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Retrospective Study

Safety and efficacy of metallic stent for unresectable distal malignant biliary obstruction in elderly patients

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Abstract

AIM

To study the safety of insertion of metallic stents in elderly patients with unresectable distal malignant biliary obstruction.

METHODS

Of 272 patients with unresectable distal malignant biliary obstruction, 184 patients under the age of 80 were classified into Group A, and 88 subjects aged 80 years or more were classified into Group B. The safety of metallic stent insertion, metal stent patency period, and the obstruction rate were examined in each group.

RESULTS

In Group B, patients had a significantly worse performance status, high blood pressure, heart disease, cerebrovascular disease, and dementia; besides the rate of patients orally administered antiplatelet drugs or anticoagulants tended to be higher ($P < 0.05$). Metallic stents were successfully inserted in all patients. The median patency period was 265.000 ± 26.779 (1-965) d; 252.000 ± 35.998 (1-618) d in Group A and 269.000 ± 47.885 (1-965) d in Group B, with no significant difference between the two groups. Metallic stent obstruction occurred in 82 of the 272 (30.15%) patients; in 53/184 (28.80%) patients in Group A and in 29/88 (32.95%) of those in Group B, showing no significant difference between the two groups. Procedural accidents due to metal stent insertion occurred in 24/272 (8.8%) patients; in 17/184 (9.2%) of patients in Group A and in 7/88 (8.0%) of those in Group B, with no significant difference between the two groups, either.

CONCLUSION

These results suggested that metallic stents can be safely inserted to treat unresectable distal malignant biliary obstruction even in elderly patients aged 80 years or more.

Key words: Elderly patients; Metallic stent; Malignant biliary obstruction

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Core tip: It was suggested that metallic stent insertion for unresectable distal malignant biliary obstruction in the elderly can be conducted safely and with a high success rate, without any significant difference in the occurrence of procedural accidents when compared with the non-elderly group, even though the elderly tend to have more underlying diseases.

Sakai Y, Iwai T, Shimura K, Gon K, Koizumi K, Ijima M, Chiba K, Nakatani S, Sugiyama H, Tsuyuguchi T, Kamisawa T, Maetani I, Kida M. Safety and efficacy of metallic stent for unresectable

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INTRODUCTION

Endoscopic retrograde cholangiopancreatography (ERCP) related procedure is a minimally invasive diagnostic and therapeutic method for biliary and pancreatic diseases and plays a very important role. As for biliary drainage, endoscopic drainage by ERCP is considered to be noninvasive and the first choice of treatment^[1,2]. Either plastic or metallic stents are used in endoscopic drainage for patients with unresectable malignant biliary obstruction. However, it is desirable to use a metallic stent because of its long patency period and low obstruction rate, which reduce the need for retreatment and the total treatment cost^[1-4]. It is considered that metallic stents can be safely inserted in patients with unresectable malignant biliary obstruction, they are useful and the drainage effect is excellent^[5-8]. Yet, to our knowledge, there are no reports that examined the safety of insertion of metallic stents in the elderly with an unresectable malignant biliary obstruction. Therefore, we studied the safety and usefulness of metallic stents for unresectable distal malignant biliary obstruction in a multicenter, collaborative, retrospective study.

MATERIALS AND METHODS

There were 272 patients diagnosed with unresectable distal malignant biliary obstruction, at the 7 institutions participating in this study, from January 2012 to July 2016. Metallic stents were inserted transpapillary using the ERCP route. In all patients, endoscopic sphincterotomy (EST) was performed previous to metal stent insertion. The metallic stent used was BONA stent (Sewoon Medical Co., Ltd. Delivery system, 8Fr, 10 mm diameter, fully covered stent). Inclusion criteria were: (1) written informed consent for the study obtained previous to the endoscopic treatment; (2) patients aged 20 years or more; (3) patients hospitalized on ERCP day who could be followed for one week after ERCP; (4) patients not subjected to stomach reconstruction with Billroth II method or Roux-en Y anastomosis; (5) patients who could orally administered antiplatelet drugs or anticoagulants, and could discontinue drug treatment for one week before and after ERCP or EST; and (6) patients with a platelet count of 50000/mL or more, and PT-INR 1.5 or less. Exclusion criteria were (1) patients whose medical record could not be reviewed after treatment; and (2) other patients who were judged as inappropriate by the investigator. There were 157 men and 115 women, whose mean age was 74.165 ± 11.649

