Safety and effectiveness of vascular endoprosthesis for malignant superior vena cava syndrome

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ABSTRACT

Background: Superior vena cava syndrome management has been traditionally radiation therapy, chemotherapy or chemoradiation, depending on the underlying malignancy involved and individual clinicopathological features of the case. Recent emergence of endovascular stents offer the opportunity for immediate relief of the venous stenosis. This review examines findings from the published series which used endovascular prosthesis for this syndrome with regards to efficacy and safety.

Methods: Literature search identified studies using endovascular stents as initial therapy or for recurrence of malignant superior vena cava syndrome. Effectiveness and toxicity from stent placement was assessed.

Results: Endovascular stent placement provides immediate haemodynamic relief of venous compression either before or after definitive therapy in the majority of cancer patients. Severe bleedings, cardiopulmonary complications and stent migrations remain significant problems for patient management.

Conclusions: Endovascular prosthesis is an effective modality for malignant superior vena cava syndrome with acceptable morbidity. Prospective studies should be performed to determine the optimal anticoagulation regimen.

The pathology of superior vena cava syndrome (SVCS) is frequently secondary to external compression of the superior vena cava (SVC) because of the low internal venous pressure situated within rigid structures of the thorax (trachea, right bronchus, aorta, perihilar and para-aorta lymph nodes).¹ SVC compression induces venous hypertension responsible for SVCS clinical manifestations (neck and/or arm oedema, respiratory distress, cyanosis and obtundation). Although rarely fatal, these haemodynamic effects cause serious distress when the stenosis is severe.² SVCS aetiology is predominantly malignant with lung cancer as the primary cause.³ As a result, radiation therapy, chemotherapy or chemoradiation are the main traditional therapies.^{4,5} SVCS recurrence may occur after successful primary therapy for tumour recurrence.⁶ Thus alternative salvage treatment is needed for palliation. Since 1986, endovascular stent placement offered an effective therapy to relieve venous compression when primary therapy failed or at the time of cancer diagnosis.⁷⁻¹⁰ Endovascular stent popularity increased because of fast relief of the venous congestion,^{11,12} but report of fatal complications⁹ have tempered the initial enthusiasm and have prompted us to conduct this survey assessing effectiveness and safety of this interventional modality.

METHODS

This systematic review was designed to investigate the safety and efficacy of endovascular stents for the treatment of malignant SVCS. A search was undertaken from 1986, when the stent was first reported to relieve malignant SVCS, until 2007. The search was based on PubMed electronic databases. The following terms were explored and used for each database search: superior vena cava syndrome, malignant and endovascular stent. Reference lists of relevant papers were then searched for additional publications. The papers were classified into two categories: effectiveness of the stent at diagnosis of SVC or after failure of the primary therapy. The following criteria were analysed in each article: definition of the stent success, rate of re-occlusion, mortality rate, major complications and protocol for anticoagulation following stent placement.

Overview of stent placement protocol as reported by the literature

The severity and location of the venous stenosis were confirmed by venography under local anaesthesia. Patients were monitored for oxygen saturation, blood pressure and cardiac function during the procedure. The stents were usually introduced through the common femoral veins but the brachial venous route could also be used if the guidewire could not cross the stenosis through the femoral route. Following placement of the stent, a final SVC cavogram confirmed patency of the stent. Most institutions recommended anticoagulation following stent placement but the type and duration of anticoagulation therapy varied depending on the institution. Patients were assessed for resolution of their clinical symptoms. Chest x ray was usually performed following the procedure to verify location of the stent (possible stent migration) and the degree of stent expansion. Unless the SVCS recurred, venograms were not routinely repeated. Clinical patency, recurrence of SVCS and complication rates following the procedure were reported.

