Self-expandable metallic stent placement was introduced in an attempt to overcome the limitations of external biliary drainage catheters (such as tube dislodge-ment, bile leakage, and psychologic problems) and plastic endoprostheses (such as migration, occlusion, and a traumatic implantation procedure) in treating patients
with biliary obstruction (1-5). The advantages of metallic stents were found to be their relatively small introduction system and large luminal diameter. Because of the high occlusion rates usually caused by tumor ingrowth or overgrowth, or bile debris, the use of metallic stents in patients with malignant biliary obstruction was, however, disappointing (6-11).

For the palliation of cholangiocarcinoma, the use of the brachytherapy with iridium-192 in combination with conventional drainage has shown promising results and led to extended survival (14). This internal source allows a high local dose of radiation while limiting the exposure of adjacent organs.

The purpose of our study was to assess the outcome of intraluminal brachytherapy on stent patency and survival after metallic stent placement in patients with primary bile duct carcinoma.

Materials and Methods

Patients

Between August 1997 and June 2000, 13 men and 14 women aged 30-90 (mean, 62) years with inoperable primary bile duct carcinoma underwent self-expandable metallic stent placement. Sixteen of the 27 then received intraluminal brachytherapy, but the other eleven declined this option. No patient had previously undergone surgery for this condition.

Fourteen patients had obstruction at the hilar level, and the others had common bile duct obstruction without hilar involvement. In 19 patients the diagnoses were proven by biopsy and/or bile cytology, and in the remaining eight on the basis of the radiological and clinical findings.

Technique (Figs. 1, 2)

After transhepatic biliary drainage, all patients underwent placement of self-expandable metallic stents through the transhepatic tract. In ten of the 14 patients with hilar obstruction, two stents were placed in a Y-configuration through both transhepatic tracts. Two types of biliary stent were used: Hanaro (n=17) and Nitinol (n=20). The fully expanded diameter of the stents used in this study was 10 mm. They were of adequate length, varying between 6 and 10 cm and permitting overstretching of the stenotic segment.

For intraluminal brachytherapy, the drainage catheter was changed to an 8.5-F guiding catheter (GCA8/5; Nycomed, Paris, France) 3-6 days after stent placement. If difficulties due to incomplete stent expansion were encountered during the first week, balloon dilatation was performed and an iridium-192 wire was then placed inside the guiding catheter. The length of the iridium source, ranging from 5 to 16 cm, was such that it could extend 2 cm proximal and distal over and above the length of the stenotic segment. Intraluminal brachytherapy at 1 cm from the center of the source was prescribed, and using a brachytherapy unit (Nucletron) once a day or every other day, for 9-18 days, a dose of 25 Gy was delivered at a rate of 5 Gy per fraction.

Follow-up

Follow-up cholangiograms were obtained after the completion of intraluminal brachytherapy, and if good internal drainage through the stent was determined, the guiding catheter was removed. When expansion of the stent was incomplete, the guiding catheter was changed by the addition of an indwelling external drainage catheter for follow-up cholangiography and additional intervention. In patients who did not undergo intraluminal brachytherapy, a drainage catheter was left in place for two weeks in order to adequately evaluate patency after stent placement.

After intraluminal brachytherapy, 14 patients also underwent external-beam radiotherapy.

Data analysis

For statistical comparison of patients who underwent and who did not undergo intraluminal brachytherapy, stent patency and survival were calculated using the Kaplan-Meier method and an independent t test. Stent patency was determined from the time required to achieve adequate internal drainage after intraluminal brachytherapy, or was taken as two weeks after stent placement in the patients who did not undergo intraluminal brachytherapy. To evaluate patency, patients were given follow-up tests for jaundice and also underwent a serum total bilirubin test, hepatobiliary scanning, cholangiography, and US and/or CT scanning. Survival from the time of stent placement was determined.

Results

Procedure

Stents were placed at mean 17.5 days after external biliary drainage and intraluminal brachytherapy was performed 5.0 (range, 0-12) days after stent placement.
External drainage catheters were removed 26.2 (range, 6-45) days after stent placement, and 4.6 days after intraluminal brachytherapy. In five patients, the drainage catheter was not removed because of incomplete stent expansion (n=3) or early death (within 30 days of stent placement)(n=2). No severe stent-related complication occurred.

**Patency and Survival (Tables 1, 2, 3; Figs. 3, 4)**

The mean durations of stent patency and survival were 7.0 and 7.8 months, respectively, in all patients; 9.1 and 10.0 months in patients who underwent intraluminal brachytherapy, and 4.2 and 5.0 months in those who did not undergo this procedure ($p<0.05$).

