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Intraluminal Brachytherapy after Metallic Stent Placement in Primary Bile Duct Carcinoma[1]

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Purpose: To determine the effect of intraluminal brachytherapy on stent patency and survival after metallic stent placement in patients with primary bile duct carcinoma.

Materials and Methods: Twenty-seven patients with primary bile duct carcinoma underwent metallic stent placement; in 16 of the 27 intraluminal brachytherapy with an iridium-192 source (dose, 25 Gy) was the performed. Obstruction was due to either hilar (n = 14) or non-hilar involvement (n = 13). For statistical comparison of patients who underwent/did not undergo intraluminal brachytherapy, stent patency and survival were calculated using the Kaplan-Meier method and an independent t test.

Results: The mean durations of stent patency and survival were 9.1 and 10.0 months respectively in patients who underwent intraluminal brachytherapy, and 4.2 and 5.0 months in those who did not undergo this procedure ($p < 0.05$). The mean durations of stent patency and survival among the 22 patients who died were 7.6 (range, 0.8 - 16.1) and 8.3 (range, 0.8 - 17.3) months, respectively, 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 those whom the procedure was not performed ($p < 0.05$).

Conclusion: Intraluminal brachytherapy after stent placement extended both stent patency and survival in patients with primary bile duct carcinoma.

Index words : Bile ducts, interventional procedure
Bile ducts, neoplasms
Bile ducts. stents and prostheses
Bile ducts, stenosis or obstruction
Bile ducts, therapeutic radiology

Self-expandable metallic stent placement was introduced in an attempt to overcome the limitations of external biliary drainage catheters (such as tube dislodgement, bile leakage, and psychologic problems) and plastic endoprostheses (such as migration, occlusion, and a traumatic implantation procedure) in treating patients

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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 ually 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 overstenting 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 1cm 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 cholangiograhy 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

