Thrombolysis and Iliofemoral Vein Stent Placement in Cancer Patients with Lower Extremity Swelling Attributed to Lymphedema

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ABSTRACT

Purpose: To assess the effects of iliofemoral vein stent placement on symptomatic lower extremity swelling (LES), presumed to be lymphedema, in patients with cancer.

Materials and Methods: During the period 2005–2013, 62 patients (38 female; age, 60.4 y ± 15.4) with histology-proven metastatic disease and LES resistant to standard therapies were evaluated and found to have venous outflow obstruction. Stents were placed in the iliofemoral veins or inferior vena cava, or both, and evaluated by color Doppler ultrasound or contrast-enhanced computed tomography during the follow-up period. Patient symptoms were assessed using the Venous Disability Score (VDS) and the Galway Limb Swelling score, a patient-directed, 5-question symptom scoring system.

Results: Stents were successfully placed in all patients. During the follow-up period, in-stent thrombosis occurred in 13 patients, and additional stents were placed in 3 patients to treat luminal narrowing. The mean VDS improved significantly ($P < .05$): from 3.0 ± 0 on the day of the procedure to 2.95 ± 0.22 on day 3, 2.0 ± 0.33 on day 7, and 1.87 ± 0.34 on day 30. The mean Galway Limb Swelling score also improved significantly ($P < 0.001$): from 3.6 ± 0.74 on the day of the procedure to 1.96 ± 0.91 on day 3, 1.06 ± 0.78 on day 7, and 0.6 ± 0.66 on day 30. During the follow-up period, 60 patients died as a result of their underlying malignancy (mean, 230 d; range, 5–1,080 d).

Conclusions: Iliofemoral or iliocaval venous stent placement may have a valuable role in patients with metastatic disease and symptomatic LES associated with venous obstruction.

ABBREVIATIONS

CDT = catheter-directed intrathrombus thrombolysis, GALS = Galway Limb Swelling score, IVC = inferior vena cava, LES = lower extremity swelling, VDS = Venous Disability Score

Lower extremity swelling (LES) in patients with metastatic disease may be associated with congestive heart failure, liver impairment, hypoalbuminemia, lymphedema from radiotherapy or lymph node dissection, venous obstruction (which may develop secondary to compression or thrombosis), or a combination of these, among other causes. In practice, LES in patients with metastatic disease is typically attributed to secondary lymphedema (1–3). The available literature on this topic is quite limited; incidence and prevalence data as well as quality studies describing patient assessment and treatment outcomes are lacking. It was previously reported that patients with lymphedema received incorrect diagnosis or management presumably because lymphedema itself remains poorly understood (4,5).

Patients with an initial diagnosis of lymphedema may actually have a more treatable cause of LES associated with inferior vena cava (IVC) or iliofemoral venous obstruction. The treatment of venous obstruction (with various etiologies) with stent placement has been widely reported, with positive patient outcomes and few complications (6–18). Although limited, the available data also suggest that patients with LES associated with

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venous obstruction and metastatic disease have favorable outcomes (ie, improved quality of life) after stent placement (6,7,19,20). This retrospective study evaluated outcomes after placement of stents in the IVC or iliofemoral veins (with or without thrombolysis) to treat LES in patients with metastatic disease and venous obstruction using a simple scoring system developed specifically for this patient population.

MATERIALS AND METHODS

This retrospective analysis comprised 62 consecutive patients with metastatic disease and LES presumed to be lymphedema that was evaluated, discovered to be venous obstruction, and subsequently treated with stent placement in the IVC or iliofemoral veins, or both, in the years 2005–2013 at a University Hospital. Institutional review board approval from the University Hospital Clinical Research Ethics Committee was obtained. A retrospective review of the patient medical records was performed to collect demographic data, details of the interventional procedure, and patency and symptom outcomes after treatment.