Twenty-two of the total of 27 patients died 0.8-17.3 (mean, 6.7) months after stent placement; one died of
massive bleeding of a gastric ulcer during the course of intraluminal brachytherapy, confirmed by emergency endoscopy and not directly related to this treatment. The mean duration of stent patency and survival among the 22 who died were 7.6 (range, 0.8 - 16.1) and 8.3 (range, 0.8 - 17.3) months in the eleven patients who underwent intraluminal brachytherapy, and 4.2 (range, 0.9 - 8.0) and 5.0 (range, 0.9 - 8.4) months in the others who did not (p < 0.05, independent t test).

When intraluminal brachytherapy was performed after stent placement in patients with hilar obstruction (two stents and two iridium-192 wires being placed in a Y-configuration through both hepatic tracts), the mean duration of stent patency was 8.3 months, a period not significantly different from that observed in all patients who underwent intraluminal brachytherapy.

Fig. 2. A 70-year-old woman with hilar cancer. Initial cholangiography shows hilar obstruction [A]. After two Nitinol stents (10 mm in diameter and 7 cm in length) were placed in a Y-configuration via both transhepatic tracts, tubes were changed by 8.5F guiding catheters [B]. Two iridium-192 wires were placed through guiding catheters for intraluminal brachytherapy [C]. After cholangiography, tubes were removed [D].
Discussion

In order to overcome the limitations of external biliary drainage catheters and plastic stents, the placement of self-expandable metallic stents for the palliative treatment of inoperable malignant biliary obstruction has recently become popular. One of the major problems of metallic stents, however, is early occlusion caused by tumor overgrowth or ingrowth (1-11). In order to decrease stent occlusion rate, overstenting of the stenotic segment and intraluminal brachytherapy have thus been attempted (9, 12-15).

In our initial study, intraluminal brachytherapy was performed, using an indwelling biliary drainage catheter before stent placement. This, though, requires a drainage catheter whose inner and outer diameter are at least 6F and 12F, respectively. One of this size, however, is difficult to pass through a stenotic segment, and in addition, it is difficult to advance an iridium-192 wire through a drainage catheter with side holes because the tip of the wire becomes ensnared. Although a 12F drainage catheter with an end hole only might be suitable, the biliary system is not drained effectively during the course of intraluminal brachytherapy, and the risk

Table 1. Patency and Survival in the All Patients (Kaplan-Meier method)

<table>
<thead>
<tr>
<th>Patients group</th>
<th>Mean patency</th>
<th>Mean survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>ILBT (+) [n = 16]</td>
<td>9.1 months</td>
<td>10.0 months</td>
</tr>
<tr>
<td>ILBT (-) [n = 11]</td>
<td>4.2 months</td>
<td>5.0 months</td>
</tr>
<tr>
<td>Total [n = 27]</td>
<td>7.0 months</td>
<td>7.8 months</td>
</tr>
</tbody>
</table>

ILBT: intraluminal brachytherapy

Table 2. Patency and Survival Among the Deceased (Independent t test)

<table>
<thead>
<tr>
<th>Patients group</th>
<th>Mean patency</th>
<th>Mean survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>ILBT (+) [n = 11]</td>
<td>7.6 months</td>
<td>8.3 months</td>
</tr>
<tr>
<td>ILBT (-) [n = 11]</td>
<td>4.2 months</td>
<td>5.0 months</td>
</tr>
<tr>
<td>Total [n = 22]</td>
<td>5.9 months</td>
<td>6.7 months</td>
</tr>
</tbody>
</table>

ILBT: intraluminal brachytherapy

Table 3. Patency in Hilar vs. Non-hilar Involvement (Kaplan-Meier method)

<table>
<thead>
<tr>
<th>Patients group</th>
<th>Hilar</th>
<th>Non-hilar</th>
</tr>
</thead>
<tbody>
<tr>
<td>ILBT (+) [n = 16]</td>
<td>8.3 [n = 10]</td>
<td>10.5 [n = 6]</td>
</tr>
<tr>
<td>ILBT (-) [n = 11]</td>
<td>2.6 [n = 4]</td>
<td>5.2 [n = 7]</td>
</tr>
<tr>
<td>Total [n = 27]</td>
<td>6.6 [n = 14]</td>
<td>7.7 [n = 13]</td>
</tr>
</tbody>
</table>