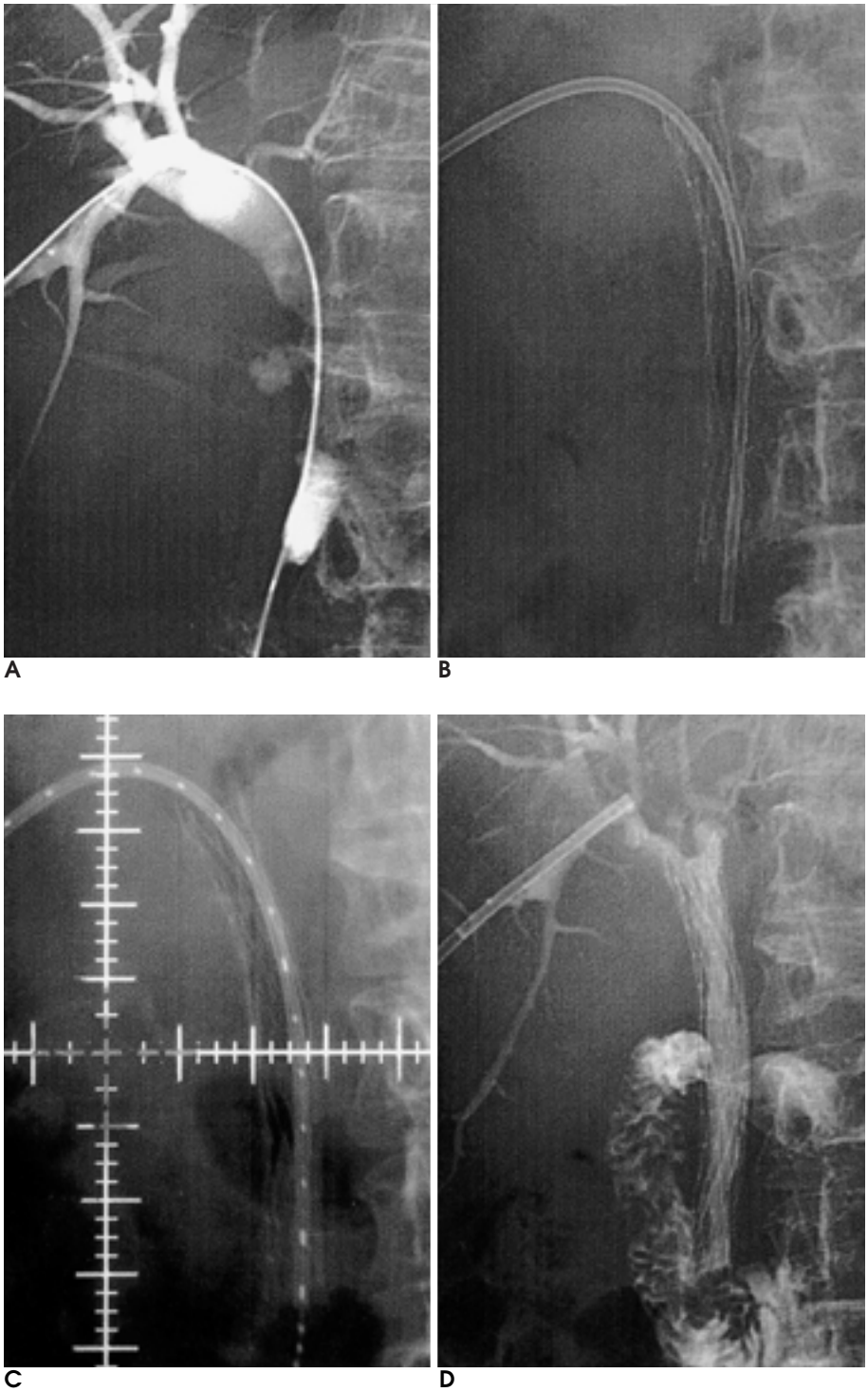

Fig. 1. A 70-year-old woman without hilar involvement. Initial cholangiography after PTBD shows common bile duct obstruction (**A**). After stent placement (a Hanaro stent, 10 mm in diameter and 7 cm in length), a pigtail catheter was changed by a 8.5F guiding catheter (**B**). An iridium-192 wire was placed through the guiding catheter for intraluminal brachytherapy (**C**). After cholangiograhpy, the tube was removed (**D**).