Types of endovascular stents

Many endovascular stents are available to relieve the stenosis.^{9,13-21} The stents come in a variety of sizes and lengths. The endoprosthesis is released across the localised site of obstruction, spanning from above and below the stricture to prevent re-occlusion.¹² Stents may be classified into two categories: self-expanding stents and balloon expanding stents. Once released, self-expanding stents (Gianturco-Z stent, Wallstent, Memotherm)^{11,13,18,21} continuously push radially outward against the stenosis until they reach

Table 1 Guidelines that may influence the choice of a specific type of stent for the treatment of superior vena cava syndrome

Stent	Characteristics of the stenosis
Gianturco Z-stent	Short, straight stenosis involving large diameter vessel.
Wallstent and Memotherm stent	Long, curved stenosis involving vessel with smaller diameter.
Palmaz stent	Short stenosis in locations where stent migration may pose a problem.

their initial size. Thus self-expanding stents may perforate the vessel wall and cause complications.

Balloon expanding stents (Palmaz and Strecker stent)¹⁵ are mounted on a balloon on the end of the delivery catheter. When the stent is positioned within the stenosis, the balloon is inflated, causing the stent to expand to a desired diameter, and is less likely to cause perforation. Balloon expanding stents have a high radial force when inflated. However, once expanded, their compressibility may lead to re-occlusion of the vessels or stent fracture. The two types of stents can be combined when there is residual stenosis after stent placement. For example, a balloon expanding stent can be placed within a self-expanding stent to maintain stent patency.¹⁸

The Gianturco-Z stent (Z-stent) was most frequently used in the first reports.^{7 14 17} It is the most rigid stent with a large diameter (up to 3 cm), excellent radial expansile strength and is commonly used in large diameter vessels. The open structure of the stent does not cause obstruction to the collateral side vessels bridged by the stent. Because of its short length, large diameter and rigidity, multiple insertions of the Z-stent for long stenosis may represent a technical challenge, especially along the curvature. The wide gap between stent wires may allow tumour ingrowth through the stent and re-stenosis.

The Wallstent is flexible, long and easy to insert.^{11 19 20} It has a smaller diameter (up to 1.6 cm) and less radial strength, and is best suited for smaller vessels such as brachiocephalic vein stenosis or along curvatures. Its mesh-like structure prevents infiltration of the tumour through the stent.

Wallstent has become more popular because of its length and ease of insertion. Once deployed, Wallstent does foreshorten by 20%.

Memotherm stent⁹ is also flexible as it is constructed of a tight mesh of nitinol (nickel–titanium compound) with super-elasticity, allowing the stent to expand to its initial size without any shortening of the length. It is best suited for stenosis along curvatures, the same as the Wallstent.

Palmaz stent is rigid^{15 18} and requires balloon assistance to distend it. It has excellent radial force but will not expand beyond the limits of the specific balloon size inflated. Its short length makes it most effective in short segmental stenosis. Advantages include ease of targeting the site of stent expansion, control of degree of stent expansion and a decreased chance of migration once released. However, because of its compressibility, vessel re-stenosis and stent fracture may occur.

Other prosthesis such as the Strecker or Symphony are of limited use because of the small diameter (up to 12 mm) but have been reported to be successful for treatment of SVCS.^{13 16}

The specific type of stent selected for use is determined by the characteristics of the stenosis (diameter, length and location) and the experience of the interventional radiologist. Table 1 summarises some of the criteria that may influence stent choice.

Haemodynamic changes following stent placement

Sudden venous lumen diameter increase reverses aberrant caval pressure distal to the pathological stenosis and improves right atrial pressure from restored venous return. Pulmonary capillary wedge pressure and cardiac output immediately increase following successful stent placement.¹⁷ Acute pulmonary oedema, which may be fatal,¹⁸ can occur in individuals with comorbid underlying coronary artery disease and heart failure. Clinical manifestations of SVCS resolve within 24–48 h post-endovascular stent placement. Endothelial intima usually covers stents and incorporates them into the physiological vascular system within a few weeks time following stent placement.⁷ During this “intimisation/vascularisation period”, the patient remains at highest risk for thrombotic events. Anticoagulation is recommended following stent placement but optimal duration and methods of anticoagulation therapy remain controversial.^{13–16} Sometimes anticoagulation is not given either before or after completion of stent placement.¹⁶ Thrombolytic therapy is usually recommended if SVC thrombosis is found pre-stenting.^{5 10 11} Thrombolysis and anticoagulation may induce