(44-96) years. The disease was pancreatic cancer in 208 patients, bile duct cancer in 30, metastatic biliary obstruction in 16, duodenal papillary carcinoma in 9, gallbladder cancer in 7, hepatocellular carcinoma in 1, and intraductal papillary mucinous carcinoma in 1 patient. Hepatic metastasis was found in 56 patients and ascites retention in 68 patients. Duodenal stenosis was detected in 40 patients and a duodenal stent was inserted in all patients. In 250 patients the diagnosis of malignancy was established by pathological examination, and in the remaining patients imaging techniques and clinical course. The bile duct diameter prior to drainage was 12.093 ± 3.336 (4-23) mm, and the stenosis length prior to the drainage was 27.276 ± 12.683 (5-59) mm. The result of hepatobiliary enzyme tests prior to the drainage was ALT 141.139 ± 105.309 (29-851) IU/L, ALP 1498.163 ± 1248.051 (409-2620) IU/L, and T-Bil 5.388 ± 6.203 (0.4-27.8) mg/dL. Performance status (PS) determined according to the criteria of the Eastern Cooperative Oncology Group was 0 in 80 patients, 1 in 10 patients, 2 in 56 patients, 3 in 66 patients and 4 in 60 patients. Underlying diseases included high blood pressure in 107 patients, diabetes mellitus in 81 patients, hyperlipidemia in 26 patients, chronic lung disease in 43 patients, heart disease in 38 patients, chronic liver disease in 24 patients, chronic kidney disease in 13 patients, cerebrovascular disease in 25 patients, and dementia in 25 patients; and there were 32 patients who were administered antiplatelet drugs or anticoagulants. Chemotherapy was carried out in 121 patients based on judgment by the attending physician. The judgment of therapeutic effect was made after 2 courses of chemotherapy. In patients for whom chemotherapy could not be continued before conducting 2 courses, the effect was judged at that time. Chemotherapy effect was judged using RECIST criteria^[9]. At the time of effect judgment, complete response: CR was defined as disappearance of all target lesions, and regarding lymph node involvement, this was defined as reduction of the shorter diameter to less than 10 mm. Partial response: PR was defined as reduction by more than 30% compared to the sum of total target lesion diameter at the baseline. Stable disease: SD was defined as no reduction corresponding to PR and no progress corresponding to PD. Progressive disease: PD was defined as an increase by 20% or more and an increase in absolute value by 5 mm or more when compared with the sum of the minimum diameter of the target lesion during the course. Patients under 80 years of age were classified into Group A and patients aged 80 or more into Group B. The safety of metallic stent insertion, patency period after metallic stent insertion, obstruction rate, and success rate of metallic stent insertion were examined and compared between the two groups. Early procedural accidents occurring in ERCP-related procedures were evaluated using Cotton's classification^[10]. All treatments were carried out with the patient's or patient's family

informed consent, and a signed consent form was obtained. This study was conducted with the approval of the ethics committee of each participating facility.

Statistical analysis

Person χ^2 test with Yates correction and Fisher's exact test, when appropriate, were used for statistical analysis of categorical variables. Stent patency and patient survival time were estimated using the Kaplan-Meier method, and the log-rank test was used to assess differences between the groups. Data were analyzed using SPSS software version 11 (SPSS, Chicago, IL, United States). Differences with a *P* value of < 0.05 were considered statistically significant.

