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Mumtaz K, Hamid S, Jafri W

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Endoscopic retrograde cholangiopancreatography with or without stenting in patients with pancreaticobiliary malignancy, prior to surgery.

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[Intervention Review]

Endoscopic retrograde cholangiopancreatography with or without stenting in patients with pancreaticobiliary malignancy, prior to surgery

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ABSTRACT

Background

Postoperative morbidity and mortality are high in patients undergoing pancreatico-duodenectomy for malignant pancreatico-biliary stricture. Different approaches have been tried to improve the outcomes, including pre-surgical biliary stenting with endoscopic retrograde cholangiopancreatography (ERCP).

Objectives

To assess the beneficial and harmful effects of biliary stenting via ERCP for pancreatico-biliary stricture confirmed or suspected to be malignant, prior to surgery.

Search methods

We identified trials through *The Cochrane Hepato-Biliary Group Controlled Trials Register* (October 2006), the *Cochrane Central Register of Controlled Trials (CENTRAL)* in *The Cochrane Library* (Issue 2, 2006), *MEDLINE* (1950 to October 2006), *EMBASE* (1980 to October 2006), and *Science Citation Index Expanded* (1945 to October 2006). We also searched the references in the published papers and wrote to stent producers.

Selection criteria

Randomised trials comparing ERCP with biliary stenting versus ERCP without biliary stenting for pancreatico-biliary malignancy prior to surgery.

Data collection and analysis

Two authors independently selected trials for inclusion and extracted data. The primary pre-surgical, post-surgical, and final outcome measures were mortality. The secondary outcomes were complications such as cholangitis, pancreatitis, bleeding, pancreatic fistula, intra-abdominal abscess, improvement in bilirubin, and quality of life. Dichotomous outcomes were reported as odds ratio (OR) with 95% confidence interval (CI) based on fixed- and random-effect models.

Endoscopic retrograde cholangiopancreatography with or without stenting in patients with pancreaticobiliary malignancy, prior to surgery (Review)

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Main results

We identified two randomised trials with 125 patients undergoing pancreatico-duodenectomy; 62 patients underwent ERCP with biliary stenting and 63 had ERCP without biliary stenting prior to surgery. Pre-surgical mortality was not significantly affected by stenting (OR 3.14, 95% CI 0.12 to 79.26), while there were significantly more complications in the stented group (OR 43.75, 95% CI 2.51 to 761.8). Stenting had no significant effect on the post-surgical mortality (OR 0.75, 95% CI 0.25 to 2.24). However, post-surgical complications were significantly less in the stented group (OR 0.45, 95% CI 0.22 to 0.91). Overall mortality (OR 0.81, 95% CI 0.17 to 3.89) and complications (OR 0.50, 95% CI 0.01 to 23.68) were not significantly different in the two groups.

Authors' conclusions

We could not find convincing evidence to support or refute endoscopic biliary stenting on the mortality in patients with pancreatico-biliary malignancy. Large randomised trials are needed to settle the question of pre-surgical biliary stenting.

PLAIN LANGUAGE SUMMARY

No evidence to support or refute endoscopic retrograde cholangiopancreatography (ERCP) with stenting in patients with malignant pancreaticobiliary diseases, awaiting surgery

Pancreatico-biliary malignancy includes cancers of pancreas, ampulla, duodenum, and cholangiocarcinoma. There is significant morbidity and mortality related to surgery in these patients. Studies have claimed the beneficial role of biliary decompression, which can be performed via endoscopic retrograde cholangiopancreatography (ERCP) with stent insertion pre-surgically. The review found that pre-surgical biliary stenting via ERCP did not improve the morbidity and mortality in patients with pancreatico-biliary malignancy. Further evidence about its efficiency is needed.

BACKGROUND

Biliary obstruction is a frequent presenting feature of pancreatico-biliary malignancy (Conio 2001). Corrective surgery is the therapy of choice, but the majority of patients with pancreatico-biliary malignancy are incurable at the time of diagnosis due to local or distant metastases (England 1996). About one third of the patients with pancreatico-biliary malignancy are amenable to surgical resection after detailed evaluation with trans-abdominal ultrasound, computerized tomographic scan, magnetic resonance cholangiopancreatography (MRCP), and endoscopic retrograde cholangiopancreatography (ERCP) (Burke 1998; Tsao 2000; Nakeeb 2002).

Surgical treatment is found to be the best available option for patients diagnosed at a stage where the tumour is confined to the biliary tract (Abu-Hamda 2004). Until recently, a postoperative morbidity of 30% to 65% and a postoperative mortality of 5% to 20% have often been reported (Lai 1992; Povoski 1999). Several authors have reported five year survival as high as 30% to 40% in the subset of patients who obtained negative histologic margins at operation (Sugiura 1994; Klempnauer 1997; Neuhaus 1999). There are two ways to approach patients who are fit for

surgical treatment: direct surgical approach or pre-surgical biliary decompression. The latter can be achieved either per-cutaneously, via per-cutaneous transhepatic cholangiography, or endoscopically, via ERCP along with stent placement (Stain 1992; Chamberlain 2000). In the latter case, a fibre optic scope is inserted through the mouth to where the bile duct has its outlet in the small intestine (duodenum). Through the scope injection of contrast can be performed so that x-ray pictures can be taken. Furthermore, stents can be inserted into the biliary tract via the ERCP scope.

Pre-surgical biliary drainage has been used in an attempt to reduce morbidity and mortality in these patients. There are multiple non-randomised studies addressing this question. They are often against the use of routine pre-surgical endoscopic or per-cutaneous stenting (Martignoni 2001; Sewnath 2001; Jagannath 2005). Several meta-analyses of observational studies have addressed this issue. Ali et al found that pre-surgical biliary drainage does not decrease morbidity and mortality (Aly 2001). Flamm et al reported more complications in pre-surgical biliary drainage patients (Flamm 2002). Despite this evidence, a great deal of controversy exists in this area and many centres routinely continue to practice

pre-surgical biliary decompression. We have been unable to identify systematic reviews or meta-analyses of randomised clinical trials on the issue. We decided to explore the utility of preoperative endoscopic biliary drainage in patients with pancreatico-biliary stricture confirmed or suspected to be malignant, prior to surgery, by examining all randomised trials in a Cochrane systematic review. We only included trials that compared ERCP with stenting versus ERCP without stenting. Clinical trials on non-endoscopic preoperative drainage will be considered in other systematic reviews.