Table 2 Effectiveness of the Wallstent endoprosthesis in relieving malignant superior vena cava obstruction following failure of primary therapy

Study	Patient No	Prior therapy	Patient with lung cancer	Effectiveness (%)	Recurrence (%)	Follow-up (months)
Monaco ¹⁹	40	RT (33) C (33)	32	90	4	6
Stock ²²	14	RT (5) C (4)	12	83	25	3
Dinkel ²³	84	RT (28) C (54)	73	99	22	NS
Kim ²⁵	10	RT (6) C (2)	10	100	20	6.7
Dyet ²⁶	17	RT (14)	12	100	12	NS
Courtheoux ²⁷	20	RT (10) C (19)	16	95	15	NS
Nicholson ²⁸	76	RT (NS) C (NS)	58	100	9.8	NS
Hennequin ²⁹	15	RT (6) C (13)	13	93	0	3

C, chemotherapy; NS, not specified; RT, radiotherapy.

Table 3 Effectiveness of the Gianturco and other types of endoprosthesis to relieve obstruction from malignant superior vena cava syndrome following failure of primary therapy

Study	Patient No	Prosthesis type	Treatment type	Lung cancer	Effectiveness (%)	Recurrence (%)	Follow-up (months)
Crowe ¹⁰	13	G (9) W (1) P (1)	RT (10) C (1)	11	91	41	35
Marcy ¹³	37	G (29) S (5) M (5)	NS	28	97	8	6
Elson ¹⁵	5	P	RT (4)	5	100	0	3
Kee ¹⁸	43	P (NS) W (NS)	RT (30) C (6)	22	97	11	7
Greillier ²¹	8	M (NS) A (NS)	RT (2) C (6)	8	100	33	NS
Tanigawa ³⁰	23	G	RT (11) C (1)	19	78	0	3
Tan ³¹	11	G (10) S (1)	RT or C (7)	11	100	18	3.9
Furui ³²	16	G	RT (7) C (3)	14	81	25	2.9
Gaines ³³	20	G	RT (11) C (5) Su (6)	15	90	25	NS
Oudkerk ³⁴	30	G (17) W (13)	RT (22) C (12)	20	96	23	2.5

A, Angiomed stent; C, chemotherapy; G, Gianturco stent; M, Memotherm stent; NS, not specified; P, Palmaz stent; RT, radiotherapy; S, Strecker stent; Su, surgery; W, Wallstent stent.

severe bleeding following endovascular stent placement and result in reported mortalities.^{19 20}

Stent effectiveness after primary therapy failure

Most endovascular prostheses salvage studies for recurrent SVCS report effective relief of the venous compression after cancer recurrence.^{22–24} The majority of these patients had lung cancer^{25–27} and were treated with either chemotherapy or radiotherapy. As a result, prognosis was very poor as stents were used late in their clinical course, primarily for palliation of severe symptoms. Mean and median follow-up ranged from 2 to 7 months. Stents provided rapid symptomatic improvement as early as a few hours after the placement.²⁸ Stent effectiveness ranged from 81% to 100% and was unrelated to stent type. Wallstent effectiveness ranged from 90% to 100%.^{19 22 23 25–29} Other stent types had 78–100% success rates in relieving the venous stenosis.^{15 30–33} Reports for multiple stents used within the same institution achieved

similar results.^{10 13 15 18 21 34} Thus the experience of the interventional radiologist is the key to achieving good results. Re-obstruction rates ranged from 0% to 33%.^{19 21–23 25–33}

Secondary SVCS recurrence following initial successful primary therapy is attributed to venous thrombosis or vessel tumour invasion.^{19 20 32} It is difficult to determine the status of optimum anticoagulant therapy post-stent placement because this policy differed among reporting institutions.

