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REVIEW ARTICLE

Meta-analysis of randomized controlled trials on the effectiveness of somatostatin analogues for pancreatic surgery: a Cochrane review

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Abstract

Background: The use of synthetic analogues of somatostatin following pancreatic surgery is controversial. The aim of this meta-analysis is to determine whether prophylactic somatostatin analogues (SAs) should be used routinely in pancreatic surgery.

Methods: Randomized controlled trials were identified from the Cochrane Library Trials Register, MEDLINE, EMBASE, Science Citation Index Expanded and reference lists. Data were extracted from these trials by two independent reviewers. The risk ratio (RR), mean difference (MD) and standardized mean difference (SMD) were calculated with 95% confidence intervals (95% CIs) based on intention-to-treat or available case analysis.

Results: Seventeen trials involving 2143 patients were identified. The overall number of patients with postoperative complications was lower in the SA group (RR 0.71, 95% CI 0.62–0.82), but there was no difference between the groups in perioperative mortality (RR 1.04, 95% CI 0.68–1.59), re-operation rate (RR 1.15, 95% CI 0.56–2.36) or hospital stay (MD –1.04 days, 95% CI –2.54 to 0.46). The incidence of pancreatic fistula was lower in the SA group (RR 0.64, 95% CI 0.53–0.78). The proportion of these fistulas that were clinically significant is not clear. Analysis of results of trials that clearly distinguished clinically significant fistulas revealed no difference between the two groups (RR 0.69, 95% CI 0.34–1.41). Subgroup analysis revealed a shorter hospital stay in the SA group than among controls for patients with malignant aetiology (MD –7.57 days, 95% CI –11.29 to –3.84).

Conclusions: Somatostatin analogues reduce perioperative complications but do not reduce perioperative mortality. However, they do shorten hospital stay in patients undergoing pancreatic surgery for malignancy. Further adequately powered trials of low risk of bias are necessary.

Keywords

pancreatic resection, somatostatin, octreotide, pancreatic fistula, systematic review

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Introduction

Pancreatic resection is performed to treat pancreatic diseases including malignancy and chronic pancreatitis. In most series, the incidence of complications following pancreatic surgery varies from 30% to 60% and the mortality rate is <5%.[1–3] The major complication following pancreatic resection is postoperative pancreatic leak or fistula. Recent reviews have described the incidence of pancreatic leak or fistula as 37%.[4] Various methods have been

suggested to decrease the incidence of pancreatic complications, but the most common approach has involved the use of somatostatin or its synthetic analogues. Somatostatin and its analogues decrease the exocrine and endocrine pancreatic secretions by binding to the somatostatin receptors on the exocrine and endocrine cells, and decrease the secretions of these cells possibly by acting as dephosphorylators and by altering the calcium transport across the cell membranes.[5] Decreasing the volume of pancreatic secretion may decrease the incidence of pancreatic leak or fistula.[6] However, the use of somatostatin and its analogues is controversial and whereas some randomized controlled trials (RCTs) and systematic reviews recommend[7,8] prophylactic somatostatin analogues (SAs) in pancreatic resections, others do not.[9,10] These treatments may potentially decrease morbidity and mortality following pancreatic surgery, but it is possible that they may have no therapeutic benefit and may be associated with negative outcomes. A systematic review was carried out to determine whether prophylactic SAs should be used routinely in pancreatic surgery.

Materials and methods

Identification of trials and data extraction

Only RCTs of parallel design, irrespective of blinding, sample size, publication status (i.e. whether published as full text or presented only as an abstract at a conference) and language, were included. Quasi-randomized trials and other study designs were excluded. Only trials involving patients undergoing a pancreatic surgical procedure (pancreatic resection, pancreatic duct drainage procedures or cyst drainage procedures) for any pancreatic disease were considered. Only trials involving the administration of perioperative somatostatin (or an analogue of this hormone, such as octreotide) against a comparator of placebo or no intervention were considered. The Cochrane Upper Gastrointestinal and Pancreatic Diseases Group Controlled Trials Register,[11] the Cochrane Central Register of Controlled Trials (CENTRAL) in the Cochrane Library, MEDLINE, EMBASE and Science Citation Index Expanded[12] were searched for trials published up to November 2009. The references of the identified trials were also searched to identify further relevant trials.