OBJECTIVES

To evaluate the beneficial and harmful effects of biliary stenting via ERCP for pancreatico-biliary stricture confirmed or suspected to be malignant, prior to surgery.

METHODS

Criteria for considering studies for this review

Types of studies

We included all randomised clinical trials, which compared pre-surgical endoscopic biliary drainage with no pre-surgical drainage in patients awaiting surgical procedure for a pancreatico-biliary stricture confirmed or suspected to be malignant. We excluded historically controlled trials, cohort studies, and case series. We included trials from journal articles and abstracts in any language, irrespective of blinding and year of publication.

We were only able to identify two randomised trials. Therefore, as a post hoc decision we also decided to analyse the non-randomised studies that we identified. This decision was taken knowing that it may only be a select group of studies we were able to identify. Furthermore, we are also aware of the weak inferences one is able to draw based on the non-randomised design. In spite of the fact that our wish to include such non-randomised studies as a kind of 'quality control' on the results from the randomised trials, we stress the risky nature of such control.

Types of participants

Patients included

All patients, with peri-ampullary carcinoma (head of pancreas, ampullary, or duodenal) or cholangiocarcinoma, found to have a pancreatico-biliary stricture that is confirmed or suspected to be malignant and which is amenable to surgical correction.

Patients excluded

(1) Those with metastatic pancreatico-biliary disease.

(2) Those not fit for surgical correction procedure, such as pancreatico-duodenectomy, etc.
(3) Patients undergoing per-cutaneous trans-hepatic stenting.
(4) Those in whom ERCP was not possible (eg, previous Billroth II operation).

Types of interventions

ERCP with biliary stenting versus ERCP without biliary stenting. Trial on non-endoscopic preoperative drainage will not be included in the present review.

Types of outcome measures

Pre-surgical primary outcome

(1) Mortality.

Pre-surgical secondary outcomes

(1) Complication, such as
(i) cholangitis,
(ii) pancreatitis, and
(iii) bleeding.
(2) Duration between ERCP and stenting.
(3) Haemoglobin, serum albumin, and serum bilirubin concentrations.
(4) Quality of life.

Post-surgical primary outcome

(1) Mortality at maximal follow-up.

Post-surgical secondary outcomes

(1) Complications, such as
(i) wound infection,
(ii) intra-abdominal abscess,
(iii) pancreatic fistula, and
(iv) bleeding.
(2) Quality of life.
(3) Length of hospital stay.

Total outcomes

(1) Overall mortality.
(2) Overall complications.

Search methods for identification of studies

We searched *The Cochrane Hepato-Biliary Group Controlled Trials Register* (October 2006), the *Cochrane Central Register of Controlled Trials (CENTRAL)* in *The Cochrane Library* (Issue 2, 2006), *MEDLINE* (1950 to October 2006), *EMBASE* (1980 to October 2006), and *Science Citation Index Expanded* (1945 to October 2006) (Royle 2003). The search strategies used are given in Appendix 1.

We identified further trials by reading the reference lists of the identified studies. We wrote to the principal authors of the relevant trials and enquired about additional trials they might know of. We could not find unpublished trials from pharmaceutical companies involved in the production of stents and ERCP accessories.

Data collection and analysis

Two authors (KM and SH) extracted the pre-specified characteristics of the included trials independently. We sought the opinion of the third author (WJ) in case of disagreement. We contacted the authors of the trials if the data were not reported sufficiently in the publication. We performed meta-analyses following the instructions given in the *Cochrane Handbook for Systematic Reviews of Intervention* (Higgins 2006) and the *Cochrane Hepato-Biliary Group Module* (Gluud 2007).

Selection and data-extraction

We retrieved full articles for assessment and applied independently the inclusion criteria to all potential studies. From each trial we extracted age, gender, symptoms, biochemical laboratory parameters, including serum bilirubin, transaminases, alkaline phosphatases; type of the tumour such as perampullary carcinoma (pancreatic head tumour, duodenal tumour, ampullary tumour), or cholangiocarcinoma involving intra-hepatic, peri-hilar or distal bile duct along with pathologic diagnosis. We recorded ERCP findings with specifications of the biliary stent used, alongside with complications arising during ERCP and stenting such as pancreatitis, cholangitis, and bleed; the mortality related to the surgical intervention in both groups; and retrieved the data of surgical outcome in patients from both the groups. We extracted the data for our outcome measures listed above.

Two of the authors analysed all the included randomised trials independently and solved eventual disagreements by discussion. We listed all included and excluded trials, the latter with the reasons for exclusion.

We extracted the details of methods of endoscopic biliary drainage and the success rates prior to surgical intervention. We recorded the surgical interventions for the pancreatico-biliary malignancy treatment.

Methodological quality

Methodological quality was defined as the confidence that the design and report of the randomised trial would restrict bias in the comparison of the intervention (Moher 1998). According to empirical evidence (Schulz 1995; Moher 1998; Kjaergard 2001), we assessed the methodological quality of the trials based on the generation of the allocation sequence, allocation concealment, and blinding. These quality components were classified as follows:

- Generation of the allocation sequence: adequate (computer generated random numbers, table of random numbers, or similar); unclear (the trial was described as randomised, but the generation of the allocation sequence was not described); or

inadequate (quasi-randomised studies, which we primarily intended to exclude, but which will be analysed together with non-randomised studies).

- Allocation concealment: adequate (concealed up to the point of treatment by central randomisation, sealed envelopes, or similar); unclear (the allocation concealment was not described); or inadequate (open table of random numbers, or similar).

- Blinding: Due to the nature of the interventions, blinding of the patient, surgeon, endoscopist, and care-giver is not practicable. However, all trials could have employed blinded outcome assessment, and if so, we registered it.

We also registered whether the investigators have performed a sample-size calculation and used an intention-to-treat analysis.

