Endovascular stent placement for treatment of malignant superior vena cava syndrome: Clinical efficacy, safety, and factors influencing stent patency

Poster No.: C-2095
Congress: ECR 2010
Type: Scientific Exhibit
Topic: Interventional Radiology - Vascular
Keywords: Malignant superior vena cava syndrome, Stent, Endovascular treatment
Keywords: Interventional vascular, Vascular, Percutaneous
DOI: 10.1594/ecr2010/C-2095

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Purpose

- Patients with malignant SVCS (superior vena cava syndrome) are typically seriously ill, and further deterioration is likely due to the presence of unresectable advanced malignant tumors. Although bypass surgery is a good palliative treatment for symptom resolution in patients with malignant SVCS, it is rarely performed because of the high morbidity and mortality. Until recently, irradiation and chemotherapy were standards in the management of malignant SVCS. However, both therapies may not be possible under certain conditions, notably when cumulative maximum dosage have been reached by previous treatments. In addition, it make several weeks before either intervention shows a clinical effect.

- Endovascular stent placement as an alternative palliative treatment increased because of quickest way to relieve symptoms. Although there have been many studies reporting the efficacy of stent placement in patients with malignant SVCS, however, SVCS recurrence following initial successful endovascular stent placement still occurs up to 18% and is attributed to tumor ingrowth inside the stent or venous thrombosis. Therefore, there is a need for further study of the influencing factors associated with stent patency.

- The purpose of our study is to evaluate the safety and clinical efficacy of endovascular stent placement for treatment of malignant SVCS and to analyze influencing factors associated with stent patency.
Methods and Materials

Patient Population

- From January 1999 to March 2009, 43 patients were enrolled in the retrospective study. This study was approved by the Institutional Review Board of our Institution and written informed consent was waived. The characteristics of the patients are presented in Fig.1 on page 7. The diagnosis of malignant SVCS was based on clinical symptoms and signs and imaging studies such as computed tomography (CT) and upper extremity venography. In all patients, pathologic diagnosis of underlying malignancy was made by biopsy, since treatment approaches could vary widely depending on the histology of the malignancy.

- Pathologic specimens were obtained by bronchoscopy (n=19), percutaneous needle (n=18), and excision (n=6). Except two (4.7%) patients who had undergone no prior treatment, 21 (48.8%) patients had undergone prior chemotherapy, 19 (44.2%) had undergone prior chemotherapy and radiation therapy, and one (2.3%) had undergone prior radiation therapy (Fig.2 on page 7).

Devices

The metallic stents used in this study were Zilver stent (Cook, Bloomington, IN), Wallstent (Boston Scientific, Galway, Ireland), and Hercules (S&G biotech, Sungnam, Korea).

Technique

- Preparation: Prior to stent insertion, CT was performed to assess the anatomy and plan the most appropriate approach for intervention. Experienced interventional radiologists (D.I.G., G.Y.K.) performed venography and stent insertion. Intervventional procedures were performed under conscious sedation using intravenous pethidine hydrochloride (Demerol, Keukdong Pharmaceuticals, Seoul, Korea) and local anesthesia using intramuscular lidocaine (Jeil Pharmaceuticals, Taegu, Korea). The stenosis of the SVC was transversed with a 5-F catheter and guide wire.

- Venography: Venography was performed to evaluate the length, severity, and location of the obstruction. The approach site for accessing the SVC was internal jugular, subclavian or common femoral vein. In some patients, pre- and poststenting pressure gradients were performed to access immediate effectiveness of stenting (Fig.3 on page 8). Prestenting pressure measurements
were performed in SVC peripheral to the stenosis to determining the significance of SVC stenosis and pressure gradient between the BCV and RA (right atrium) was also measured. After stent placement, pressure gradient was measured to access immediate effectiveness of stenting. Predilatation using a 6- to 10-mm-diameter balloon catheter (Boston Scientific, Galway, Ireland) was performed to determine stent size and allow for easy navigation of the stenosis as well as placement of the stent.