Two reviewers (RSK and KSG) independently identified the trials for inclusion. In addition, the population characteristics (such as sex, age, proportion of pancreaticoduodenectomies, disease aetiology) and the interventions used in each trial were extracted. The methodological qualities of the trials were assessed independently, without masking the trial names. Any unclear or missing information was obtained by contacting the authors of the individual trials. If there was any doubt as to whether trials had shared the same patients – completely or partially (by identifying common authors and centres) – the authors of the trials were contacted to establish whether the trial report had been duplicated. Any differences in opinion were resolved through discussion.

Outcomes

Data for the following outcomes were extracted: postoperative mortality; re-operation; postoperative complications (anastomotic leak, pancreatic fistula, pancreatitis, sepsis, renal failure, bleeding, abdominal collections, infected abdominal collections, delayed gastric emptying, pulmonary complications, shock, number of complications, number of patients with any complications); drug-related complications (treatment withdrawal, number with adverse effects resulting from treatment), and hospital stay (total hospital stay, intensive care unit [ICU] stay). Pancreatic fistula has been graded as A, B and C by consensus amongst surgeons.[13] Any pancreatic fistula, however defined, was included by the authors as one of the outcomes. Clinically significant pancreatic fistula was included as another outcome, for which only trials which featured data on grades B and C as distinct from grade A (not clinically significant) were included.

Subgroup analyses of trials with low risk of bias vs. those with high risk of bias, different interventions (somatostatin and octreotide), different aetiologies (malignancy and chronic pancreatitis), different procedures (pancreatoduodenectomy, distal pancreatectomy and pancreatic drainage procedures) and different methods of management of the pancreatic stump (pancreatogastrostomy and pancreatojejunostomy) were planned.

Assessment of risk of bias

Risk of bias can result in the incorrect estimation of the effectiveness of an intervention.[14–17] The risk of bias in the trials was assessed in different domains, including sequence generation, allocation concealment, blinding (of participants, personnel and outcome assessors), incomplete outcome data, selective outcome reporting and other sources of bias, such as baseline imbalance, early stopping bias, academic bias and sources of funding bias.[18,19] Trials which were classified as being at low risk of bias in sequence generation, allocation concealment, blinding, incomplete data and selective outcome reporting were considered as low bias-risk trials.

Statistical methods

Meta-analyses were performed according to the recommendations of the Cochrane Collaboration[18] using the software package Revman 5.0 (Nordic Cochrane Centre, Cochrane Collaboration, Copenhagen, Denmark). For dichotomous outcomes, the risk ratio (RR) was calculated with a 95% confidence interval (CI). For continuous outcomes, the mean difference (MD) or standardized mean difference (SMD) was calculated with its 95% CI. A random-effects model[20] and a fixed-effect model[21] were used. In cases of discrepancy between the two models, both the results were reported; otherwise only the results from the fixed-effect model were reported. The analysis was performed on an 'intention-to-treat' basis[22] whenever possible, but, in order to allow for dropouts and withdrawals between randomization and intervention or control, the 'available case analysis'[18]

was adopted. The degree of heterogeneity was measured by chi-squared test with significance set at a *P*-value of 0.10, and the quantity of heterogeneity was measured by I^2.[23] An I^2 value >30% was considered to represent statistically significant heterogeneity. Standard deviation was imputed from standard error or from *P*-values if it was not given directly in the trial reports, according to Cochrane Collaboration guidelines.[18] The chi-squared test for subgroup differences set at a *P*-value of 0.05 was performed to identify any subgroup differences.