RESULTS

The patient background data is shown in Table 1. In Group B there were significantly more patients with high blood pressure, heart disease, cerebrovascular disease, and dementia, as well as more patients taking antiplatelet drugs or anticoagulants. PS tended to be significantly worse in Group B, and fewer patients were subjected to chemotherapy in this group. Other factors did not show a significant difference between Group A and Group B. The results on treatment are shown in Table 2. The success rate of metallic stent insertion was 100% (272/272). The drainage effect after insertion of the metal stent was ALT 70.375 ± 123.860 (10-278) IU/L, ALP 768.400 ± 70.181 (326-1855) IU/L, and T-Bil 1.944 ± 2.873 (0.4-12.2) mg/dL, showing significant reduction ($P < 0.05$). There was no significant difference of ALT, ALP and T-Bil values after the drainage between Group A and Group B, and drainage was excellent. Chemotherapy was conducted more frequently in Group A and best supportive care was more frequently employed in Group B. As for the effect of chemotherapy, CR was achieved in 0% (0/121), PR in 13.2% (16/121), SD in 70.2% (85/121), and PD in 16.5% (20/121) of the patients, with a success rate of 13.2% (16/121). Prior to conducting 2 courses of chemotherapy, PD was observed in 8.3% (10/121) of the patients, thus it was not possible to continue with the treatment. In Group A, the number of patients with SD tended to be significantly higher. The median of survival period was 205.000 ± 21.801 (7-999) d. The median of survival period was 246.000 ± 36.056 (7-738) d in Group A and 180.000 ± 25.724 (7-999) d in Group B, showing no significant difference (Figure 1). The median patency period was 265.000 ± 26.779 (1-965) d; 252.000 ± 35.998 (1-618) d in Group A and 269.000 ± 47.885 (1-965) d in Group B, with no significant difference (Figure 2). Stent obstruction occurred in 30.15% (82/272) of the patients during the follow-up period. The cause of stent obstruction included overgrowth in 6.3% (17/272), ingrowth in 2.2% (6/272), sludge in 9.6% (26/272), migration in 8.5% (23/272), food impaction

Table 1 Patient background

	< 80 yr old (Group A)	≥ 80 yr old (Group B)	P value
Number of patients	184	88	
Male	105	52	NS
Female	79	36	NS
Pancreatic cancer	136	72	NS
Bile duct cancer	21	9	NS
Metastatic biliary obstruction	13	3	NS
Papilla vater cancer	6	3	NS
Gallbladder cancer	6	1	NS
Intraductal papillary mucinous carcinoma	1	0	NS
Hepatocellular carcinoma	1	0	NS
Hepatic metastasis	40	16	NS
Ascites	45	23	NS
Duodenal stent indwelling	30	10	NS
Pathological diagnosis	161	89	NS
Performance status			
0	72	8	0.0000
1	7	3	NS
2	44	12	0.018
3	29	37	0.0004
4	32	28	0.0064
Chemotherapy	106	15	0.0000
Hypertension	55	52	0.0002
Hyperlipidemia	20	6	NS
Diabetes mellitus	50	31	NS
Chronic respiratory disease	25	18	NS
Cardiac disease	18	20	0.0065
Chronic liver disease	18	6	NS
Chronic renal disease	10	3	NS
Cerebrovascular disease	5	20	0.0000
Dementia	5	20	0.0000
Anticoagulant/antiplatelet	9	23	0.0270

NS: Not significant.

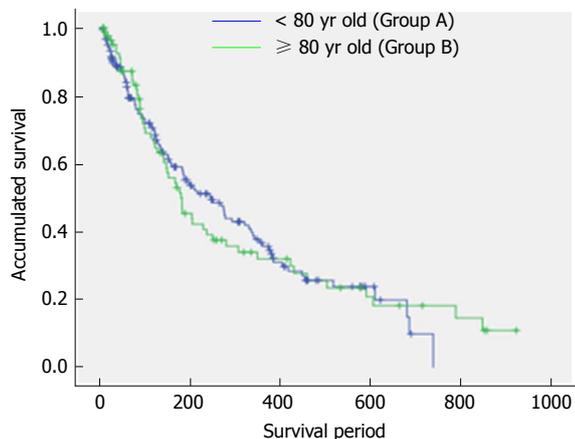


Figure 1 Comparison of the survival period. The median of survival period was 246.000 ± 36.056 (7-738) d in Group A and 180.000 ± 25.724 (7-999) d in Group B, showing no significant difference.

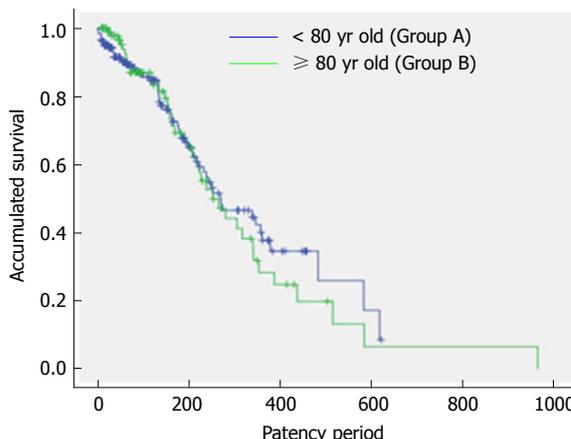


Figure 2 Metallic stent patency period. The median patency period was 265.000 ± 26.779 (1-965) d; 252.000 ± 35.998 (1-618) d in Group A and 269.000 ± 47.885 (1-965) d in Group B, with no significant difference.