Statistical methods

We used Review Manager 4.2 (RevMan 2003). We used the intention-to-treat principle when analysing the data, that is, patients with missing data were considered treatment failures. Binary outcomes were expressed as relative risks (RR) and continuous outcomes as weighted mean differences (WMD) both with 95% confidence intervals (CI). We estimated rare events (pre-surgical morbidity and mortality) by Peto odds ratio (Deeks 1998). For all analyses, we employed both random-effects (DerSimonian 1986) and fixed-effect (Demets 1987) models. We reported the fixed-effect results when there was no discrepancy between the two models (both showing a significant intervention effect and both showing no significant intervention effect). Discrepancy between the two methods occurs only when there is heterogeneity. Since the trials were small and of low methodological quality, we were unable to perform everything described in the protocol part of the review, like we could not estimate funnel plot asymmetry using regression analysis (Egger 1997) to examine potential bias. We explored heterogeneity using chi-squared test and we measured the quantity of heterogeneity by I^2 statistic (Higgins 2002). We will explore sources of heterogeneity in assessment of treatment response in meta-regression analyses and subgroup analyses if enough trials are identified. When the number of trials allow, we will perform the following subgroup analyses to determine the impact of trial characteristics:

- Methodological quality: comparison of intervention effect in trials with adequate compared to trials with inadequate or unclear generation of the allocation sequence, allocation concealment, and blinding.

- Publication status: comparison of the intervention effect in trials published as full papers compared to trials published as abstracts or letter.

- Co-interventions: comparison of the intervention effect in trials without co-interventions compared to trials with co-interventions.

- Funnel plot asymmetry: bias will be assessed by looking for funnel plot asymmetry. We will perform the Begg and Mazumdar (Begg 1994) adjusted rank correlation test and the Egger (Egger 1997) regression asymmetry test for bias.

RESULTS

Description of studies

In total, we identified 12 studies presented in 12 publications.

Included trials

Two randomised trials fulfilled the inclusion criteria of this review. There were 125 patients randomised (Lygidakis 1987; Lai 1994). Both trials investigated patients with malignant pancreatico-biliary stricture in which pancreatico-duodenectomy was done; one group with 62 patients underwent endoscopic biliary drainage prior to surgery, and the other group with 63 patients had a direct pancreatico-duodenectomy. Both trials had similar entry criteria of generally good quality, making it highly likely that all or almost all patients did, in fact, have malignant pancreatico-biliary stricture. The diagnostic modalities used for finding malignant diseases included ultrasonography, computerized tomography scan of abdomen, and ERCP in both the groups of patients. The distribution of the diagnosis in the two groups did not differ significantly and is presented in Table 1.

The main outcome measures of both trials were divided into following categories: pre-surgical outcomes and post-surgical outcomes (mortality and complications). There were 41 males and 21 females in the stent group, and 39 males and 24 females were in the control group, ie, ERCP without biliary stenting. The mean age of patients in the stented and the no stented (control) groups was 62.5 and 63 years, respectively. Mortality was the primary outcome in both the trials. Only Lai 1994 et al described the details of pre-surgical secondary outcome, such as cholangitis, pancreatitis, and bleeding. Stenting was successful in Lai 1994 et al in 37/43 patients; two patients after stent insertion refused surgery. Only 33/87 patients underwent resection of tumour; choledocho-enteric bypass was done in 25, and intra-hepatic biliary enteric bypass was performed in 19. The details of 10 patients who could not undergo tumour resection were not given. Endoscopic biliary prosthesis was inserted successfully in all patients in the other group (Lygidakis 1987).

Neither Lai 1994 nor Lygidakis 1987 provided information on the length of hospital stay after surgery.

Quality of life was not addressed in any of the two trials, neither as pre-surgical outcome nor as post-surgical outcome.

Excluded studies

The 10 excluded studies are listed with the reasons for exclusion in Characteristics of excluded studies table.

Risk of bias in included studies

The two identified trials had high risk of bias. Both trials were described as randomised trials. In the Lai 1994 trial, the allocation concealment was performed by drawing of a consecutively numbered envelope. There was no description on how the allocation sequence was generated. In the Lygidakis 1987 trial, the generation of allocation sequence and allocation concealment were not described.

The sample size was calculated by Lai 1994 only; 33/87 patients had resection of tumour and the trial was terminated as the analysis of available data showed that the estimated sample size was inadequate. In addition, the hospital mortality rates of the two groups were close and it was considered that inclusion of the remaining patients as planned would have added no further information.

None of the two trials used blinded outcome assessment.

Effects of interventions

Presurgical primary outcome

Mortality

Combining the results of the two randomised trials, 1/62 patients died in the stented group versus 0/63 patients in the no stented group (OR 3.14, 95% CI 0.12 to 79.3). This patient died due to bleeding after precut for placing the stent (Lai 1994).

Presurgical secondary outcomes

Overall complications

We found a total of 14/62 patients with complications in the stented group versus 0/63 patients in the no stented group (OR 43.75, 95% CI 2.51 to 761.8).

Cholangitis

Cholangitis was reported in 10/62 patients in the stented group versus 0/63 patients in the no stented group (OR 27.90, 95% CI 1.58 to 493.1).

Pancreatitis

None of the patients was reported to develop pancreatitis.

Bleeding

Bleeding occurred in 1/62 patients in the stented group versus 0/63 patients in the no stented group (OR 3.14, 95% CI 0.12 to 79.26). This patient died of uncontrollable bleeding (Lai 1994).

Duration between ERCP and stenting

The exact duration was not mentioned in any of the two trials, but it seems that stenting was performed during the index ERCP.

Haemoglobin, serum albumin, and serum bilirubin

There was no difference in the haemoglobin and serum albumin levels in the two trials. Lai 1994 reported number of patients with improvement of serum bilirubin in 25/43 patients in the stented group versus 0/44 patients in the no stented group (OR 122.68, 95% CI 7.09 to 2122.7). Lygidakis 1987 did not mention the number of patients with improvement in bilirubin. Lai 1994 provided data for serum bilirubin concentration.

Quality of life

None of the two trials addressed the quality of life issues.

Post-surgical primary outcome

Mortality at maximal follow-up

A total of 6/62 patients in the stented group versus 8/63 patients in the no stented group died (OR 0.75, 95% CI 0.25 to 2.24). The inter-trial heterogeneity (I^2) was 6.4%.

Post-surgical secondary outcomes

Overall complications

Complications were seen in 19/62 patients in the stented group versus 32/63 patients in the no stented group (OR 0.45, 95% CI 0.22 to 0.91). Lai 1994 et al did not report each complication separately.

Wound infection

Lygidakis 1987 reported the post-surgical wound infection in 1/19 patients in the stented group versus 4/19 patients in the no stented group (OR 0.21, 95% CI 0.02 to 2.07).