- Stent placement: 5000-unit bolus of heparin was administrated at the beginning of the intervention. The stent was introduced over a 0.035-inch, 150-cm-long stiff hydrophilic guide wire (Terumo, Tokyo, Japan) or over an extra stiff Amplatz guide wire (Cook) and then deployed across the obstruction. The stent was placed approximately 2-4 cm distal and proximal from the obstruction to prevent tumor overgrowth. In patients with unilateral BCV obstruction, one stent was placed from the obstructed BCV into the SVC via ipsilateral IJV route or from the SVC into the obstructed BCV via right femoral vein route (Fig.4 on page 9). In patients with bilateral BCV obstruction, one stent was placed because of operator preference via right femoral vein route or two stents were placed from both of the obstructed BCVs into the SVC via both SCV routes (Fig.5 on page 10). If the affected venous segment was longer than the longest available stent, an additional stent was placed coaxially, overlapping the first. If stent dilatation was insufficient or pressure gradient was higher than 5mmHg, poststenting balloon dilatation was performed (Fig.6 on page 11).

- Post-stent management: After the procedure, all patients received continuous infusion of heparin (500 IU/hour) for 2 to 5 days. Subsequently, patients received a long-term oral anticoagulant agent (warfarin; titrated to an INR [International Normalized Ratio] of 2.0) or an antiplatelet agent (aspirin).

Study Endpoints.

- Technical success: Technical success was considered as the following: placement of the stent in an adequate position without migration; the degree of expansion greater than 80% of the diameter of the unconstrained stent as seen on venography; and pressure gradient between the BCV and the RA less than 5mmHg.

- Clinical success and failure: Clinical success was considered as major improvement or elimination of symptoms. Clinical failure was considered as persistence of the cardinal symptoms of SVCS. In patients with dyspnea, persistent dyspnea alone was not equated with clinical failure, since it is a symptom of the underlying pulmonary disease and is frequently found in patients with tumor invasion into bronchus or pulmonary vessels.
• Patient survival: Patient survival was defined as the time interval between the initial stent placement and the patient's death or last follow-up. If patient had not died by the last follow-up, the survival rate was considered to be equal to the follow-up duration.

• Stent patency: Primary stent patency was defined as the time interval between initial stent placement and obstruction recurrence or last follow-up. Secondary stent patency was defined as the time interval between obstruction was not evident during a patient's life, the patency was considered to be equal to the survival duration. At the time of a patient's death, the stent was assumed to be patent if the patient had no cardinal symptoms of SVCS. If the patient had obvious symptoms of SVCS, the stent was assumed to be obstructed.

• Complication: Complications were classified as major and minor according to the guidelines of the Society of Interventional Radiology Standards of Practice Committee. Major complications were defined as those necessitating major therapy, those necessitating an unplanned increase in the level of care or prolonged hospitalization (>48 hours), and those in permanent adverse sequelae or death. Minor complications were defined as those requiring no therapy or nominal therapy, including overnight admission for observation only.

Statistical analysis

• Stent patency and patient survival: life-table analysis according to the Kaplan-Meier method.
• Factors related to the stent patency: Multivariate Cox regression analysis
• Statistical analysis was conducted using of SPSS software (version 14.0. SPSS, Chicago, IL).
Table 1. Demographic data of 43 patients with malignant SVC obstruction.

<table>
<thead>
<tr>
<th></th>
<th>Number of patients</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (male/female)</td>
<td>39/4</td>
<td>91.9</td>
</tr>
<tr>
<td>Mean age, year (range)</td>
<td>62.6 (31—81)</td>
<td></td>
</tr>
<tr>
<td>Underlying diseases</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Squamous cell carcinoma</td>
<td>19</td>
<td>44</td>
</tr>
<tr>
<td>Adenocarcinoma</td>
<td>12</td>
<td>28</td>
</tr>
<tr>
<td>Small cell carcinoma</td>
<td>8</td>
<td>19</td>
</tr>
<tr>
<td>Others*</td>
<td>4</td>
<td>9</td>
</tr>
<tr>
<td>Symptoms and signs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neck edema</td>
<td>43</td>
<td>100</td>
</tr>
<tr>
<td>Face edema</td>
<td>41</td>
<td>95</td>
</tr>
<tr>
<td>Prominent vein</td>
<td>17</td>
<td>40</td>
</tr>
<tr>
<td>Arm edema</td>
<td>15</td>
<td>35</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>14</td>
<td>33</td>
</tr>
</tbody>
</table>

* Including thymic carcinoma (n=2), diffuse large B cell lymphoma (n=1), and large cell carcinoma (n=1)