in 2.6% (7/272), and others in 1.1% (3/272). Stent obstruction occurred in 28.80% (53/184) of patients in Group A, and in 32.95% (29/88) of those in Group B with no significant difference between the two groups. There was no significant difference between Group A and Group B regarding the cause-specific obstruction rate (Table 3). Early procedural accidents due to ERCP related procedures were observed in 8.8% (24/272)

of the patients. Early procedural accidents included pancreatitis in 2.9% (8/272, mild 8), cholecystitis in 3.7% (10/272, mild 8, moderate 2), cholangitis in 1.1% (3/272 mild 3), stent migration in 0.4% (1/272), and pneumonia in 0.7% (2/272). As shown in Table 4, there was no significant difference in the incidence of procedural accidents between Group A and Group B, whereas the onset of pancreatitis showed a

Table 2 Treatment effect judgment

Drainage effect	< 80 yr old (Group A; n = 184)	≥ 80 yr old (Group B; n = 88)	P value
Bile duct diameter prior to drainage (mm)	11.350 ± 3.6310 (4-23)	12.819 ± 3.3148 (5-22)	NS
Stenosis length prior to drainage (mm)	27.216 ± 12.688 (5-59)	27.292 ± 12.702(6-52)	NS
ALT prior to drainage (IU/L)	162.767 ± 104.768 (29-851)	127.567 ± 104.760(30-838)	NS
ALT post drainage (IU/L)	78.875 ± 159.482 (10-278)	66.039 ± 143.106 (13-270)	NS
ALP prior to drainage (IU/L)	1529.375 ± 1465.465 (409-2620)	1489.447 ± 1102.192 (432-2512)	NS
ALP post drainage (IU/L)	871.000 ± 803.131 (326-1855)	665.622 ± 557.643 (331-1811)	NS
T-Bil prior to drainage (mg/dl)	5.438 ± 6.512 (0.4-27.8)	5.276 ± 5.858 (0.6-27)	NS
T-Bil post drainage (mg/dl)	2.387 ± 3.879 (0.4-12.2)	1.580 ± 3.943 (0.6-12)	NS
Chemotherapeutic effect			
CR	0	0	NS
PR	12	4	NS
SD	78	7	0.0000
PD	16	4	NS
Total	106	15	0.0000
Best supportive care	78	73	0.0000

NS: Not significant.

Table 3 Cause of metallic stent obstruction

Related complications	< 80 yr old (Group A; n = 184)	≥ 80 yr old (Group B; n = 88)	P value
Overgrowth	10	7	NS
Ingrowth	6	0	NS
Sludge	16	10	NS
Stent migration	15	8	NS
Food impaction	3	4	NS
Others	3	0	NS
Total	53	29	NS

NS: Not significant.

Table 4 Comparison of early procedural accidents after conducting endoscopic retrograde cholangiopancreatography

Related complications	< 80 yr old (Group A; n = 184)	≥ 80 yr old (Group B; n = 88)	P value
Bleeding	0	0	
Perforation	0	0	NS
Pancreatitis	7 (mild)	1 (mild)	0.003
Cholangitis	1 (mild)	2 (mild)	NS
Cholecystitis	8 (6 mild, 2 moderate)	2 (mild)	NS
Stent migration	1	0	NS
Pneumoniae	0	2	NS

NS: Not significant.

significantly lower tendency in Group B: 0.01% (1/88) when compared with in Group A: 3.8% (7/184). All procedural accidents resolved without requiring a surgical procedure.