The study included consecutive patients with histologically proven malignancy and persistent leg edema unresponsive to standard therapies (eg, leg elevation, compression stockings, manual lymphatic drainage). Patients with a life expectancy of < 4 weeks, previous groin lymph node dissection in the affected limb, or sepsis were excluded. Mean age of patients was 60.4 years ± 15.4 (range, 4–92 y), and 38 patients were female. Table 1 lists the types of cancer affecting the study patients. Eight patients had undergone previous iliac lymph node dissection.

Imaging before the Procedure

Before 2008, imaging before the procedure included an abdominal computed tomography (CT) scan (focused on the underlying malignancy) and a lower limb duplex ultrasound (US) examination (n = 28 patients). Beginning in 2008, imaging before the procedure included CT venography and lower limb duplex US (n = 34 patients). For CT venography (SOMATOM Sensation 64-slice CT scanner; Siemens, Erlangen, Germany), patients received a 150-mL injection of iodinated contrast agent, iohexol, 300 mg/mL (GE Healthcare, Oslo, Norway), at a rate of 2–4 mL/s through a peripheral intravenous cannula (this was usually placed in the wrist or forearm but not in the swollen limb). Imaging was performed axially in 5-mm increments from the diaphragm to the ankle at 150 seconds.

Table 1. Malignancy Type

Type of Malignancy	No. Patients
Ovarian	9
Breast	8*
Cervical	8
Prostate	8
Colon	6
Lung	4
Pancreatic	3
Bladder	2
Endometrial	2
Other	12†

*One patient in this group also had pancreatic cancer.
†Other cancers included lymphoma, penile, testicular, groin, liver, renal, gastric, mesothelioma, melanoma/skin, retroperitoneal liposarcoma, rhabdomyosarcoma, and metastatic of unknown primary origin.

Thrombus Removal and Stent Placement

Acute occlusive thrombus visualized on CT venography was removed before stent placement. Methods of thrombus removal or dissolution included catheter-directed intrathrombus thrombolysis (CDT) and pharmacomechanical CDT (Trellis; Covidien, Mansfield, Massachusetts, or AngioJet Solent; Medrad, Inc, Pittsburgh, Pennsylvania) (21). Pharmacomechanical CDT was the preferred method; CDT was used for below-knee thrombus (posterior tibial vein access) and when pharmacomechanical CDT did not clear > 95% of the thrombus.

Stent placement was the primary treatment for patients with a nonthrombotic obstruction; it was performed after thrombus removal in patients with acute thrombus. Balloon angioplasty on its own was not used. Briefly, patients were brought to the interventional radiology suite and positioned prone on the table, and the skin of the popliteal fossa was prepared and draped in the usual sterile fashion. Using US guidance, access was gained to the popliteal vein, and ascending venography was performed. The causative lesion in the iliofemoral vein or IVC was crossed using fluoroscopic assistance, and an Amplatz wire (Cook, Inc, Bloomington, Indiana), 0.035-inch diameter, 180 cm long, was placed. Patients were given 5,000 units of heparin intravenously for systemic heparinization. Self-expanding stents, including WALLSTENT (Boston Scientific, Marlborough, Massachusetts) (n = 82), Zilver Vena (Cook Medical Inc, Bloomington, Indiana) (n = 17), Protege (ev3 Endovascular, Inc, Plymouth, Minnesota) (n = 8), Bard LUMINEXX (Bard Peripheral Vascular, Tempe, Arizona) (n = 4), sinus-Venous (OptiMed, Ettlingen, Germany) (n = 2), Zilver Vascular (Cook, Inc) (n = 1), and S.M.A.R.T. (Cordis Corporation, Fremont, California) (n = 1) in 12- to 18-mm diameters, were placed to cover the target lesion completely so that the stents extended from "flow to flow." At the beginning of this series, WALLSTENT stents were used almost exclusively; however, as stents designed specifically for the iliofemoral vein have become commercially available (first in January 2011), our institution has begun using those. Stent diameter was chosen based on comparison of the diameter of the dilated vein below and the normal vein above the lesion, and a stent diameter