Intra-abdominal abscess

Intra-abdominal abscess was reported by Lygidakis 1987 in 1/19 patients in the stented group versus 3/19 patients in the no stented group (OR 0.30, 95% CI 0.03 to 3.14).

Pancreatic fistula

None of the two trials reported on pancreatic fistula.

Bleeding

Bleeding occurred in 0/19 patients in the stented group versus 1/19 in patients in the no stented group (OR 0.32, 95% CI 0.01 to 8.26) (Lygidakis 1987).

Quality of life

Neither of the two trials addressed it.

Length of hospital stay

It could not be calculated due to missing data.

Final outcome

Overall mortality

There were 15/125 deaths (OR 0.81, 95% CI 0.17 to 3.89); seven in the stented group versus eight in the no stented group. The inter-trial heterogeneity (I^2) was 24%.

All complications

There were 65/125 complications (OR 0.50, 95% CI 0.01 to 23.68, random-effects model) seen in the two groups; 33 in the stented group versus 32 in the no stented group. The inter-trial heterogeneity (I^2) was 94.4%.

Subgroup analyses

None of the subgroups of patients grouped according to diagnosis were statistically significant (Comparison 06; Table 1).

Post-hoc analysis of observational studies

We also evaluated the observational studies identified during our searches. As only two small randomised trials were available for analysis, we performed a post-hoc analysis of eight non-randomised studies comparing ERCP with stenting to ERCP without stenting (control group) in pancreatico-biliary malignancy awaiting surgery (Table 2).

Post-hoc analysis of eight non-randomised studies with 878 patients in the endoscopic stenting group and 635 patients in the ERCP without stenting group showed no pre-surgical mortality

in either group, but complications were not reported adequately. There were no statistically significant differences in post-surgical mortality (OR 0.91, 95% CI 0.51 to 1.60) and complications (OR 1.02, 95% CI, 0.80 to 1.29) among the stented and the control groups. The total mortality was not different in the two groups, but there were more overall complications in the stented group.

Pre-surgical primary outcome

Mortality

In a total of eight non-randomised studies, 1513 patients were enrolled and one peri-operative mortality was reported by Heslin 1998 in the stented group (OR 2.77, 95% CI 0.11 to 70.14). The death occurred in the ERCP with stenting group, though it was not related to the pre-surgically placed stent.

Pre-surgical secondary outcomes

Overall complications

Jagannath 2005 reported 5/74 cases of cholangitis and pancreatitis each (OR 11.16, 95% CI 0.61 to 205.6); 4/74 patients also developed post stenting bleed in the same study (OR 9.00, 95% CI 0.48 to 170.3). The remaining seven studies did not mention on these events. In none of the studies overall complications were discussed.

Improvement in serum bilirubin

Two non-randomised studies reported number of patients with improvement of serum bilirubin, ie, 225/547 patients in ERCP with stenting group (OR 338, 95% CI 46.63 to 2450). The remaining six studies have not mentioned the number of patients with improvement of serum bilirubin.

Quality of life

None of the non-randomised study looked into the quality of life issues.

Post-surgical secondary outcomes

Mortality at maximal follow-up

In eight non-randomised studies, there was no difference in mortality between the two groups (OR 0.91, 95% CI 0.51 to 1.60); 25/878 patients in ERCP with stenting group versus 25/635 patients in the ERCP without stenting group died. The inter-trial heterogeneity was negligible (I^2 0%).

Post-surgical secondary outcomes

Overall complications

In eight non-randomised studies, complications were equally divided in the two groups (OR 1.02, 95% CI 0.80 to 1.29); there were 312/878 complications in the ERCP with stenting group versus 208/632 in the ERCP without stenting group.

Wound infection

In eight non-randomised studies, wound infections were reported in 139/1513 patients (OR 1.57, 95%CI 1.06 to 2.32); 88/878 in the ERCP with stenting group versus 51/635 in the ERCP without stenting group.

Intra-abdominal abscess

Intra-abdominal abscess developed in a total of 135/1513 patients (OR 1.01, 95%CI 0.68 to 1.50); 83/878 patients in the ERCP with stenting group versus 52/635 patients in the ERCP without stenting group.

Pancreatic fistula

There were five non-randomised studies that reported pancreatic fistula in 49/985 patients (OR 1.00, 95%CI 0.54 to 1.86); 29/518 in the ERCP with stenting group versus 20/440 in the ERCP without stenting group.

Bleeding

Four studies reported bleeding in 80/752 patients (OR 0.57, 95%CI 0.34 to 0.96); 43/459 in the ERCP with stenting group versus 37/293 in the ERCP without stenting group.

Quality of life

Not addressed by any of the non-randomised trials.

Length of hospital stay

Three non-randomised studies reported length of stay, but there was not any uniformity in it.

Final outcomes

Overall mortality

There was similar mortality in the two groups (OR 0.94, 95% CI 0.54 to 1.66); 26/878 in the ERCP with stenting group versus 25/635 in the ERCP without stenting group.

All complications

There were 534/1513 complications seen in the two groups (OR 1.15, 95% CI 0.90 to 1.46); 326/878 in the stent group versus 208/635 in the ERCP without stenting group.

DISCUSSION

We found that ERCP with stenting has no significant harmful or beneficial effect on post-surgical mortality. There are too limited numbers of randomised trials with too sparse data to answer this question.

There has been a significant evolution in biliary drainage procedures over the last three decades in order to improve morbidity and mortality in patients with biliary obstruction awaiting corrective surgery. Earlier attempts at biliary drainage mainly related to the per-cutaneous route. The concept of biliary drainage in this context was proposed in 1970s, when [Takada 1976](#) and colleagues in a non-randomised study found that mortality fell from 28% to 8% when percutaneous biliary drainage was performed in patients with malignant jaundice before a surgical procedure. Further non-randomised studies by [Nakayam and Gobien 1984](#) also found pre-surgery percutaneous biliary drainage to be useful. In 1980s, [Denning 1981](#) and [Grundy 1984](#) again demonstrated effectiveness of percutaneous biliary drainage in non-randomised cohort studies ([Denning 1981](#); [Grundy 1984](#)). In order to confirm this finding, [Hatfield 1982](#), [McPherson 1984](#), and [Pitt 1985](#) conducted randomised trials and showed that, in fact, mortality

and morbidity were higher in percutaneous biliary drainage patients as compared to those who went to surgery directly.