A funnel plot was used to explore bias.[24,25] Asymmetry in the funnel plot of trial size against treatment effect was used to assess the risk of bias. The linear regression approach was performed to determine the funnel plot asymmetry.[24]

Results

Description of studies

A total of 742 references were identified through electronic searches of the Cochrane Upper Gastrointestinal and Pancreatic Diseases Group Controlled Trials Register[11] and the Cochrane Central Register of Controlled Trials (CENTRAL) in the Cochrane Library (n = 74), MEDLINE (n = 390), EMBASE (n = 176), Science Citation Index Expanded (n = 102). A total of 192 duplicates and 505 clearly irrelevant references identified by reading the abstracts were excluded (Fig. 1). Forty-five references were retrieved for further assessment. No references were identified through scanning the reference lists of the RCTs identified. Of the 45 references, 16 were excluded because they referred to quasi-randomized studies, prospective non-randomized studies or comments that did not contain data from an RCT. Of the remaining 29 references, 12 were multiple reports, which resulted in the identification of a total of 17 RCT reports which fulfilled the inclusion criteria. All 17 trials were completed trials and were able to provide data for the analyses. Important details of the included trials are shown in Table 1. Only two trials were considered to be at low risk of bias.[26,27]

Participants

The 17 trials included 2143 patients (Table 1). A total of 237 patients were involved in six trials comparing somatostatin vs. control[27–32] and 1564 patients were involved in 10 trials comparing octreotide vs. control.[7,8,10,27,33–38] The remaining patients were involved in one trial comparing vapreotide vs. control.[9] Overall, 1457 patients underwent pancreatoduodenectomy, 1143 patients had malignancy and 587 had chronic pancreatitis in the trials that reported these characteristics. The mean age of the individuals in the trials varied between 43 years and 65 years. The mean proportion of females varied between 15% and 48%. There was no difference in the characteristics of patients in the intervention and control groups in any of the trials that reported these baseline characteristics.

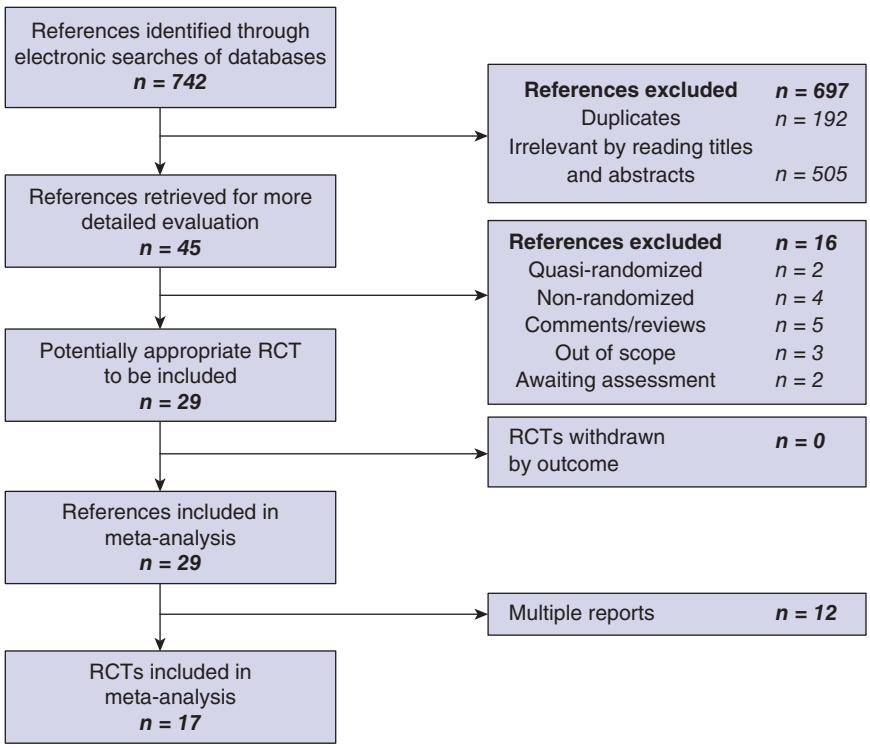


Figure 1 Flow chart showing the search strategy used to identify trials. RCT, randomized controlled trial

Table 1 Important characteristics of included studies. All trials are randomized controlled trials (parallel design)