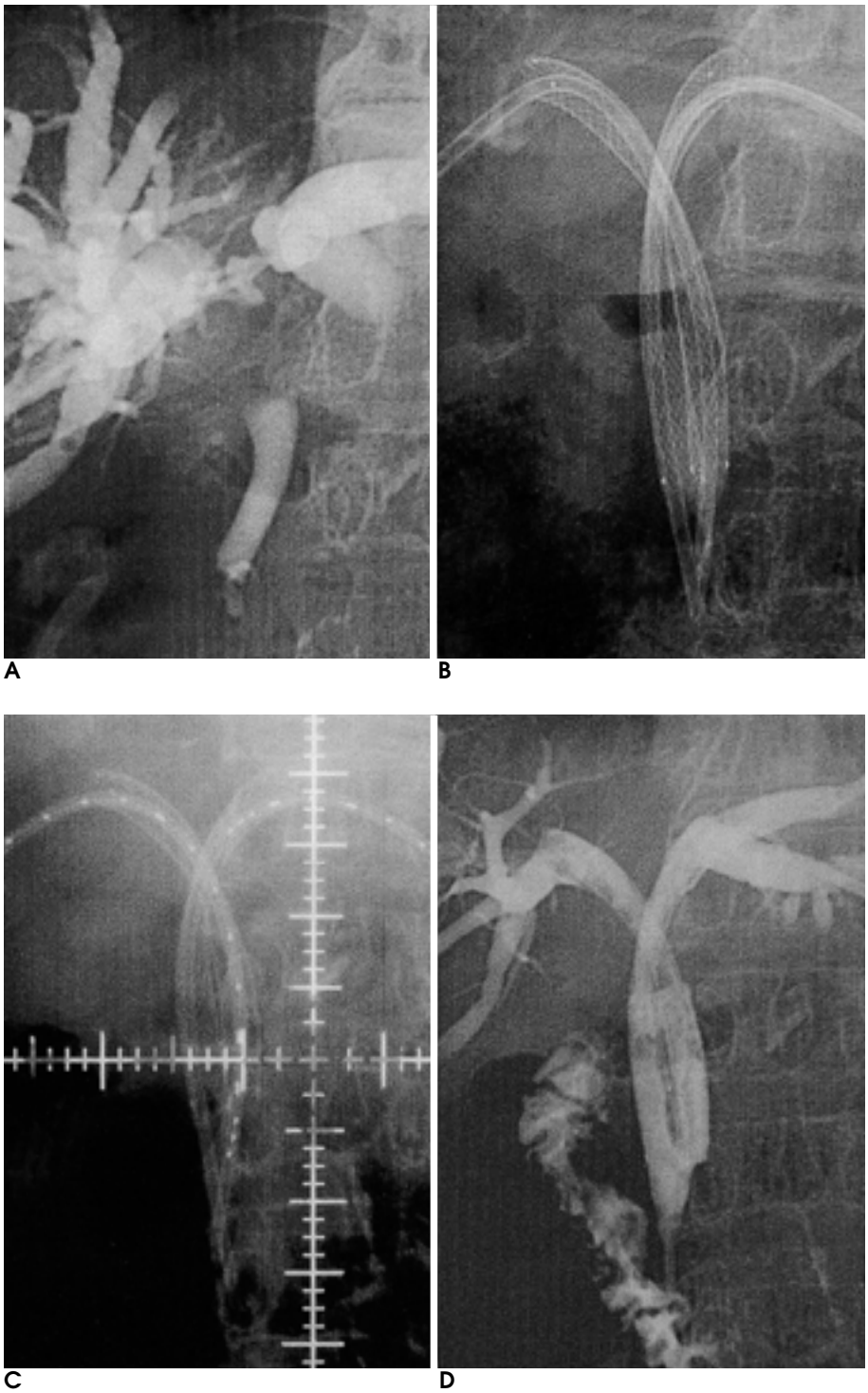

Fig. 2. A 70-year-old woman with hilar cancer. Initial cholangiography shows hilar obstruction (**A**). After two Nitinol stents (10 mm in diameter and 7 cm in length) were placed in a Y-configuration via both transhepatic tracts, tubes were changed by 8.5F guiding catheters (**B**). Two iridium-192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

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.

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)

	$p < 0.05$	months
Patients group	Mean patency	Mean survival
ILBT (+) (n = 16)	9.1	10.0
ILBT (-) (n = 11)	4.2	5.0
Total (n = 27)	7.0	7.8

ILBT: intraluminal brachytherapy

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

	$p < 0.05$	months
Patients group	Mean patency	Mean survival
ILBT (+) (n = 11)	7.6	8.3
ILBT (-) (n = 11)	4.2	5.0
Total (n = 22)	5.9	6.7

ILBT: intraluminal brachytherapy

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

		months
Patients group	Hilar	Non-hilar
ILBT (+) (n = 16)	8.3 (n = 10)	10.5 (n = 6)
ILBT (-) (n = 11)	2.6 (n = 4)	5.2 (n = 7)
Total (n = 27)	6.6 (n = 14)	7.7 (n = 13)

