may contribute to vascular remodeling and thrombus formation. These hemodynamic effects materialized only at retrieval which is consistent with the clinical literature that filters do not have an increased risk of thrombus formation in the short term. However, there was no apparent correlation between the changes in 2D-perfusion variables and filter dwell time. Further study will be required to evaluate the hemodynamic effects of various filter types and filters with shorter dwell times.

Author contributions

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