Author(s), year	Sample size, *n*	Mean age, years	Intervention	Dose	Aetiology, *n*		Pancreatoduodenectomy, *n*	Follow-up	Pancreatic fistula definition
					Malignancy	Chronic pancreatitis			
Beguiristain *et al.*, 1995[31]	35	59.4	Somatostatin	4.5 mg/day continuous infusion for 7 days	30 (85.7%)	3 (8.6%)	35 (100%)	Not reported	≥10 ml fluid with amylase concentration of >5 somogyi units
Briceno Delgado *et al.*, 1998[38]	34	52.5	Octreotide	0.1 mg s.c. t.i.d. for 7 days	28 (82.4%)	5 (14.7%)		Not reported	≥50 ml/day ARF for >2 weeks
Buccoliero *et al.*, 1992[32]	16	58.2	Somatostatin	250 mcg/h infusion for 6 days	NS	NS	16 (100%)	Not reported	Not reported
Buchler *et al.*, 1992[34]	246	52	Octreotide	100 mcg s.c. t.i.d. for 7 days	111 (45.1%)	112 (45.5%)	200 (81.3%)	90 days	Amylase and lipase >3 times serum concentration, >3 days postop, >10 ml/h
Friess *et al.*, 1995[8]	247	48	Octreotide	100 mcg s.c. t.i.d. for 7 days	0	247 (100%)	124 (50.2%)	90 days	Amylase and lipase >3 times serum level, >3 days postop, >10 ml/h
Gouillat *et al.*, 2001[27]	75	60.2	Somatostatin	6 mg/day infusion for 7 days	61 (81.3%)	4 (5.3%)	75 (100%)	Not reported	>100 ml/day ARF (>5 times normal serum amylase), after day 3, persisting after day 12, or in association with ↑temp or symptoms requiring surgery, drainage or intensive care
Hesse *et al.*, 2005[33]	105	59.5	Octreotide	0.1 mg s.c. t.i.d. for 7 days	71 (67.6%)	26 (24.8%)	80 (76.2%)	Not reported	>100 ml/day of ARF (>5 times normal serum amylase), after day 3, persisting after day 7, with ↑temp and preseptic conditions
Klempa *et al.*, 1991[30]	24	56.5	Somatostatin	250 mcg/h i.v. for 6 days	24 (100%)	0	24 (100%)	Not reported	Not reported
Kollmar *et al.*, 2008[26]	67	62.8	Octreotide	100 mcg s.c. t.i.d. for 7 days	33 (49.3%)	16 (23.9%)	67 (100%)	Not reported	Any volume after day 3 with amylase content >3 times normal serum amylase
Lange *et al.*, 1992[35]	21	46.5	Octreotide	s.c. 8-hourly 50 mcg on day 1, 100 mcg on day 2, 150 mcg until 3 days after drain removal	21 (100%)	0	NS	Not reported	Recurrent pancreatic drainage
Montorsi *et al.*, 1995[36]	218	58.2	Octreotide	100 mcg s.c. t.i.d. for 7 days	139 (63.8%)	18 (8.3%)	143 (65.6%)	Not reported	>10 ml/day ARF (>3 times normal serum amylase) after day 3
Pederzoli *et al.*, 1994[37]	252	53.1	Octreotide	100 mcg s.c. t.i.d. for 7 days	162 (64.3%)	90 (35.7%)	105 (41.7%)	Until discharge	>10 ml/day for >4 days after day 4, amylase >3 times normal
Sarr, 2003[9]	275	62	Vapreotide	0.6 mg s.c. b.i.d for 7 days	138 (50.2%)	0	108 (39.3%)	30 days	>30 ml/day ≥day 5, amylase or lipase >5 times normal
Shan *et al.*, 2005[28]	54	67	Somatostatin	250 mcg/h i.v. for 7 days	45 (83.3%)	0	54 (100%)	60 days	>10 ml/day ARF (amylase >3 times serum level), for >7 days
Suc *et al.*, 2004[7]	230	56.5	Octreotide	100 mcg s.c. t.i.d. for 10 days	154 (67%)	30 (13%)	177 (77%)	Not reported	Any volume with amylase >4 times normal serum value for 3 days or clinical/radiological anastomotic leak
Tulassay *et al.*, 1993[29]	33	43	Somatostatin	125 mcg/h infusion for 48 h	0	14 (42.4%)	0	Not reported	Not reported
Yeo *et al.*, 2000[10]	211	64.7	Octreotide	100 mcg s.c. t.i.d. for 7 days	147 (69.7%)	22 (10.4%)	211 (100%)	Not reported	>50 ml/day ARF (>3 times normal serum value) on or after day 10 or radiological pancreatic anastomosis disruption

NS, not specified; s.c. subcutaneous; ARF, amylase rich fluid

Somatostatin analogues vs. no intervention

Primary outcomes

There was no difference between the two groups in either perioperative mortality (RR 1.04, 95% CI 0.68–1.59) or re-operation rates (RR 1.15, 95% CI 0.56–2.36) (Fig. 2).

