*Gut*, 1989, **30**, 1132–1135

# Randomised trial of endoscopic endoprosthesis versus operative bypass in malignant obstructive jaundice

J R ANDERSEN, S M SØRENSEN, A KRUSE, M ROKKJÆR, AND P MATZEN

*From the Departments of Medical Gastroenterology, Hepatology, and Surgical Gastroenterology, Hvidovre Hospital, University of Copenhagen, Denmark and Department of Surgical Gastroenterology L, Aarhus Kommunehospital, University of Aarhus, Denmark*

SUMMARY **In patients with obstructive jaundice caused by malignant stricture of the extrahepatic bile duct we compared survival time, complication rates, hospitalisation requirements, and quality of life after palliation by endoscopic endoprosthesis or bypass surgery. During diagnostic endoscopic cholangiography 50 patients were randomised to the two treatment alternatives. All 25 patients randomised to endoprosthesis were treated by this procedure, whereas only 19 of 25 patients randomised to bypass surgery underwent operative biliary-digestive anastomosis. Life table analysis revealed no difference in survival between treatment groups or randomisation groups. No differences were found when other variables were compared. We conclude, that palliation of obstructive jaundice in malignant bile duct obstruction with endoscopically introduced endoprosthesis is as effective as operative bypass.**

In recent years, endoscopically placed endoprosthesis has become an alternative to traditional operative biliary-digestive bypass in palliative treatment of patients with non-resectable biliary obstruction caused by malignant stricture of the extrahepatic bile duct. In an uncontrolled series the endoscopic approach has been recommended as the treatment of choice.[1] Alternatively surgery has been recommended primarily because 13% of the survivors needed a later operation for duodenal obstruction.[2] The combined intraoperative and postoperative mortality (30 days mortality) after bypass surgery is reported to be 15–30%,[2] and the corresponding mortality for the endoscopic approach 10–18%.[1 3] The procedure related mortality of endoprosthesis insertion was low (0–2%),[1 3] and success rates in the application of the stent were high (90%).[1 3] Sonnenfeld *et al*[4] reported a non-randomised comparison of endoprosthesis *versus* bypass with 20 patients in each group and found no difference in survival, but the hospitalisation time was longer and major complications were more frequent in the operated group. Bornman *et al*[5] found no major differences in survival, hospitalisation time or complication rate in a random study comparing bypass surgery with percutaneous endoprostheses. Endoscopic stent insertion seemed to carry a lower mortality and fewer complications than the percutaneous stent insertion.[6] The present study was initiated in order to compare short and long time survival, quality of life and complication rates in a randomised study of endoscopic endoprosthesis *versus* bypass surgery for palliative treatment of patients with bile duct obstruction caused by malignant disease.

Address for correspondence: Jens Rikardt Andersen, MD, Dept. Medicine, Section of Gastroenterology 261, Hvidovre Hospital, DK-2650 Hvidovre, Denmark.

Accepted for publication 16 January 1989.

## Methods

### PATIENTS

The trial included 50 jaundiced patients consecutively referred for ERCP (endoscopic retrograde cholangiopancreaticography). Patients were randomised if over 60 years of age, if ERCP showed a low stricture of the common bile duct with strong suspicion of malignant aetiology, and if judged fit for

Table 1 *Fifty patients with malignant stricture of the common bile duct randomised to operative or endoscopic palliation*

| | *Endoscopy* | *Operation* |
|---|---|---|
| n | 25 | 25 |
| Women/men | 14/11 | 17/8 |
| Median age yr (range) | 77 (62–86) | 76 (69–86) |
| Pancreatic cancer (histology) | 21 (16) | 22 (14) |
| Biliary carcinoma (histology) | 4 (3) | 3 (3) |
| Treated according to randomisation | 25 | 19 |
| Se-bilirubin (μmol/l) mediun (range) | 224 (69–577) | 180 (44–551) |
| Se-alkaline phosphatase (U/l) median (range) | 1505 (472–4210) | 1408 (340–4290) |