ILBT: intraluminal brachytherapy

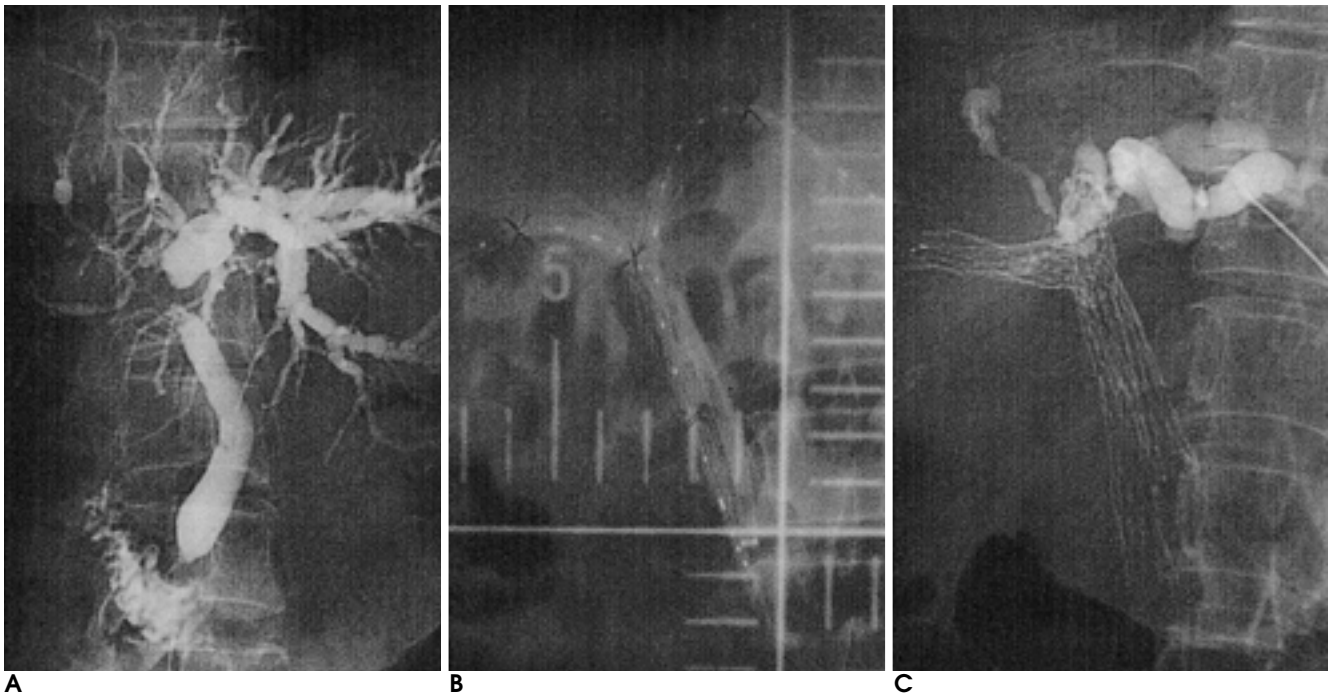

Fig. 3. A 57-year-old man with hilar involvement. Initial cholangiography shows occlusion of hilum (**A**). Two Hanaro stents (10 mm in diameter and 7 cm in length) were placed in a Y-configuration via both transhepatic tracts. After stent placement, he received intraluminal brachytherapy (**B**). After 16 months, recurrent jaundice developed. Tubogram shows stent occlusion (**C**). He died 1 month later.