Secondary outcomes

Postoperative complications There were statistically significant lower incidences of pancreatic fistula (RR 0.64, 95% CI 0.53–0.78) (Fig. 3) and sepsis (RR 0.47, 95% CI 0.23–0.97) in the SA group than in the control group. Likewise, decreases in the numbers of complications (rate ratio 0.72, 95% CI 0.61–0.85) and of patients with any complication (RR 0.71, 95% CI 0.62–0.82) in the SA group over the control group were statistically significant (Fig. 4). There were no differences between the groups in incidences of anastomotic leak rates (RR 0.81, 95% CI 0.51–1.27), clinically significant pancreatic fistulas (RR 0.69, 95% CI 0.34–1.41) (Fig. 3), postoperative pancreatitis (RR 0.63, 95% CI 0.32–1.22), renal failure (RR 0.67, 95% CI 0.25–1.77), bleeding (RR 1.00, 95% CI 0.70–1.44), abdominal collections (RR 0.79, 95% CI 0.58–1.09), infected abdominal collections (RR 0.97, 95% CI 0.68–1.38), delayed gastric emptying (RR 0.81, 95% CI 0.52–1.28), pulmonary complications (RR 0.86, 95% CI 0.54–1.36) or shock (RR 0.92, 95% CI 0.41–2.05).

Drug-related complications There was no difference in treatment withdrawal (RR 1.55, 95% CI 0.56–4.33) or number of patients with adverse effects caused by treatment (RR 1.27, 95% CI 0.95–1.71) between the groups.

Hospital stay There was no difference in the duration of hospital stay (MD −1.04, 95% CI −2.54 to 0.46) or ICU stay (MD 0.90, 95% CI −1.76 to 3.56) between the groups.

Subgroup analysis

The following planned subgroup analyses were performed: different interventions (somatostatin and octreotide); different aetiologies (malignancy and chronic pancreatitis), and different procedures (pancreatoduodenectomy). A planned subgroup analysis of other procedures (distal pancreatectomy and pancreatic drainage procedures), and the different methods of management of pancreatic stump (pancreatogastrostomy and pancreatojejunostomy) could not be performed as the outcome data for the different subgroups were not available from the trials.

Subgroup analysis based on the risk of bias in the trials could not be performed as only two trials were at low risk of bias.[26,27] There was no difference in any of the primary outcomes between intervention and control groups in the different subgroups.

The secondary outcomes for which there were statistically significant differences between the two groups are described below.

Stratified by intervention

Somatostatin vs. no intervention The decrease in incidences of pancreatic fistula (RR 0.35, 95% CI 0.14–0.88), reduced number of patients with any complications (RR 0.50, 95% CI 0.27–0.93) and reduction in duration of hospital stay (MD −6.79 days, 95% CI −10.65 to −2.94; mean hospital stay 22.1 days in the somatostatin group vs. 27.6 days in controls) in the somatostatin group compared with the control group were statistically significant. There was no difference between the two groups in any of the other outcomes.

Octreotide vs. no intervention The lower incidences of pancreatic fistula (RR 0.61, 95% CI 0.49–0.77) and abdominal collections (RR 0.61, 95% CI 0.42–0.89), lower number of complications (rate ratio 0.66, 95% CI 0.55–0.80) and lower number of patients with any complications (RR 0.68, 95% CI 0.58–0.80) in the octreotide group compared with the control group were statistically significant. There was no difference in any of the other outcomes between the two groups.

The only outcome in which the test for subgroup differences was positive was that of hospital stay ($P = 0.001$).