In the late 1980s, the trend changed towards firstly internal percutaneous drainage and then towards endoscopic drainage. Internal percutaneous drainage had been reported to have complications of its own and, therefore, could not gain support ([Smith 1985](#)). On the other hand, many non-randomised studies and their meta-analyses were performed to determine the role of endoscopic biliary drainage. However, the majority of these studies could not demonstrate any reduction in morbidity and mortality in patients with malignant jaundice awaiting surgery.

We found only two randomised trials looking at the issue of pre-surgical endoscopic biliary stenting compared with no stenting in patients with pancreatobiliary malignancy awaiting surgery. Both trials were high-bias risk trials with poor methodology because of the unclear generation of randomisation sequence and lack of blinded outcome assessment and the unclear allocation concealment procedure in one of them. Pre-surgical mortality was reported in one patient related to ERCP after precut papillotomy prior to stent placement. The patient died due to exsanguinating bleeding. There were also a significant number of patients who developed cholangitis after ERCP ([Lai 1994](#)).

The two randomised trials show variable results when they are analysed separately. For example, in the study by [Lygidakis 1987](#), 38 patients were assigned to undergo pancreatoduodenectomy; 19 with prior endoscopic stent placement and 19 without stent placement. There were 16% complications and no deaths in the stented group as compared to 74% complications and 2 deaths in the no stented group. This is the only study that demonstrated a highly significant reduction in post-surgical morbidity or mortality between the groups with or without pre-surgical stent placement. On the other hand, the study by [Lai 1992](#) did not report any difference in post-surgical morbidity and mortality between the groups with or without stent placement. Only 23 patients underwent pancreatoduodenectomy in this trial and, though it is not possible to extract the data pertaining to complications, mortality was similar in the two groups.

When we analysed the results of two trials together, we found that the rate of overall post-surgical mortality was not significantly different in the groups that did or did not have pre-surgical stent placement, but that there was weak evidence of benefit of pre-surgical stenting in preventing post-surgical complications.

The results of non-randomised studies are consistent with the findings of the two small randomised trials in showing no significant benefit or harm related to prior endoscopic biliary drainage in patients with pancreatobiliary malignancy awaiting surgery ([Table 2](#)).

What happens to the patients intra-operatively after stent placement? There are different kinds of intra-operative problems when

endoprosthesis (stent) is placed before surgery; there is inflammatory response to stent which causes difficulty in dissection, increased blood loss, and anastomosis difficulty in fibrotic ducts. In a retrospective study of 212 patients, [Hodul 2003](#) reported longer operative time (mean 6.8 hours versus 6.5 hours) and increased intra-operative blood loss (mean: 1207 ml versus 1122 ml). Contrary to this, [Peskova 2004](#) in their 304 patients, did not find any significant difference in the surgical procedure duration and the peri-operative blood loss. The effects of stents on bile duct morphology and consequent technical problems encountered at surgery were studied in 31 consecutive patients undergoing pancreaticoduodenectomies by [Waghlikar 2003](#). Stented ducts were significantly narrower (luminal diameter 9 [7 to 12] mm compared to 17.5 [8 to 23] mm; $P = 0.0001$) and had thicker walls (2.3 [1.3 to 3.5] mm compared to 1.85 [0.8 to 2.2] mm; $P = 0.004$) compared to non-stented ones. On microscopy, stented ducts had advanced grades of sub-mucosal gland hypertrophy, fibrosis, and inflammatory cell infiltrate. The author has reported difficulty in bile duct dissection which was encountered more often in patients who had been stented than in those without stents, though the difference was not statistically significant.

Similarly [Karsten 1992](#) in their 30 patients studied the morphological changes of the extra-hepatic biliary tract during obstruction and the effects of biliary decompression by means of an endoprosthesis on the bile duct wall by light microscopy and scanning electron microscopy. They found that their patients with endoprosthesis were having severe inflammatory changes with considerable fibrosis and ulcerative lesions, resulting in markedly thickened ducts with lumina approximating the diameter of the stent. On the other hand, the patients with obstructed ducts without endoprosthesis had mild inflammation, a moderate degree of fibrosis, and local epithelial disintegration. Though the above evidence is not conclusive, it appears that there is likelihood that the local inflammation due to stent can cause operative problems, such as difficult dissection, increased per-operative bleeding and thickening of the bile duct with fibrosis causing anastomosis problems.

There is a need for a large randomised trial with good collaboration between gastroenterologists and surgeons to settle this very important issue of presurgical drainage in patients with pancre-

atic-biliary malignancy. Furthermore, whenever such trials are designed, they must address the issue of surgical problems with or without stenting.

AUTHORS' CONCLUSIONS

Implications for practice

On the basis of the only two randomised high-bias risk trials included in this systematic review, pre-surgical endoscopic biliary drainage in patients with malignant pancreaticobiliary stricture awaiting surgery cannot be supported or refuted.

Implications for research

Further properly designed randomised trials with sufficient statistical power, adequate generation of the allocation sequence and allocation concealment, and adequate blinding of outcome assessment should be initiated to evaluate the use of pre-surgical endoscopic biliary drainage in patients with malignant pancreaticobiliary stricture awaiting surgery. This clinical practice of endoscopic biliary drainage must be avoided until result from such trials can guide future practice. Furthermore, future trials should also provide data regarding additional, clinically relevant aspects, such as duration of hospital stay, frequency of post ERCP cholangitis, pancreatitis, individual post-surgical complications, and problems during the following surgery. None of the trials has dealt with the important issue of quality of life so it has to be incorporated in the future trials also. Future trials ought to be reported following the CONSORT Guidelines (<http://www.consort-statement.org>).