surgical bypass, both technically and with respect to concommitant disease and general health, and if curative resection was not considered a realistic option (Table 1). The malignant disease was histologically proven during the study in 36 patients (Table 1). In the remaining 14 patients the diagnosis rested on typical findings on ERCP, a course of disease compatible with the diagnosis, the finding of metastases, and typical macroscopic appearance during operation. Autopsy was performed in 22 patients. Six patients randomised to operative treatment were not operated according to the protocol. Two patients wanted endoscopic treatment after randomisation to surgery. In one patient the anastomosis could not be constructed because of massive mestastases in the portal area, and this patient had no palliative treatment of the jaundice. Two patients were endoscopically treated because of concommitant psychiatric illness in one, and severe dementia in the other. The sixth had endoscopic treatment because of lack of operative capacity during summer vacation.

During the initial endoscopy patients were randomised by means of sealed envelopes to endoscopical treatment with 7 or 10 French endoprosthesis or to treatment with bypass surgery (Table 2). Twenty two patients had their endoprosthesis inserted at the time of randomisation; three patients had the endoscopy repeated with a delay of median three days, range two to four days, before the stent could be placed. The therapeutic delay in the operation group was median 1 day, range 0–17 days. No prophylactic antibiotics were used. The initial treatment was considered successful if the serum bilirubin dropped to less than 50% of the initial value, if not patients were treated as the alternative group. Every patient was seen in the outpatient clinic every 100 days until death. An estimate of the patients' quality of life was performed at every control visit by the investigators, ranking the patients' degree of immobilisation in five groups: normal, limited but no need for aid for basic activities, limited with need for aid, bedridden, and massive aid needed. The percentage of survival time the individual spent in the various selfcare ability groups was calculated from this information.

Table 2 *Types of operation performed in 19 patients with bile duct occlusion as a result of malignant disease*

| | |
|---|---|
| Cholecysto-jejunostomy | 13 |
| Choledocho-jejunostomy | 3 |
| Choledocho-duodenostomy | 3 |
| Supplementary gastro-enterostomy | 4 |

Patients gave informed consent and had the chance to change the treatment at any time during the course of their disease. As mentioned above two patients used this option. The consent was given before the ERCP: if the investigator judged that both endoprosthesis and operation was equally favourable for the patient, then randomisation was performed. Information about the malignant diagnosis was given after the investigation, and the patient had the opportunity to reconsider the decision. The protocol was approved by the regional ethical committee. For statistical evaluation the $\chi^2$ test, and the Mann-Whitney rank sum test for unpaired samples were used. Life tables were constructed according to the Kaplan-Meier method supplemented by the Gehan test.

## Results

### SURVIVAL

The median survival of the 25 patients randomised to endoscopic treatment was 84 days (range 3–498), whereas the 25 patients randomised to operative treatment survived median 100 days (10–642) after randomisation. The equivalent figures for the 30 patients treated endoscopically were 81 days (three to 564), and for the 19 patients who had a biliary bypass 108 days (20–642). Life table analysis (Figure) showed no significant differences in survival, neither according to randomisation nor ot actual treatment. None of the patients developed duodenal stenosis after the initial treatment. The number of deaths within 30 days after randomisation was five in the endoscopy group and six in the operative group. Of the 17 patients surviving for more than 200 days, 12 had histological verification of the malignant diagnosis. Two had their diagnosis verified because of typical macroscopic findings during operation, and in three cases the diagnosis rested on ERCP-findings and the clinical course.

