Venous thromboembolism (VTE) is a frequent complication of cancer and carries a significant risk of mortality. \(^1\) Anticoagulation serves as the mainstay of treatment for VTE in patients with cancer and deep venous thrombosis (DVT) or pulmonary embolus (PE), but the associated risk of bleeding may be prohibitive in some patients. In this situation, or in a scenario wherein patients experience recurrent or progressive VTE despite anticoagulation, inferior vena cava (IVC) filters may be used as a means of mechanical thromboprophylaxis. Placement of an IVC filter itself, though, is not without risk. The evidence to support the use of IVC filters in patients with cancer, specifically, is limited.

Balabhadra et al\(^2\) sought to address this knowledge gap and leverage administrative data in a population-based cohort study that evaluated the association of IVC filters with PE in patients with cancer and acute DVT. Through this study, they found that patients with risk factors for bleeding or bleeding complications were more likely to receive an IVC filter. Those that did undergo IVC filter placement experienced significant improvement in PE-free survival compared with those who did not receive an IVC filter in both the unadjusted and propensity-matched analyses. When stratified by the type of cancer and the risk of VTE with the specific diagnosis, IVC filters were associated with a reduced risk of PE for very high-risk, high-risk, and low-risk types of cancer. Finally, IVC filters were not associated with an increased risk of new DVT development after accounting for anticoagulation and bleeding risk factors.

When placed in the context of the broader clinical data surrounding the use of IVC filters, it is difficult to draw a clear conclusion. A small RCT comparing fondaparinux anticoagulation plus IVC filter placement with fondaparinux alone in patients with cancer found no difference in recurrent VTE, bleeding, or mortality at 3 years.\(^3\) The Prevention du Risque d’Embolie Pulmonaire par Interruption Cave (PREPIC) study, which randomized patients with proximal DVT to either permanent IVC filter plus anticoagulation or to anticoagulation alone, included only a small proportion of patients with cancer.\(^4\) While this study demonstrated IVC filters reduced the incidence of PE and increased the incidence of DVT, there was no improvement in survival at 8 years of follow-up. The PREPIC 2 study, which randomized patients with acute PE to either temporary IVC filter plus anticoagulation or to anticoagulation alone, was similarly limited in the number of enrolled patients with cancer.\(^5\) No significant differences in the rate of recurrent PE, symptomatic DVT, or bleeding were identified. It should be noted that none of these 3 trials included patients with contraindications to anticoagulation. Taken all together, these studies found IVC filters convey no clinical benefit in patients who are candidates for anticoagulation and have supported the development of consensus guidelines echoing the same.\(^6\)

At first glance, it would seem the findings of Balabhadra et al\(^2\) are in conflict with those of the randomized clinical trials pertaining to IVC filter use. Rather, this speaks to the heterogeneity in the trial populations as well as the study designs. The PREPIC and PREPIC 2 studies enrolled very few patients with cancer and all patients were candidates for anticoagulation.\(^4,5\) Similarly, while Bargineur et al\(^3\) enrolled only patients with cancer, this trial also included only those who were candidates for anticoagulation. Conversely, Balabhadra et al\(^2\) found that patients with risk factors for bleeding or bleeding complications such as gastrointestinal bleeding, intracranial hemorrhage, hematuria, or coagulopathy were more likely to receive an IVC filter. Therefore, it is reasonable to assume that in this study cohort many of those who received an IVC filter were likely not suitable for anticoagulation.
therapy and represent a fundamentally different study population than those enrolled in the comparator clinical trials. This difference may explain, at least in part, the conflicting study conclusions.

In the absence of randomized clinical trials, the use of administrative data, as demonstrated by Balabhadra et al., may provide an avenue for robust evaluation of IVC filter use in patients with cancer. Utilization of population-level claims data allows for large-sample, real-world analysis of outcomes outside the specific and highly structured clinical trial environment. Longitudinal follow-up, which is notoriously costly and burdensome in clinical trials, is a strength of claims-based analyses and allows for long-term outcomes evaluation. There are, of course, limitations as well. Population administrative data studies, including the work of Balabhadra et al., lack some of the granular patient-level information such as laboratory values, complete medical history, or device-specific implantation records provided in randomized clinical trials. Even strong approaches such as propensity matching can only match patients based on measurable confounders. Unmeasurable differences in the populations compared in their study may harbor confounders in patient selection, and, as such, sicker patients may not have received filters if their survival appeared limited to the clinicians involved in their care. An instrumental variable analysis may help account for such unmeasurable confounders and may allow future work to better estimate long-term survival effects in a pseudorandomized approach. Despite these limitations, Balabhadra et al. should be commended for utilizing population-based study techniques to clarify the role of IVC filters in patients with cancer and supplement the paucity of evidence therein.

ARTICLE INFORMATION


Open Access: This is an open access article distributed under the terms of the CC-BY License. © 2020 Barnes JA et al. JAMA Network Open.

Corresponding Author: Philip P. Goodney, MD, MS, Section of Vascular Surgery, Dartmouth-Hitchcock Medical Center, One Medical Center Drive, Lebanon, NH 03756 (Philip.P.Goodney@hitchcock.org).

Author Affiliations: Section of Vascular Surgery, Dartmouth-Hitchcock Medical Center, Lebanon, New Hampshire.

Conflict of Interest Disclosures: None reported.

REFERENCES