**Fig. 0:** Demographic data of 43 patients with malignant SVC obstruction.

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Table 2. Pathologic diagnosis and combined therapy of the 43 patients with malignant SVC obstruction

<table>
<thead>
<tr>
<th>Pathological diagnosis</th>
<th>Number of patients</th>
<th>Percentage</th>
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</thead>
<tbody>
<tr>
<td>Bronchoscopy</td>
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<td>44</td>
</tr>
<tr>
<td>Percutaneous needle biopsy</td>
<td>18</td>
<td>42</td>
</tr>
<tr>
<td>Excisional biopsy</td>
<td>6</td>
<td>14</td>
</tr>
<tr>
<td>Location of obstruction</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SVC only</td>
<td>21</td>
<td>49</td>
</tr>
<tr>
<td>SVC + unilateral BCV</td>
<td>7</td>
<td>16</td>
</tr>
<tr>
<td>SVC + bilateral BCV</td>
<td>15</td>
<td>35</td>
</tr>
<tr>
<td>Other treatments before stenting</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>40</td>
<td>93</td>
</tr>
<tr>
<td>Radiation therapy</td>
<td>20</td>
<td>47</td>
</tr>
<tr>
<td>None</td>
<td>2</td>
<td>5</td>
</tr>
</tbody>
</table>

**Fig. 0:** Pathologic diagnosis and combined therapy of the 43 patients with malignant SVC obstruction

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**Fig. 0:** A 69 year-old male with small cell lung cancer in the right upper lobe of the lung and infiltrate to the central airway. A. Coronal reconstructed CT image shows invasion of the tumor into the SVC causing near total occlusion of SVC. B. Superior vena cavaogram shows occlusion of the SVC. The pressure gradient was 24 to 27 mmHg. C, D. Images show stenting and post-stenting balloon angioplasty. E. Images show improved contrast flow through the SVC to the RA. The pressure gradient was decreased to 6 mmHg.

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Fig. 0: A 56 year-old mail with primary lung cancer in the right lung upper lobe with metastatic lymphadenopathies in the mediastinum. He was suffered from face and neck edema for 20 days. A.Image shows tight stenosis at proximal to mid SVC (arrow) extending to the right and left innominate vein(arrowheads) due to invasion via metastatic lymph nodes. B.The length of stenosis were approximately 6 cm(Scale is mm). C.Successful stenting was done using 14 mm x 7 cm Zilver stent(Cook, Bloomington, IN). D.Final superior venocavogram shows slight improvement of contrast flow through the narrowed segment. Although there was mild improvement on final angiography, the symptoms were effectively alleviated within 2 days.

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**Fig. 0**: A 59 year-old male with squamous cell carcinoma of the right lung. A. CT image reveals conglomerated lymphadenopathy (asterisk) in the mediastinum compressing the left innominate vein and SVC (arrows). B, C. Images show narrowing of both innominate veins and SVC (arrow heads) causing obstructive symptoms for 14 days. D. Image shows successful placement of a 10mm x 7cm stent across the right SVC and successful placement of a 10mm x 8cm stent across the left innominate vein (Wall stent, Boston Scientific, Galway, Ireland). E, F. Phlebograms obtained after bilateral stent placement show no residual SVC stenosis. Symptoms caused by venous obstruction disappeared within 1 day.

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**Fig. 0:** A 65 year-old male with small cell lung cancer. A. CT scan shows infiltrative soft tissue mass (asterisk) invasion to the SVC and right pulmonary artery. B. Superior venacavogram shows total occlusion of the SVC. There was collateral venous flow via azygose vein (arrowheads). C, D. Stent placement with 12 mm x 8cm stent across the lesion and balloon angioplasty via right femoral venous approach was successful. D. Final superior venacavogram obtained after unilateral stent placement shows good angiographic result with no collateral venous networks.

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Results

Stent placement and Clinical outcomes

- Stent placement was not performed in two patients because of extensive thrombosis of BCV and IJV. Therefore stent placement was performed in the remaining 41 patients and was technically successful in all patients. Venography immediately after stent placement confirmed the correct positioning of the stent and none of the stents migrated immediately after deployment. There was no complication related to the interventional procedures and no procedure-related mortality.

- Clinical symptoms improved from 1 to 5 days (mean, 1.2 days) after stent placement in 38 (93%) patients. Among them, 32 (78%) patients experienced symptomatic improvement immediately or within 1 day. Three (7%) patients experienced no symptomatic improvement (Fig.1 on page 15).