Stratified by aetiologies

Malignancy Decreases in the incidence of pancreatic fistula (RR 0.52, 95% CI 0.35–0.77) and sepsis (RR 0.28, 95% CI 0.08–0.97), number of complications (rate ratio 0.61, 95% CI 0.48–0.77) and number of patients with complications (RR 0.60, 95% CI 0.45–0.79) in the SA group over the control group were statistically significant. The decrease in the duration of hospital stay in the SA group over that in the control group (MD −7.57 days, 95% CI −11.29 to −3.84; mean hospital stay 25.0 days in the SA group vs. 32.1 days in controls) was statistically significant (Fig. 5). There was no difference in any of the other outcomes between the two groups.

Chronic pancreatitis Reductions in the incidence of pancreatic fistula (RR 0.40, 95% CI 0.24–0.64) and number of patients with any complications (RR 0.54, 95% CI 0.38–0.77) in the intervention group compared with the control group were statistically significant. There was no difference in any of the other outcomes between the two groups.

The only outcome in which the test for subgroup differences was positive was hospital stay ($P = 0.03$).

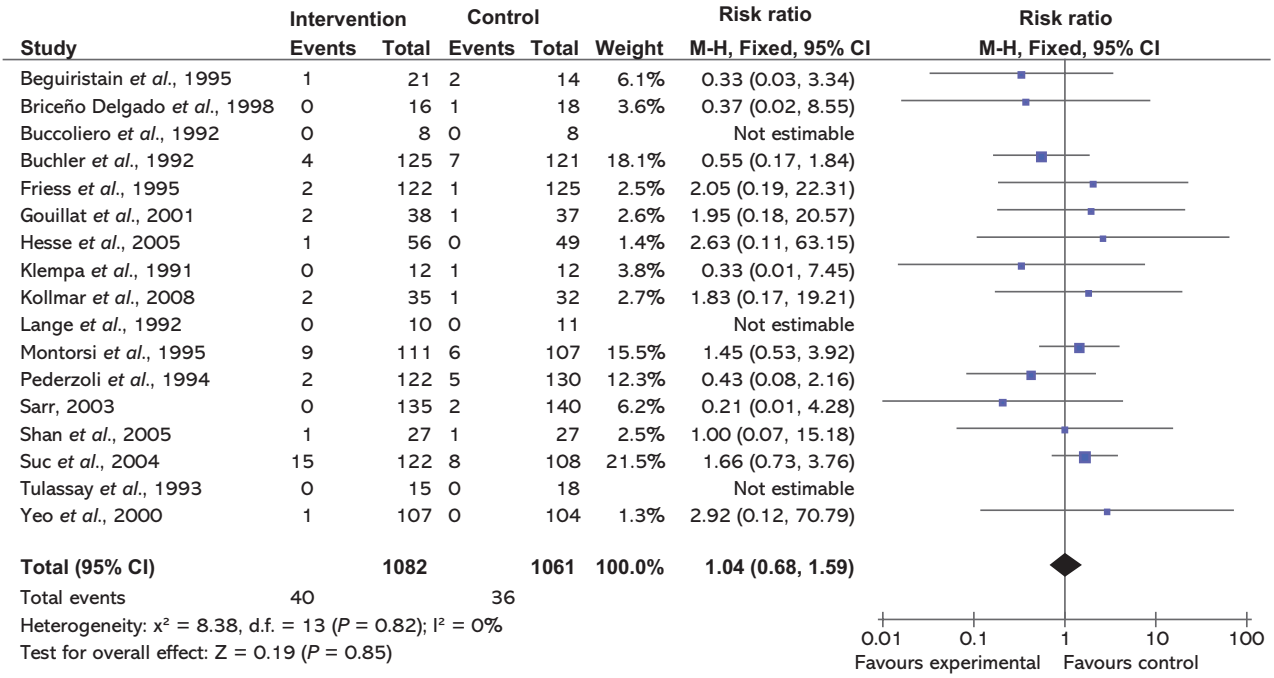
Stratified by procedure

A planned subgroup analysis of distal pancreatectomy and pancreatic drainage procedures could not be performed as the data for these procedures were not available from the trials. Only the subgroup of patients undergoing pancreatoduodenectomy was reported.

