The RETRIEVE Trial: Safety and Effectiveness of the Retrievable Crux Vena Cava Filter

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ABSTRACT

Purpose: To evaluate the safety and effectiveness of the Crux vena cava filter in patients at risk for pulmonary embolism (PE).

Materials and Methods: The Crux Biomedical Evaluation of the Crux Inferior Vena Cava Filter System trial was an international prospective, multicenter, single-arm clinical trial in 125 patients implanted with the Crux filter between June 2010 and June 2011. Follow-up was 180 days after filter placement and 30 days after filter retrieval. The primary objective was to determine whether the clinical success rate was at least 80%. Clinical success was defined as technical success of deployment and freedom from definite PE, filter migration, and device-related adverse events requiring intervention.

Results: The clinical success rate was 96.0% (120 of 125), with a one-sided lower limit of the 95% confidence interval of 91.8%. The rate of technical success was 98.4% (123 of 125). There were three cases of definite PE (2.4%), two cases of deployment failure, and no cases of device migration, embolization, fracture, or tilting. Investigators observed nine cases of thrombus (all nonocclusive) in or near the filter (six during retrieval evaluation vena cavography, two during computed tomography [CT] scans for PE symptoms, and one during CT for cancer management) and 13 cases of deep vein thrombosis. Device retrieval was attempted at a mean of 84.6 days ± 57.6 (range, 6–190 d) after implantation and was successful for 98.1% of patients (53 of 54). All deaths (n = 14) were determined to be unrelated to the filter or PE.

Conclusions: The Crux vena cava filter performed safely, with high rates of clinical, technical, and retrieval success.

ABBREVIATIONS

CI = confidence interval, DVT = deep vein thrombosis, ePTFE = expanded polytetrafluoroethylene, FDA = Food and Drug Administration, IVC = inferior vena cava, PE = pulmonary embolism, RETRIEVE = Crux Biomedical Evaluation of the Crux Inferior Vena Cava Filter System [trial], VTE = venous thromboembolism

Permanently deployed inferior vena cava (IVC) filters have been effective in reducing the short-term and long-term risk of pulmonary embolism (PE), but they have been associated with increased incidence of proximal deep vein thrombosis (DVT), with the risk appearing to increase with the indwelling duration (1–3). Other complications include venous access site thrombosis, hematoma, and infection; filter misplacement; penetration of the vessel wall; and filter migration, tilting, obstruction, and fracture (4,5). In 2003 and 2004, the United States Food and Drug Administration (FDA) approved changes in the instructions for use of three then-available permanent filters to allow for percutaneous retrieval, without modification of the indications for placement or the addition of indications for retrieval (6,7). The subsequent development of devices specifically designed to offer the option of permanent retention or appropriately timed removal has led to increased use of vena cava filters, with application expanded to patients with clearly short-term indications (eg, in a setting of trauma). The potential long-term complications associated with the permanent devices may be avoided by filter retrieval if and when the risks of

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bleeding or PE resolve or substantially decrease (7,8). Although several retrievable filters have been approved by the FDA, there has been limited publication of supportive data from prospective randomized trials (9–14). Concerns have been raised related to reported low rates of actual retrieval of the devices, and about the occurrence of time-dependent and device-dependent serious complications including filter migration or fracture and IVC perforation or occlusion (8,15–17). Although the complication rates of the retrievable devices may increase with prolonged indwelling time, the risk of retrieval failure may also increase (8,16,18).

The Crux Vena Cava Filter (Crux Biomedical, Menlo Park, California) is a new retrievable device with a non-conical, opposing-helix design including a thrombus-trapping web of expanded polytetrafluoroethylene (ePTFE) filaments and atraumatic, radiopaque retrieval tails at both ends to allow the option of jugular or femoral access for retrieval as well as for delivery. The Crux Biomedical Evaluation of the Crux Inferior Vena Cava Filter System (RETRIEVE) trial was undertaken to assess the safety and effectiveness of the Crux filter as both a permanent and a retrievable device.

MATERIALS AND METHODS

Study Design and Conduct

The RETRIEVE trial was a prospective, multicenter, single-arm, nonrandomized clinical trial conducted in patients with temporary or permanent risk of PE, and in whom IVC filtration was clinically indicated as a result of contra-indication to or failure of anticoagulation. The RETRIEVE trial outcomes reported here are pooled from three clinical trials that were conducted during the same time period: RETRIEVE 2 (clinicaltrials.gov identifier NCT01120509), conducted in the United States with an FDA-approved investigational device exemption; RETRIEVE 3 (clinicaltrials.gov identifier NCT01120522), conducted in Belgium with Federal Agency for Medicines and Health Products notification; and RETRIEVE 4 (clinicaltrials.gov identifier NCT01120535), conducted in Australia and New Zealand with Therapeutic Goods Agency notification. RETRIEVE 1 (clinicaltrials.gov identifier NCT00605332) was an earlier trial of a different design of the filter. For the three current RETRIEVE trials, the filters implanted, the site training methods, the subject eligibility criteria, the case report forms, the Data and Safety Monitoring Board (DSMB), the study definitions, the monitoring plan, and the database were all identical, and procedures to ensure data quality were applied with equal rigor.

Each RETRIEVE trial site (see Appendix) obtained ethics committee or institutional review board approval, and all patients provided written informed consent before trial enrollment. The RETRIEVE trial was conducted in accordance with the ethical principles of the Declaration of Helsinki, and in compliance with local and national regulations. Analyses of primary and secondary endpoints were performed by an independent statistician and the trial principal investigator. An independent physician served as the medical monitor.

Patient Selection

The trial inclusion and exclusion criteria were consistent with previous prospective studies with retrievable filters (11–14). Enrolled patients were older than 18 years of age, had temporary or permanent risk of PE, and had clinical indications for filter placement as a result of contra-indication to or failure of anticoagulation or the presence of temporary risk factors such as trauma or planned surgical procedures (eg, bariatric or pelvic surgery) or medical conditions known to increase the risk of venous thromboembolism (VTE). The indications for enrollment were consistent with the therapeutic (ie, documented thromboembolic disease) and prophylactic (ie, no current thromboembolic disease) categories in the 2011 Quality Improvement Guidelines for IVC filter placement from the Society of Interventional Radiology (SIR) Standards of Practice Committee (**Table 1**) (19). To be eligible, patients were required to have a documented infrarenal IVC diameter of 17–28 mm and venous anatomy and access vessels adequate for infrarenal IVC placement of the filter. Patients were excluded if they were pregnant, if they

Table 1. Society of Interventional Radiology Standards of Practice Committee Classification of Indications for IVC Filter Placement (19)

Therapeutic indications (documented thromboembolic disease)
Evidence of PE or IVC/iliac/femoropopliteal DVT and one or more of the following:
Absolute or relative contraindication to anticoagulation
Complications of anticoagulation
Failure of anticoagulation
Recurrent PE despite adequate therapy
Inability to achieve/maintain adequate anticoagulation
Propagation/progression of DVT during therapeutic anticoagulation
Massive PE with residual DVT in a patient at risk for further PE
Free-floating ileofemoral or IVC thrombus
Severe cardiopulmonary disease and DVT (eg, cor pulmonale with pulmonary hypertension)
Prophylactic indications (no current thromboembolic disease)
Temporary risk of PE in one of the following settings:
Severe trauma without documented PE or DVT
Closed head injury
Spinal cord injury
Multiple long-bone or pelvic fractures
High-risk situations (eg, patient immobilized or in ICU)

DVT = deep vein thrombosis, ICU = intensive care unit, IVC = inferior vena cava, PE = pulmonary embolism.