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Lai 1994

Methods	Randomised clinical trial. Generation of the allocation sequence: unclear, not reported Allocation concealment: adequate, by drawing of consecutively numbered envelopes, that contained assigned treatment: either early surgery or a trial of pre-surgical drainage before definitive surgery Blinding: not performed. Follow-up: no. Intention-to-treat: no. Sample size calculation: yes.	
Participants	Country: Hong Kong. Number of participants randomised: 87; 59 males and 28 females, mean age was 66 years Inclusion criteria: Patients with malignant obstructive jaundice due to carcinoma of pancreas (41), ampullary carcinoma (5), gall bladder carcinoma (7), common bile duct carcinoma (16), intrahepatic cholangiocarcinoma (5), metastatic tumor (3) Exclusion criteria: 37 patients were excluded during trial due to: refusal for surgery (8), high operative risk (11), disseminated disease (3), prior biliary drainage before referral (9), bleeding peptic ulcer (2), biliary sepsis (3), and previous gastrectomy (1) The following investigations were performed for diagnosing cancer in all the participants: ultrasound of abdomen, computerised tomography scan of abdomen, and ERCP	
Interventions	Participants were divided into two groups: Group 1: underwent ERCP with stenting (n = 43) prior to surgery Group 2: underwent ERCP without stenting (n = 44) prior to surgery ERCP was performed with a side view duodenoscope (Olympus JF-IT20 or TJF-10), under local pharyngeal anaesthesia supplemented by intravenous diazepam as per need. A straight endoprosthesis of appropriate length and largest possible size was inserted in patients randomised to pre-surgical stenting. When stent insertion was successful, drainage was performed for 2 weeks. If stenting failed, then the patient was subjected to early surgery	
Outcomes	Pre-surgical outcome measures: Complications such as cholangitis and bleed; effective biliary decompression Post-surgical outcome measures: Complications and mortality.	
Notes	Drop outs or withdrawals: 7 patients could not be stented, 2 patients successfully stented refused surgery after resolution of jaundice Resection of tumor was possible in only 33/85. Trial was terminated as analysis of available data showed that estimated sample size was inadequate	
Risk of bias		
Bias	Authors' judgement	Support for judgement

Lai 1994 (Continued)

Allocation concealment?	Low risk	A - Adequate
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Lygidakis 1987

Methods	Randomised clinical trial. Generation of allocation sequence: unclear. Allocation concealment: unclear. Double blinding: not performed. Follow-up: no. Intention to treat analysis: no. Sample size calculation: no.
Participants	Country: The Netherlands. Number of participants randomised: 38; 21 males and 17 females, mean age was 59 years Inclusion criteria: obstructive jaundice secondary to carcinoma of pancreatic head, serum bilirubin > 15 umol/litre, serum creatinine < 2 gm/litre and resectable tumor Exclusion criteria: non-resectable tumor. Following investigations were performed for diagnosing cancer in all the participants: ultrasound of abdomen, computed tomography of abdomen and ERCP; selective hepatic arteriography and late phase splenoportography was performed in 28 cases
Interventions	Participants were divided into two groups: Group 1 underwent ERCP with stenting (n = 19) prior to surgery; Group 2 underwent ERCP without stenting (n = 19) prior to surgery
Outcomes	Pre-surgical outcome measures: Decrease in bilirubin, coagulation profile improvement, complications Post-surgical outcome measures: Mortality and complications.
Notes	Two patients died in group 2 (ERCP without stenting), one due to uncontrolled sepsis and the other due to rupture of aneurysm of hepatic artery None died in group 1 (ERCP with stenting). Postsurgical complications were seen in 3 patients in group 1 and 14 in group 2 This study favours endoscopic pre-surgical stenting in patients who are awaiting pancreatic head surgery

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

ERCP = endoscopic retrograde cholangiopancreatography.

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Aly 2001	This is a meta-analysis of retrospective cohort studies. Patients undergoing both percutaneous and endoscopic biliary drainage were included
Heslin 1998	This is an analysis of a retrospective data. 39 patients had ERCP with biliary stenting and 35 had direct surgery after ERCP
Hodul 2003	This is an analysis of a retrospective data. 154 patients underwent ERCP with biliary stenting and 58 had direct surgery after ERCP
Jagannath 2005	This is an analysis of a retrospective data. 74 patients underwent ERCP with biliary drainage and 70 had direct surgery after ERCP
Marcus 1998	This is an analysis of a retrospective data. 22 patients underwent ERCP and biliary drainage and 30 had direct surgery after ERCP
Martignoni 2001	This is an analysis of a retrospective data. 85 patients underwent ERCP and biliary stenting and 158 had direct surgical after ERCP
Pisters 2001	This is an analysis of a retrospective hospital database. 98 patients underwent ERCP and biliary drainage and 93 had direct surgery after ERCP
Sewnath 2001	This is an analysis of a retrospective data. 232 patients underwent ERCP and biliary stenting and 58 had direct surgery after ERCP
Sohn 2000	This is an analysis of a retrospective data. Majority of patients underwent percutaneous biliary drainage and few had ERCP and biliary stenting
Srivastava 2001	This is an analysis of a retrospective data. 50 patients underwent ERCP and biliary stenting and 67 had direct surgery after ERCP

ERCP = endoscopic retrograde cholangiopancreatography

DATA AND ANALYSES

Comparison 1. Pre-surgical primary outcome

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Mortality	2	125	Odds Ratio (M-H, Fixed, 95% CI)	3.14 [0.12, 79.26]

Comparison 2. Pre-surgical secondary outcomes

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Overall complications	2	125	Odds Ratio (M-H, Fixed, 95% CI)	43.75 [2.51, 761.84]
2 Cholangitis	2	125	Odds Ratio (M-H, Fixed, 95% CI)	27.90 [1.58, 493.10]
3 Bleeding	2	125	Odds Ratio (M-H, Fixed, 95% CI)	3.14 [0.12, 79.26]
4 Number of patients with improvement of serum bilirubin	1	87	Odds Ratio (M-H, Fixed, 95% CI)	122.68 [7.09, 2122.66]
5 Serum bilirubin concentration before surgery	1	87	Mean Difference (IV, Fixed, 95% CI)	-24.89 [-34.56, -15.22]

Comparison 3. Post-surgical primary outcome

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Moratlity (death in 30 days or maximum follow-up	2	125	Odds Ratio (M-H, Fixed, 95% CI)	0.75 [0.25, 2.24]

Comparison 4. Post-surgical secondary outcomes

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Overall complications	2	125	Odds Ratio (M-H, Fixed, 95% CI)	0.45 [0.22, 0.91]
2 Wound infection	1	38	Odds Ratio (M-H, Fixed, 95% CI)	0.21 [0.02, 2.07]
3 Intra-abdominal abscess	1	38	Odds Ratio (M-H, Fixed, 95% CI)	0.30 [0.03, 3.14]
4 Bleeding/haemorrhage	1	38	Odds Ratio (M-H, Fixed, 95% CI)	0.32 [0.01, 8.26]

Comparison 5. Overall mortality and complications

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Overall mortality	2	125	Odds Ratio (M-H, Random, 95% CI)	0.81 [0.17, 3.89]
2 Overall complications	2	125	Odds Ratio (M-H, Random, 95% CI)	0.50 [0.01, 23.68]