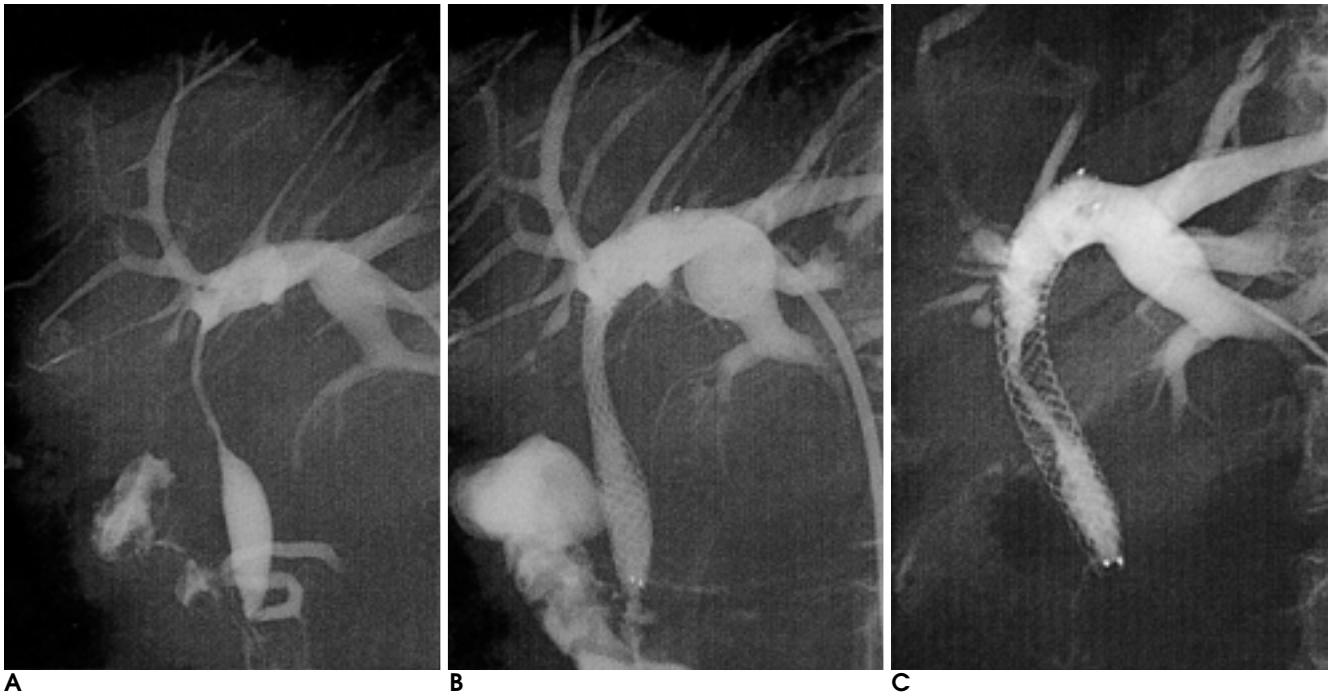

Fig. 4. A 54-year-old woman without hilar involvement. Initial cholangiography shows occlusion of common hepatic duct (**A**). A Nitinol stent (10 mm in diameter and 7 cm in length) was placed in common hepatic duct. After stent placement, tubogram shows biliary drainage (**B**). She did not receive intraluminal brachytherapy. After 6 months, recurrent jaundice developed. Tubogram shows stent occlusion due to tumor ingrowth (**C**). She died 2 months later.

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 in 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

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 reportd 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