DISCUSSION

In medical care treatment should be safer and minimally invasive in consideration of the patient's quality of life. ERCP related procedures can be carried out rather safely as they are minimally invasive and a reasonable treatment method for removal of a

calculus from the common bile duct, or drainage in patients with obstructive jaundice. There are many reports indicating that ERCP related procedures can be safely performed even in the elderly^[11-14]. However, sufficient attention is necessary because there also are reports describing that procedural accidents easily become serious once they occur^[15]. In the present study we assessed the feasibility of metallic stent insertion in elderly patients with unresectable distal malignant biliary obstruction. The study was conducted because there have been no such reports so far. In general, elderly people tend to have various underlying diseases^[11-15], and this study also showed that tendency. Although it is obvious that the patient condition is not so good in such a situation, we showed that a metal stent can be safely inserted even in the elderly. In this study, there was no significant difference in the survival period and the metallic stent patency period. In recent years, patient prognosis has improved thanks to advances in chemotherapy for pancreatic cancer and bile duct cancer^[16-18]. There is a report showing that not only the survival period but also metal stent patency period is prolonged by chemotherapy for bile duct cancer^[19]. However, in this study, no significant difference was found in the survival period and the patency period, though the number of patients who underwent chemotherapy in the elderly group was significantly small. The reason may be that the success rate of chemotherapy was low in this study. The success rate of metal stent insertion was 100% in both groups. Though it is a retrospective study, the success rate of transpapillary metallic stent insertion is generally high even in past reports^[5-8]. Therefore, this result seems not to be a particularly good result. There was no significant difference in procedural accidents between the two groups, but the incidence of pancreatitis tended to be lower in Group B. The reason may be that in the elderly, pancreatic function is deteriorated, which lowers the possibility of

developing pancreatitis^[20]. In addition, pneumonia was observed in Group B but not in Group A. Since elderly people have sometimes reduced sputum excretion capacity, they may suffer from aspiration pneumonia. Therefore, especially for the elderly it was considered necessary to frequently conduct sputum aspiration during and after surgery. This study suggested that metallic stents can be safely inserted and are a useful treatment for unresectable distal malignant biliary obstruction in the elderly. However, since this was a retrospective, multicenter study, a prospective study is considered necessary in the future to further evaluate the feasibility and usefulness of this procedure in elderly patients.

In conclusion, it was suggested that metallic stent insertion for unresectable distal malignant biliary obstruction in the elderly can be conducted safely and with a high success rate, without any significant difference in the occurrence of procedural accidents when compared with the non-elderly group, even though the elderly tend to have more underlying diseases.

ARTICLE HIGHLIGHTS

Research background

The related procedure of endoscopic retrograde cholangiopancreatography (ERCP) is a minimally invasive diagnostic and therapeutic method for biliary and pancreatic diseases and plays a very important role. As for biliary drainage, endoscopic drainage by ERCP is considered to be noninvasive and the first choice of treatment.

Research motivation

To our knowledge, there are no reports that examined the safety of insertion of metallic stents in the elderly with an unresectable malignant biliary obstruction. Therefore, we studied the safety and usefulness of metallic stents for unresectable distal malignant biliary obstruction in a multicenter, collaborative, retrospective study.

Research objectives

This study aims to evaluate the safety of insertion of metallic stents in elderly patients with unresectable distal malignant biliary obstruction.

Research methods

There are total 272 patients with unresectable distal malignant biliary obstruction in this study. Group A (184 patients under the age of 80) and Group B (88 subjects aged 80 years or more) were examined by the safety of metallic stent insertion, metal stent patency period, and the obstruction rate.

Research results

In Group B, patients had a significantly worse performance status, high blood pressure, cerebrovascular disease, heart disease, and dementia; besides the rate of patients orally administered antiplatelet drugs or anticoagulants tended to be higher ($P < 0.05$). Metallic stents were successfully inserted in all patients. The median patency period was 265.000 ± 26.779 d (1-965); 252.000 ± 35.998 d (1-618) in Group A and 269.000 ± 47.885 d (1-965) in Group B, with no significant difference between the two groups. Metallic stent obstruction occurred in 30.15% (82/272) patients; in 28.80% (53/184) patients in Group A and in 32.95% (29/88) of those in Group B, showing no significant difference between the two groups.

Research conclusions

This study suggested that metallic stents can be safely inserted and are a

useful treatment for unresectable distal malignant biliary obstruction in the elderly. It was suggested that metallic stent insertion for unresectable distal malignant biliary obstruction in the elderly can be conducted safely and with a high success rate. We should insert metallic stent in unresectable distal malignant biliary obstruction in the elderly patients for improvement of quality of life positively.

Research perspectives

A prospective study is considered necessary in the future to further evaluate the feasibility and usefulness of metallic stent for unresectable distal malignant biliary obstruction in elderly patients.

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