Comparison 6. Diagnosis

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Pancreatic carcinoma	2	125	Odds Ratio (M-H, Fixed, 95% CI)	0.59 [0.28, 1.23]
2 Periapillary carcinoma	2	125	Odds Ratio (M-H, Fixed, 95% CI)	1.43 [0.45, 4.58]
3 Gallbladder carcinoma	1	87	Odds Ratio (M-H, Fixed, 95% CI)	1.40 [0.29, 6.67]
4 Common bile duct carcinoma	1	87	Odds Ratio (M-H, Fixed, 95% CI)	1.29 [0.51, 3.23]
5 Intrahepatic cholangiocarcinoma	1	87	Odds Ratio (M-H, Fixed, 95% CI)	1.58 [0.25, 9.93]
6 Metastatic tumour	1	87	Odds Ratio (M-H, Fixed, 95% CI)	2.10 [0.18, 24.02]

Analysis 1.1. Comparison 1 Pre-surgical primary outcome, Outcome 1 Mortality.

Review: Endoscopic retrograde cholangiopancreatography with or without stenting in patients with pancreaticobiliary malignancy, prior to surgery

Comparison: 1 Pre-surgical primary outcome

Outcome: 1 Mortality

Analysis 2.1. Comparison 2 Pre-surgical secondary outcomes, Outcome 1 Overall complications.

Review: Endoscopic retrograde cholangiopancreatography with or without stenting in patients with pancreaticobiliary malignancy, prior to surgery

Comparison: 2 Pre-surgical secondary outcomes

Outcome: 1 Overall complications

Analysis 2.2. Comparison 2 Pre-surgical secondary outcomes, Outcome 2 Cholangitis.

Review: Endoscopic retrograde cholangiopancreatography with or without stenting in patients with pancreaticobiliary malignancy, prior to surgery

Comparison: 2 Pre-surgical secondary outcomes

Outcome: 2 Cholangitis

Analysis 2.3. Comparison 2 Pre-surgical secondary outcomes, Outcome 3 Bleeding.

Review: Endoscopic retrograde cholangiopancreatography with or without stenting in patients with pancreaticobiliary malignancy, prior to surgery

Comparison: 2 Pre-surgical secondary outcomes

Outcome: 3 Bleeding

Analysis 2.4. Comparison 2 Pre-surgical secondary outcomes, Outcome 4 Number of patients with improvement of serum bilirubin.

Review: Endoscopic retrograde cholangiopancreatography with or without stenting in patients with pancreaticobiliary malignancy, prior to surgery

Comparison: 2 Pre-surgical secondary outcomes

Outcome: 4 Number of patients with improvement of serum bilirubin

Analysis 2.5. Comparison 2 Pre-surgical secondary outcomes, Outcome 5 Serum bilirubin concentration before surgery.

Review: Endoscopic retrograde cholangiopancreatography with or without stenting in patients with pancreaticobiliary malignancy, prior to surgery

Comparison: 2 Pre-surgical secondary outcomes

Outcome: 5 Serum bilirubin concentration before surgery

Analysis 3.1. Comparison 3 Post-surgical primary outcome, Outcome 1 Moratlity (death in 30 days or maximum follow-up).

Review: Endoscopic retrograde cholangiopancreatography with or without stenting in patients with pancreaticobiliary malignancy, prior to surgery

Comparison: 3 Post-surgical primary outcome

Outcome: 1 Moratlity (death in 30 days or maximum follow-up)

Analysis 4.1. Comparison 4 Post-surgical secondary outcomes, Outcome 1 Overall complications.

Review: Endoscopic retrograde cholangiopancreatography with or without stenting in patients with pancreaticobiliary malignancy, prior to surgery

Comparison: 4 Post-surgical secondary outcomes

Outcome: 1 Overall complications

Analysis 4.2. Comparison 4 Post-surgical secondary outcomes, Outcome 2 Wound infection.

Review: Endoscopic retrograde cholangiopancreatography with or without stenting in patients with pancreaticobiliary malignancy, prior to surgery

Comparison: 4 Post-surgical secondary outcomes

Outcome: 2 Wound infection

Analysis 4.3. Comparison 4 Post-surgical secondary outcomes, Outcome 3 Intra-abdominal abscess.

Review: Endoscopic retrograde cholangiopancreatography with or without stenting in patients with pancreaticobiliary malignancy, prior to surgery

Comparison: 4 Post-surgical secondary outcomes

Outcome: 3 Intra-abdominal abscess

Analysis 4.4. Comparison 4 Post-surgical secondary outcomes, Outcome 4 Bleeding/haemorrhage.

Review: Endoscopic retrograde cholangiopancreatography with or without stenting in patients with pancreaticobiliary malignancy, prior to surgery

Comparison: 4 Post-surgical secondary outcomes

Outcome: 4 Bleeding/haemorrhage

Analysis 5.1. Comparison 5 Overall mortality and complications, Outcome 1 Overall mortality.

Review: Endoscopic retrograde cholangiopancreatography with or without stenting in patients with pancreaticobiliary malignancy, prior to surgery

Comparison: 5 Overall mortality and complications

Outcome: 1 Overall mortality

Analysis 5.2. Comparison 5 Overall mortality and complications, Outcome 2 Overall complications.

Review: Endoscopic retrograde cholangiopancreatography with or without stenting in patients with pancreaticobiliary malignancy, prior to surgery

Comparison: 5 Overall mortality and complications

Outcome: 2 Overall complications

Analysis 6.1. Comparison 6 Diagnosis, Outcome 1 Pancreatic carcinoma.

Review: Endoscopic retrograde cholangiopancreatography with or without stenting in patients with pancreaticobiliary malignancy, prior to surgery

Comparison: 6 Diagnosis

Outcome: 1 Pancreatic carcinoma

Analysis 6.2. Comparison 6 Diagnosis, Outcome 2 Periampullary carcinoma.

Review: Endoscopic retrograde cholangiopancreatography with or without stenting in patients with pancreaticobiliary malignancy, prior to surgery

Comparison: 6 Diagnosis

Outcome: 2 Periampullary carcinoma

Analysis 6.3. Comparison 6 Diagnosis, Outcome 3 Gallbladder carcinoma.