1. Adam A, Chetty N, Roddie M, Yeung E, Benjamin IS. Self expandable stainless steel endoprostheses for treatment of malignant bile duct obstruction. *AJR Am J Roentgenol* 1991;156:321-325
2. Yoshioka T, Sakaguchi H, Yoshimura H, et al. Expandable metallic biliary endoprostheses: preliminary clinical evaluation. *Radiology* 1990;177:253-257
3. Yang GS, Kim SW, Kim WH, Kim YJ. Treatment of malignant biliary obstruction with Wallstent endoprosthesis. *J Korean Radiol* Soc 1995;32:71-76
4. Lee BH, Do YS, Byun HS, Kim KH, Chin SY. Metallic stents for management of malignant biliary obstruction. *J Korean Radiol Soc* 1992;28:959-967
5. Han JK, Choi BI, Chung JW, Park JH, Han GS, Han MC. The use of self expandable metallic stent in the management of malignant biliary obstruction. *J Korean Radiol Soc* 1993;29:457-463
6. Hausegger KA, Kleinert R, Lammer J, Klein GE, Fluckiger F. Malignant biliary obstruction: histologic findings after treatment with self-expandable stents. *Radiology* 1992;185:461-464
7. Rho BS, Kim CS, Lee KS, et al. Gianturco metallic biliary stent in malignant obstruction: results of follow-up in dead patients. *J Korean Radiol Soc* 1994;30:659-664
8. Mueller PR, Ferrucci JT Jr, Teplick SK, et al. Biliary stent endoprostheses: analysis of complications in 113 patients. *Rdiology* 1985;156:637-639
9. Lee MJ, Dawson SL, Mueller PR, et al. Percutaneous management of hilar biliary malignancies with metallic endoprostheses: results, technical problems, and causes of failure. *Radiographics* 1993;13: 1249-1263
10. Hausegger KA, Thurnher S, Bodendor fer G, et al. Treatment of malignant biliary obstruction with polyurethane-covered Wallstents. *AJR Am J Roentgenol* 1998;170:403-408
11. Stoker J, Lameris JS. Complications of percutaneously inserted biliary Wallstents. *J Vasc Interv Radiol* 1993;4:767-772
12. Lameris JS, Stoke J, Nijs HGT, et al. Malignant biliary obstruction: percutaneous use of self-expandable stents. *Radiology* 1991;179: 703-707
13. Rho TS, Kim YH, Lee CH, Jung HS, Kim CY. Combined treatment with stent placement and radiotherapy in malignant biliary obstruction. *J Korean Radiol Soc* 1994;31:1045-1049
14. Eschelman DJ, Shapiro MJ, Bonn J, et al. Malignant biliary duct obstruction: long-term experience with Gianturco stents and combined-modality radiation therapy. *Radiology* 1996;200:717-724
15. Mayo-Smith WW, Dawson SL, Mauceri T, Mueller PR. Attenuation effects of biliary endoprostheses on therapeutic radiation. *Radiology* 1996;199:571-572
16. Karani J, Fletcher M, Brinkley D, Dawson JL, Williams R, Nunnerley H. Internal biliary drainage and local radiotherapy with iridium-192 wire in treatment of hilar cholangiocarcinoma. *Clin Radiol* 1985;36:603-306
17. Coons H. Metallic stents for the treatment of biliary obstruction : a report of 100 cases. *Cardiovasc Intervent Radiol* 1992;15:367-374
18. Becker CD, Glattli A, Maibach R, Baer HU. Percutaneous palliation of malignant obstructive jaundice with the Wallstent endoprosthesis: follow-up and reintervention in patients with hilar and non-hilar obstruction. *J Vasc Interv Radiol* 1993;4:597-604
19. Gilliams A, Dick R, Dooley JS, Wallsten H, El-Din A. Self-expandable stainless steel braided endoprosthesis for biliary stricture. *Radiology* 1990;174:137-140
20. Leung JT, Kaun R. Intraluminal brachytherapy in the treatment of bile duct carcinoma. *Australas Radiol* 1997;41:151-154

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원발성 담관암에서 금속 스텐트 설치후 관내 방사선치료[1]

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목적: 원발성 담관암 환자에서 금속 스텐트 설치후 관내 방사선치료의 효과를 스텐트의 개존기간과 환자의 생존기간을 중심으로 알아보고자 하였다.

대상과 방법: 원발설 담관암 환자중 스텐트를 설치한 27명을 대상으로 하였고, 이중 16명은 관내 방사선치료를 시행하였다. 관내 방사선치료로 iridium-192를 사용하여 25 Gy를 5회에 나누어 시행하였다. 담도 폐쇄의 부위는 간문부를 침범한 경우가 14 예였으며, 나머지는 간문부 침범이 없었다. 관내 방사선치료를 시행한 군과 시행하지 않은 군 사이에 스텐트의 개존 기간과 환자의 생존기간을 Kaplan-Meier 방법 및 독립표본 T검정을 이용하여 비교하였다.

결과: 관내 방사선치료를 시행한 군에서 스텐트의 평균 개존기간은 9.1개월이었으며, 시행하지 않은 군에서 4.2개월이었다($p<0.05$). 환자의 평균 생존기간은 관내 방사선치료를 시행한 군에서 10.0개월이었으며, 시행하지 않은 군에서 5.0개월이었다($p<0.05$). 사망 환자(n=22)중 관내 방사선치료를 시행한 군(n=11)의 스텐트 개존기간은 평균 7.6(0.8-16.1)개월, 시행하지 않은 군(n=11)에서는 평균 4.2(0.9-8.0)개월이었으며($p<0.05$), 환자의 평균 생존기간도 관내 방사선치료를 시행한 군에서 8.3(0.8-17.3)개월, 시행하지 않은 군에서 5.0(0.9-8.4)개월이었다($p<0.05$).

결론: 원발성 담관암 환자에서 스텐트 설치후 관내 방사선치료는 스텐트의 개존 기간과 환자의 생존기간을 연장시킬 수 있는 유용한 치료방법으로 사료된다.