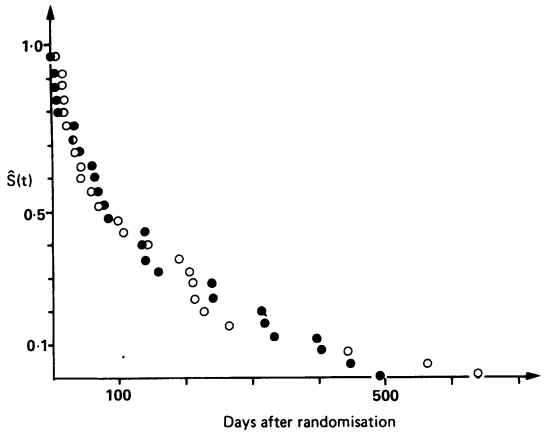


Figure *Lifetable (Kaplan-Meier) – 50 patients with jaundice caused by malignant occlusion randomised to treatment by operative by-pass (○) or endoscopic endoprosthesis (●), 25 patients in each group.*

## COMPLICATIONS

Among the patients randomised to endoscopic treatment seven (28%) developed cholangitis in the course of their disease. Additionally, one patient developed a subhepatic abscess and fistulation secondary to empyema of the gall bladder that contained stones. One patient was secondarily operated (choledochojejunostomy) and developed a subphrenic abscess postoperatively. Accordingly, nine patients randomised to endoscopic treatment developed severe infectious complications (36%). In the group randomised to operation four patients developed cholangitis (16%). One patient developed a subphrenic abscess postoperatively. A total of five patients randomised to operation (20%) had infectious complications. The difference was not statistically significant. Corresponding figures calculated according to the treatment actually applied were: endoprosthesis – 30%, operative bypass – 20%, and this difference too was not significant.

Table 3 *Cholangitis and type of endoscopic endoprosthesis in 33 patients with malignant biliary obstruction*

| | *Endoprosthesis* | |
|---|---|---|
| | *7 French* | *10 French* |
| Total (n) | 42 | 12 |
| Initial insertion | 29 | 4 |
| Replacement | 13 | 8 |
| Cholangitis (n) | 6 | 3 |
| Days with endoprosthesis | 3097 | 1009 |

## TREATMENT FAILURES

Three patients were successfully treated with endoprosthesis 13–53 days after operative shunting because of persistence or relapse of jaundice. One patient was operated because of persisting jaundice after primary endoscopic treatment.

## FUNCTIONING TIME OF ENDOPROSTHESES

In the 33 patients treated with endoprostheses (Table 3) during the course of their disease, the functioning time of the 42 7-F prostheses was from two days to more than 450 days. The 12 10-F prostheses functioned from 68 days to more than 234 days. Calculation of the median functioning time was not meaningful as the majority of the patients died with an indwelling and functioning endoprosthesis. The number of endoscopic sessions ranged from one to five in patients treated with endoprosthesis alone.

## RESOURCES

The 25 patients randomised to endoscopic treatment were hospitalised for a median of 26 days (range 3–210) which constituted median 26% (3–100) of their survival time. The corresponding figures for the 25 patients randomised to operation were 27 days (10–202), or 54% (2–100) of the survival time. These differences were not significantly different. When analysed according to the treatment applied, the difference was still not significant. In the endoscopy group seven patients were never discharged from the hospital compared with seven patients in the operated group.

Table 4 *Level of selfcare ability during the period from randomisation to death in 50 patients treated with either endoscopic endoprosthesis or operative bypass. Mean values, range*

| | | *Survival time (%)* | | | | |
|---|---|---|---|---|---|---|
| | *Patients (n)* | *Normal activity* | *Limited activity No aid* | *Limited activity Aid needed* | *Bedridden* | *Massive aid needed* |
| Endoscopy randomised | 25 | 21 (0–86) | 36 (0–95) | 8 (0–100) | 19 (0–100) | 16 (0–100) |
| Endoscopy treated | 30 | 19 (0–86) | 35 (0–95) | 10 (0–100) | 22 (0–100) | 14 (0–100) |
| Operation randomised | 25 | 20 (0–91) | 31 (0–80) | 14 (0–100) | 18 (0–100) | 17 (0–100) |
| Operation treated | 19 | 21 (0–91) | 31 (0–80) | 14 (0–100) | 14 (0–60) | 20 (0–100) |

QUALITY OF LIFE

An estimate of the patients quality of life is shown in Table 4. No significant differences were revealed, neither considering randomisation groups, nor when patients were grouped according to the treatment applied.