Secondary stent re-stenosis may be resolved with further stenting.¹⁸ Tables 2 and 3 summarise the effectiveness of the Wallstent prosthesis and other types of stents, respectively, for malignant SVCS following failure of primary therapy.

Stent effectiveness for treatment of malignant SVCS at initial presentation

Although endovascular stents are traditionally offered to salvage recurrent SVCS after primary therapy failure, vascular

Table 4 Effectiveness of endovascular prosthesis in relieving obstruction at diagnosis of malignant superior vena cava syndrome prior to primary therapy

Study	Patient No	Prosthesis type	Treatment after stent	Lung cancer	Effectiveness (%)	Recurrence (%)	Follow-up (months)
Chatziioannou ⁹	18	M	RT (18)	15	100	0	NS
Biedrager ¹⁶	17	S	RT (4) C (10)	11	88	0	5
Gross ²⁴	13	W	RT (11) C (6)	11	100	0	3
Lanciego ³⁵	52	W	RT (2) C (22) RT+C (12)	49	100	11	6.4
Lopez-Muniz ³⁶	16	W	RT (NS) C (NS)	12	100	18	NS
Nagata ³⁷	71	Z	RT or C (30)	58	87	7	5.4

C, chemotherapy; M, Memotherm stent; NS, not specified; RT, radiotherapy; S, Symphony stent; W, Wallstent; Z, Gianturco stent.

Table 5 Fatal complications rate following endovascular stent placement for malignant SVCS

Study	Death	Cause of death	Other complications
Wilson ⁸	1/18	Not specified	
Crowe ¹⁰	1/12	Cardiac arrest	2 haematemeses
Thony ¹¹	1/26	Haemorrhage	1 pneumonia, 1 infection of venous line
Kee ¹⁸	2/43	Respiratory failure (1), pulmonary embolism (1)	1 stent migration, 1 gastrointestinal haemorrhage
Monaco ¹⁹	3/40	Haemoptysis (1), pulmonary oedema (1), respiratory failure (1)	
Urruticoechea ²⁰	1/52	Lung haemorrhage	1 stent migration, 1 cardiac arrhythmia, 1 sepsis
Stock ²²	1/14	Not specified	
Dinkel ²³	1/84	Cardiac tamponade (1)	
Gross ²⁴	1/13	Cardiac arrhythmia	
Dyet ²⁶	1/17	Cerebral haemorrhage	
Courtheoux ²⁷	1/20	Myocardial infarction	
Nicholson ²⁸	1/76	Brain haemorrhage	1 groin haematoma, 1 DVT
Gaines ³³	1/20	Haemoptysis	
Oudkerk ³⁴	1/30	Haemoptysis	

prosthesis is now considered firstline therapy in an increasing number of institutions because of device efficacy in relieving patient symptoms.^{9 16 24 35–37} Rapid relief of the venous compression allows early cisplatin based chemotherapy initiation for small cell lung cancer and metastatic non-small cell carcinomas which require hydration. Selected studies show almost all patients achieved immediate relief of the venous congestion allowing underlying aetiology specific therapy to be initiated.^{9 24 37} SVCS recurrence still occurs up to 18%, despite anticoagulation.^{35 36} Short term clinical follow-up in these studies limits survival analysis; it remains to be reported if this new approach will be affiliated with improved survivals. Table 4 summarises the effectiveness of various stent types for the treatment of SVCS prior to definitive antineoplastic therapy.

Complication rate following stent placement

In 32 studies,^{8–39} 17 deaths occurred (2%) during or shortly after 884 malignant SVCS stent placements. Seven of the 17 deaths (41%) were attributed to severe haemorrhage: two cerebral, three pulmonary and two unspecified sites. Four of 17 deaths (23%) were attributed to cardiac events: two arrhythmia, one myocardial infarction and one tamponade. Three of 17 deaths (17%) were attributed to respiratory failure.