Patient survival

- According to the Kaplan-Meier life-table analysis, the median patient survival was 105 days (95% CI, 64-146 days) (Fig.2 on page 15).

- At mean follow-up period of 172 days (range; 2-1590 days) after stent placement, 32 patients (78%) had died. Four patients (6%) had died within 7 days after stent placement. In these patients, death was caused by advanced cancer and their poor clinical condition and was not directly related to the procedure.

Stent patency

- The mean stent patency was 203 days (95% CI, 537-1335 days) (Fig). Cumulative stent patency rates at 1, 3, 6, and 12 months were 94%, 80%, 68%, and 55%. Stent occlusion occurred in eight (19.5%) patients after a mean of 101 days (range, 21-315 days) (Fig.3 on page 16). Factor possibly related to stent patency were also calculated. Age, sex, tumor type, combined adjacent organ invasion of the tumors, stent type, stent placement technique (unilateral or bilateral), anticoagulation, poststenting chemoradiotherapy. In our multivariate Cox regression analysis, combined adjacent organ invasion was the only significant factor associated with the stent occlusion (odds ratio, 0.19; 95%; confidence interval, 0.04-0.94; p=0.04) (Fig.4 on page 17, Fig.5 on page 19).
Complication

There was no complication related to the interventional procedures and no procedure-related mortality.
Table 3. Technical and clinical outcomes of 41 patients underwent endovascular treatment.

<table>
<thead>
<tr>
<th></th>
<th>Number of patients</th>
<th>Percentage</th>
</tr>
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<tbody>
<tr>
<td>Technical Success</td>
<td>41</td>
<td>100</td>
</tr>
<tr>
<td>Unilateral Stenting</td>
<td>35</td>
<td>85</td>
</tr>
<tr>
<td>Bilateral Stenting</td>
<td>6</td>
<td>15</td>
</tr>
<tr>
<td>Clinical Improvement in 1 to 5 days</td>
<td>38</td>
<td>93</td>
</tr>
<tr>
<td>Immediately or within 1 day</td>
<td>32</td>
<td>84</td>
</tr>
<tr>
<td>2 days to 5 days</td>
<td>6</td>
<td>16</td>
</tr>
<tr>
<td>No Symptomatic Improvement</td>
<td>3</td>
<td>7</td>
</tr>
</tbody>
</table>

Fig. 0: Technical and clinical outcomes of 41 patients underwent endovascular treatment.

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Fig. 0: Cumulative patient survival according to the Kaplan-Meier life-table analysis.

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Fig. 0: Cumulative stent patency according to the Kaplan-Meier analysis.

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Fig. 0: A 65 year-old male with malignant superior vena cava syndrome due to small cell lung cancer. A. Image shows multiple filling defects and eccentric wall irregularity (arrowheads) involving the right innominate vein and SVC due to invasion of the metastatic lymphadenopathies in the mediastinum. B. Successful placement of 16 mm x 9 cm metallic stent across the narrowed segment was revealed in the final angiograph (Wall stent, Boston Scientific, Galway, Ireland). C. 2 months later, there was near total occlusion of the proximal SVC within the stent. The pressure gradient was 22 mmHg. D, E. Images show additional stent placement and balloon angioplasty. F. Final superior venacavogram after procedure shows satisfactory result. Pressure gradient was decreased to 1 mmHg.

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Fig. 0: A 57 year-old female with recurred lung cancer after right upper lobectomy 3 years ago. A. CT image shows invasion of the SVC by the recurred tumor. B. Superior venacavography revealed severe narrowing of the SVC. Patient has undergone stent placement in the right main bronchus (arrow) and pulmonary artery (arrowhead). C. Image shows percutaneous balloon angioplasty and stent placement using 12x6cm Zilver stent (Cook, Bloomington, IN). Obstructive symptoms were disappeared within 1 day after endovascular treatment. D. After 90 days, CT image shows occlusion of the stent due to filling defect within the stent suggesting tumor ingrowth.

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Conclusion

1. Stent placement seems to be a safe and effective treatment method in patients with malignant SVCS because of its rapid alleviation of symptoms of malignant SVCS.
2. Combine adjacent organ invasion is significantly associated with stent occlusion.
References