ILBT: intraluminal brachytherapy

Fig. 3. A 57-year-old man with hilar involvement. Initial cholangiography shows occlusion of hilum (A). Two Hanaro stents (10 mm in diameter and 7 cm in length) were placed in a Y-configuration via both transhepatic tracts. After stent placement, he received intraluminal brachytherapy (B). After 16 months, recurrent jaundice developed. Tubogram shows stent occlusion (C). He died 1 month later.
of cholangitis increases. For this reason we performed stent placement prior to intraluminal brachytherapy, easily passing a relatively small stent introducer (7-10F) through the stenotic segment and accomplishing biliary drainage through the space between an 8.5F guiding catheter with an end hole only, and the stent. Because metallic stents do not have clinically important attenuation or scatter of therapeutic radiation, there was no significant difference in stent patency and survival between patients who underwent intraluminal brachytherapy before, and after, stent placement [13, 15]. When a change of catheters for intraluminal brachytherapy was difficult because of incomplete stent expansion, plain abdominal radiography and cholangiography were first performed, followed by balloon dilatation was performed.

In five patients, because of incomplete stent expansion and early death, the external drainage catheter was not removed. In such cases, because adequate internal drainage was demonstrated and the external catheter kept clamped, stent patency was determined from the time of cholangiography. The catheter was used only to permit additional intervention when symptoms of stent occlusion recurred.

We performed intraluminal brachytherapy combined with stent placement in attempts to extend stent patency and survival. The mean duration of stent patency (9.1 months) and survival (10.0 months) were greater in patients who underwent intraluminal brachytherapy than in those who did not (mean stent patency of 4.2 days and mean survival time of 5.0 months) \( p < 0.05 \). Other authors reported even better results: a mean stent patency of 19.5 months and mean survival time of 22.6 months with intraluminal brachytherapy and stent placement [Eschelman et al. (14)]; mean survival time of 8.5 months with brachytherapy only [Karani et al. (16)]; and mean survival time of 14 months with stent placement only [Coon (17)]. These findings might be accounted for by early death not related to the procedure \( n = 2 \), or the presence of advanced tumors involving massive invasion and metastases. In a larger patient population, furthermore, the question of whether they are related to the procedure or are due to other factors present in the patient population may be solved.

Becker et al. [18] and Gilliams et al. [19] reported that in patients with hilar obstruction, the period of stent patency was shorter than in patients with non-hilar obstruction, but survival time was similar. However, after placing two stents (in a Y-configuration) in patients with hilar obstruction through both transhepatic tracts and

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**Fig. 4.** A 54-year-old woman without hilar involvement. Initial cholangiography shows occlusion of common hepatic duct (A). A Nitinol stent (10 mm in diameter and 7 cm in length) was placed in common hepatic duct. After stent placement, tubogram shows biliary drainage (B). She did not receive intraluminal brachytherapy. After 6 months, recurrent jaundice developed. Tubogram shows stent occlusion due to tumor ingrowth (C). She died 2 months later.
then treating them with intraluminal brachytherapy, the mean duration of stent patency (8.3 months) was not different from that in all patients who underwent intraluminal brachytherapy. It thus appears that intraluminal brachytherapy after stent placement effectively extends stent patency in cases involving either hilar or non-hilar obstruction.

Other than mild gastrointestinal troubles and one case of cholangitis reported by Leung et al. (20), almost no complications of intraluminal brachytherapy have been reported. This internal source allows a high local dose of radiation while limiting the exposure of adjacent organs.

In conclusion, intraluminal brachytherapy after stent placement effectively extends stent patency and survival time in patients with primary bile duct carcinoma. Because of the type of primary tumor, tumor stage, the general condition of the patients involved, and external-beam radiotherapy, there may, however, has been a selection bias in our study.

References

Kyu-Hong Park, et al: Intraluminal Brachytherapy after Metallic Stent Placement in Primary Bile Duct Carcinoma

1. 배경 및 연구목적
2. 연구 방법
3. 결과
4. 결론
5. 참고문헌

배경: 전신적 치료가 불가능한 주요 간관절암의 치료에 있어서 내장기구내 브라키테라피는 최근 주목을 받고 있다. 본 연구는 주요 간관절암 환자에서 금속 슬린트 배치 후 브라키테라피의 효과를 평가하고자 하였다.


결과: 14일 동안 생존한 환자는 27명이었으며, 10명의 환자가 16일 이내에 사망하였다. 슬린트 배치 후 브라키테라피를 받은 환자의 생존율은 71%로 나타났다. 슬린트 배치 후 브라키테라피를 받지 않은 환자의 생존율은 35%로 나타났다. (p<0.05)

결론: 본 연구결과, 슬린트 배치 후 브라키테라피는 주요 간관절암의 치료에 있어 효과적인것으로 보인다.