Pancreatoduodenectomy There was no statistically significant difference between the SA and control group for any of the outcomes.

Variations in statistical analysis

Adopting the random-effects model or calculating the risk difference did not change the results. Sensitivity analysis using empirical continuity correction factors[39] was not performed because



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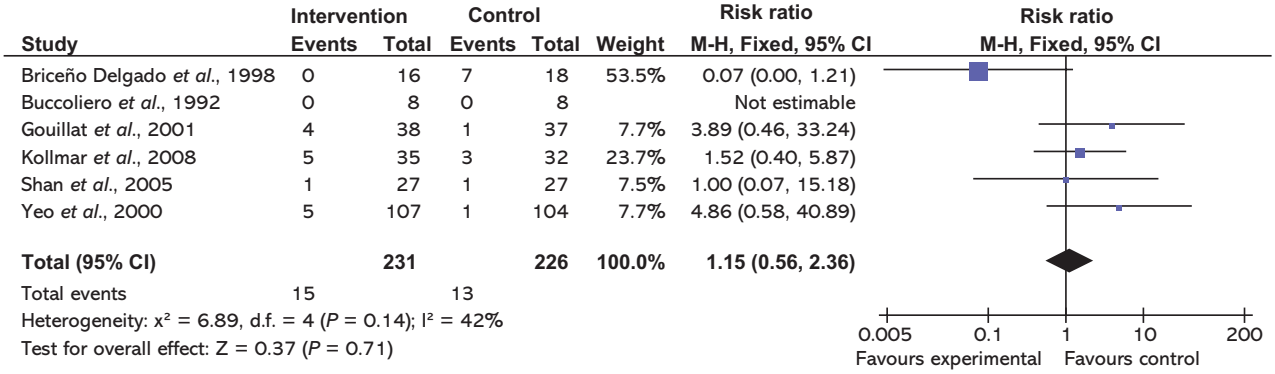

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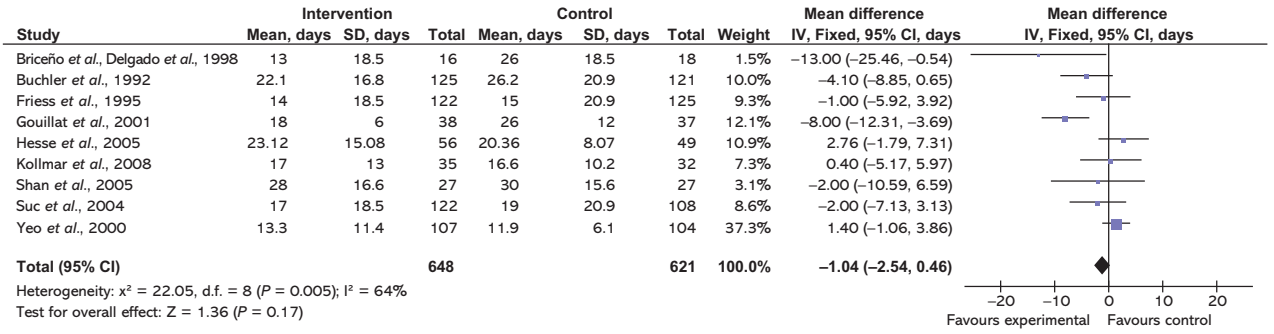
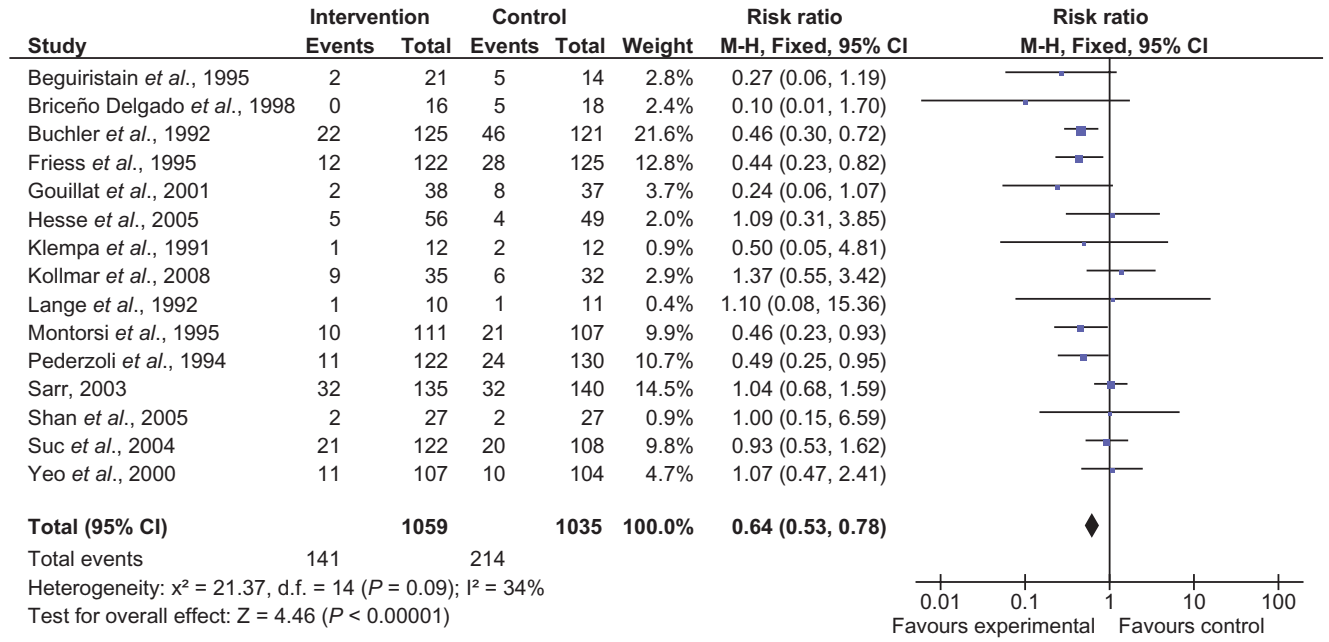