Review: Endoscopic retrograde cholangiopancreatography with or without stenting in patients with pancreaticobiliary malignancy, prior to surgery

Comparison: 6 Diagnosis

Outcome: 3 Gallbladder carcinoma

Analysis 6.4. Comparison 6 Diagnosis, Outcome 4 Common bile duct carcinoma.

Review: Endoscopic retrograde cholangiopancreatography with or without stenting in patients with pancreaticobiliary malignancy, prior to surgery

Comparison: 6 Diagnosis

Outcome: 4 Common bile duct carcinoma

Analysis 6.5. Comparison 6 Diagnosis, Outcome 5 Intrahepatic cholangiocarcinoma.

Review: Endoscopic retrograde cholangiopancreatography with or without stenting in patients with pancreaticobiliary malignancy, prior to surgery

Comparison: 6 Diagnosis

Outcome: 5 Intrahepatic cholangiocarcinoma

Analysis 6.6. Comparison 6 Diagnosis, Outcome 6 Metastatic tumour.

Review: Endoscopic retrograde cholangiopancreatography with or without stenting in patients with pancreaticobiliary malignancy, prior to surgery

Comparison: 6 Diagnosis

Outcome: 6 Metastatic tumour

ADDITIONAL TABLES

Table 1. Distribution of the different pancreatobiliary malignancies in the two groups

Diagnosis	Stented group	No stented group	(OR; 95% CI)
Pancreatic carcinoma	31/62	39/63	0.59; 0.28 to 1.23
Periampullary carcinoma	08/62	06/63	1.43; 0.45 to 4.58
Gallbladder carcinoma	04/43	03/44	1.40; 0.29 to 6.67
Common bile duct carcinoma	14/43	12/44	1.29; 0.51 to 3.23
Intrahepatic cholangiocarcinoma	03/43	02/44	1.58; 0.25 to 9.93
Metastatic tumour	02/43	01/44	2.10; 0.18 to 24.02

Table 2. Post-hoc analysis of non-randomised studies

Outcome Measures	Studies	Patients	Stented group	No stented group	(OR; 95% CI)
Presurgical primary outcome (mortality)	08	1513	01/878	00/635	2.77; 0.11 to 70.14
Post-surgical primary outcome (mortality)	08	1513	25/878	25/635	0.91; 0.51 to 1.60
Post-surgical secondary outcomes					
Overall complications	08	1513	312/878	208/635	1.02; 0.80 to 1.29
Wound infections	08	1513	88/878	51/635	1.57; 1.06 to 2.32
Intrabdominal abscess	08	1513	83/878	52/635	1.01; 0.68 to 1.50
Pancreatic fistula	05	958	29/518	20/440	1.00; 0.54 to 1.86
Haemorrhage	04	752	43/459	37/293	0.57; 0.34 to 0.96
Total outcomes					
Total mortality	08	1513	26/878	25/635	0.94; 0.54 to 1.66

Table 2. Post-hoc analysis of non-randomised studies (Continued)

Total complications	08	1513	326/878	208/635	1.15; 0.90 to 1.46
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APPENDICES

Appendix I. Search strategies

Database	Time span	Search strategy
The Cochrane Hepato-Biliary Group Controlled Trials Register	October 2006.	(ERCP OR 'endoscopic retrograde cholangiopancreatography' OR 'endoscopic retrograde cholangiopancreatography') AND (pancreaticobiliary OR pancreatobiliary OR (pancreat* AND biliary)) AND stricture*
Cochrane Central Register of Controlled Trials (CENTRAL) in The Cochrane Library	Issue 2 of 2006.	#1 MeSH descriptor Cholangiopancreatography, Endoscopic Retrograde explode all trees in MeSH products #2 ERCP or endoscopic retrograde cholangiopancreat*graphy in All Fields in all products #3 (#1 OR #2) #4 pancreat*biliary and stricture* in All Fields in all products #5 (#3 AND #4)
MEDLINE (WinSPIRS 5.0)	1950 to October 2006.	#1 explode "Cholangiopancreatography-Endoscopic-Retrograde"/ all subheadings #2 ERCP or endoscopic retrograde cholangiopancreat*graphy #3 #1 or #2 #4 pancreat*biliary and stricture* #5 #3 and #4 #6 random* or blind* or placebo* or meta-analysis #7 #5 and #6
EMBASE (WinSPIRS 5.0)	1980 to October 2006.	#1 explode "endoscopic-retrograde-cholangiopancreatography"/ all subheadings #2 ERCP or endoscopic retrograde cholangiopancreat*graphy #3 #1 or #2 #4 pancreat*biliary and stricture* #5 #3 and #4 #6 random* or blind* or placebo* or meta-analysis #7 #5 and #6

(Continued)

Science Citation Index EXPANDED (http://portal.isiknowledge.com/portal.cgi?DestApp=WOS&Func=Frame)	1945 to October 2006.	#1 TS=(ERCP or endoscopic retrograde cholangiopancreat*graphy) #2 TS=(pancreat*biliary and stricture*) #3 #2 AND #1 #4 TS=(random* or blind* or placebo* or meta-analysis) #5 #4 AND #3
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WHAT'S NEW

Last assessed as up-to-date: 22 May 2007.

Date	Event	Description
11 November 2008	Amended	Converted to new review format.

CONTRIBUTIONS OF AUTHORS

Khalid Mumtaz drafted the protocol and performed the literature searches, data extraction, and drafted the final review.

Saeed Hamid revised the protocol and helped in literature searches, reviewed the trials, extracted data, and helped in writing the final review.

Wasim Jafri helped in reviewing the studies and revising the final protocol and review.

DECLARATIONS OF INTEREST

None known.

SOURCES OF SUPPORT

Internal sources

- The Cochrane Hepato-Biliary Group, Copenhagen, Denmark.

External sources

- Aga Khan University Hospital, Department of Medicine, Karachi, Pakistan.

INDEX TERMS

Medical Subject Headings (MeSH)

*Cholangiopancreatography, Endoscopic Retrograde [adverse effects]; *Pancreaticoduodenectomy; *Stents [adverse effects]; Carcinoma, Pancreatic Ductal [diagnostic imaging; mortality; *surgery]; Cholestasis, Extrahepatic [diagnostic imaging; *surgery]; Constriction, Pathologic [diagnostic imaging; mortality; surgery]; Pancreatic Neoplasms [diagnostic imaging; mortality; *surgery]; Randomized Controlled Trials as Topic

MeSH check words

Humans