Cause of death was unattributed in two cases (12%); one death (6%) was documented pulmonary embolism.

Only 38 of 884 (4%) patients experienced major complications attributed to caval stenting, and these were most commonly stent migration or poor stent positioning ($n = 18$) followed by bleeding ($n = 8$), infection ($n = 2$), deep venous thrombosis ($n = 4$), pulmonary oedema ($n = 3$), cardiac arrhythmia ($n = 2$) and pulmonary embolism ($n = 1$).

Fatal haemorrhages reported were generally attributed to thrombolytic agent administration, including streptokinase, urokinase and tissue plasminogen activator to dissolve intracaval clot prior to vascular prosthesis insertion. Occult cerebral metastases may also explain brain haemorrhage during fibrinogen lysis.²⁸ Massive haemoptysis may also occur during thrombolytic therapy³⁴ or during maintenance anticoagulation

Table 6 Non-fatal complications resulting from endovascular stent placement for malignant vena cava syndrome

Study	Type of complications	Complication rate
Chatzioannou ⁹	1 stent migration	1/18 (5%)
Marcy ¹³	2 pulmonary oedema	2/37 (5%)
Biedrager ¹⁶	1 stent migration 1 cardiac arrhythmia	2/17 (11%)
Greillier ²¹	1 haemorrhage 2 thrombosis	3/8 (37%)
Hennequin ²⁹	1 retroperitoneal haematoma	1/15 (6%)
Tanigawa ³⁰	1 phlebitis	1/23 (4%)
Tan ³¹	2 stent migration 1 haemorrhage of femoral puncture	3/11 (27%)
Furui ³²	4 stent migration	4/16 (25%)
Gaines ³³	1 haemoptysis	1/20 (5%)
Lopez-Muniz ³⁶	2 stent migration	2/16 (12%)
Lanciego ³⁵	1 stent migration 2 poor positioning of stent	2/52 (3%)
Nagata ³⁷	3 stent migration 1 pulmonary embolism	4/71 (5%)
Kishi ³⁸	1 pulmonary oedema	1/11 (9%)

therapy.²⁰ Paraneoplastic hypercoagulation state combined with the presence of a foreign body increased the risk of thrombosis after stent placement. However, parameters for optimal anticoagulation therapy have not been determined. Some authors advocated no antithrombotic therapy post-stenting,¹⁶ but most reported studies recommended prolonged anticoagulation, including heparin, warfarin and antiplatelet agents.^{9–15 17–36}

As a result, extremes of haemorrhage versus venous thrombosis attributed to excessive versus inadequate anticoagulation remains a significant problem during follow-up in reported studies.^{21 29 31 33}

Endovascular stent placement also exposes patients to significant cardiopulmonary complication risks. Most malignancies were bronchogenic carcinoma and most patients had underlying comorbid coronary artery disease attributed to smoking and age. Stenting promptly dilated SVC diameter and increased venous return and pulmonary wedge pressure. Comorbid factors, such as borderline cardiac function, arrhythmias, pulmonary oedema, myocardial infarction and respiratory failure predisposed patients to an adverse outcome.^{10 13 16 19 24 27} Close haemodynamic monitoring during stenting may prevent or mitigate these types of complications.^{17 38}

Stent migration or malposition remains a significant long term complication and is occasionally fatal,²³ although most stent migrations did not result in long term morbidity.^{9 16 31 32 35–37} Migration/malposition likely decreases as the experience of the interventional radiologist increases. Tables 5 and 6 summarise fatal and non-fatal complications following stent placement for malignant SVCS.

CONCLUSIONS

Endovascular stent placement provides fast and effective relief of the vascular stenosis associated with malignant SVCS with acceptable morbidity. Patient management requires careful haemodynamic and coagulation profile monitoring of the patient both during and after stenting. Prospective studies are needed to address optimal anticoagulation therapy pre-stent preparation and post-stent follow-up as patients remain at risk for thrombosis as well as haemorrhagic death.

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