## Discussion

Scientifically based guidance is poor as to the method of choice for palliation of obstructive jaundice in non-resectable malignant disease. Two randomised studies have previously been published. Speer *et al*[6] showed that the endoscopic route for introduction of an endoprosthesis was significantly better than the percutaneous transhepatic route. As in the present investigation they evaluated their results according to the principle of intention of treat; the only reliable method if the question of a future routine procedure is to be answered. In a similar trial including younger patients (mean age 62 years) Bornman *et al*[5] found no differences in survival, complication rates or duration of hospitalisation between percutaneous transhepatic endoprosthesis and bypass surgery. Hospitalisation for terminal care, however, was not included in the analysis. The present investigation is the third randomised trial and the first study comparing endoscopic endoprosthesis to bypass surgery. The results are almost identical in the two treatment groups, whether evaluated according to the intention to treat principle, or according to the treatment applied. One might have expected a shorter hospitalisation time in the endoscopically treated patients, but the need for changing the stent in some patients and the slightly higher rate of cholangitis balanced the longer initial hospitalisation time in the operated group. Additionally, the large fraction of patients that were never discharged from hospital tended to blur any minor difference. We experienced no failures as to insertion of the endoprosthesis. Success rates of 89%[3,6] and 90%[1,7] have been reported. These figures indicate that the published results are from centres with considerable experience and might be valid for such centres only. Duodenal obstruction have occurred in 7·5%,[1] 13%, 14%, and 3%[6] in published data comparable with the present. None of our patients developed duodenal obstruction, and nor did any of the patients in other investigations on endoscopically placed stents.[3,4] The explanation might well be that patients with an incomplete duodenal obstruction have not been included in these studies as the obstruction prevented the initial ERCP. The survival time in the present study is compatible with those previously reported,[2-6] and probably reflected the spontaneous course of the malignant disease rather than treatment results.

We conclude that if the routine procedure for diagnosing the cause of obstructive jaundice in a hospital is ERCP and if the potential for stent insertion is present, then endoscopically introduced endoprosthesis seems to be as beneficial as operative treatment for palliation of malignant biliary obstruction.

## References

1 Hvibregtse K, Katon RM, Coene PP, Tytgat GNJ. Endoscopic palliative treatment in pancreatic cancer. *Gastrointest Endosc* 1986; **32:** 334–8.
2 La Ferla G, Murray WR. Carcinoma of the head of the pancreas: bypass surgery in unresectable disease. *Br J Surg* 1987; **74:** 212–3.
3 Siegel JH, Snady H. The significance of endoscopically placed prostheses in the management of biliary obstruction due to carcinoma of the pancreas: results of nonoperative decompression in 277 patients. *Am J Gastroenterol* 1986; **81:** 634–41.
4 Sonnenfeld T, Gabrielsson N, Granqvist S, Perbeck L. Nonresectable malignant bile duct obstruction. Surgical bypass or endoprosthesis? *Acta Chir Scand* 1986; **152:** 297–300.
5 Bornman PC, Harries-Jones EP, Tobias R, Van Stiegmann G, Terblanche J. Prospective controlled trial of transhepatic biliary endoprosthesis versus bypass surgery for incurable carcinoma of head of pancreas. *Lancet* 1986; i: 69–71.
6 Speer AG, Cotton PB, Russell RCG, *et al*. Randomised trial of endoscopic versus percutaneous stent insertion in malignant obstructive jaundice. *Lancet* 1987; ii: 57–62.
7 Matzen P, Andersen JR, Jensen AR. Endoscopic biliary drainage. *Ann Radiol* 1986; **29:** 151–2.