(C)

Figure 2 Comparison of somatostatin analogues vs. no intervention showing effects on (A) perioperative mortality, (B) re-operation rates and (C) hospital stay. M-H, Mantel-Haenszel; 95% CI, 95% confidence interval, SD, standard deviation



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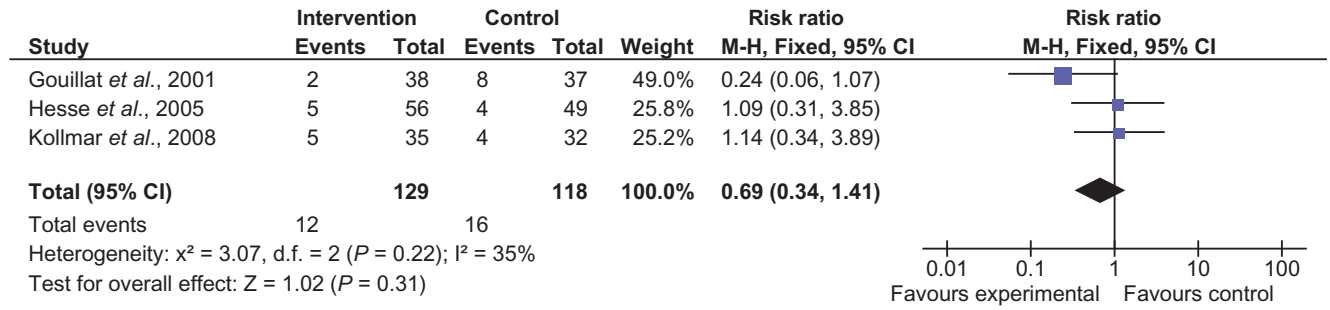


(B)

Figure 3 Comparison of somatostatin analogues vs. no intervention showing effects on pancreatic fistula rates. (A) Pancreatic fistula (all): studies did not differentiate between clinically significant and clinically insignificant fistulas. (B) Pancreatic fistula (clinically significant): studies included only clinically significant fistulas. M-H, Mantel-Haenszel; 95% CI, 95% confidence interval

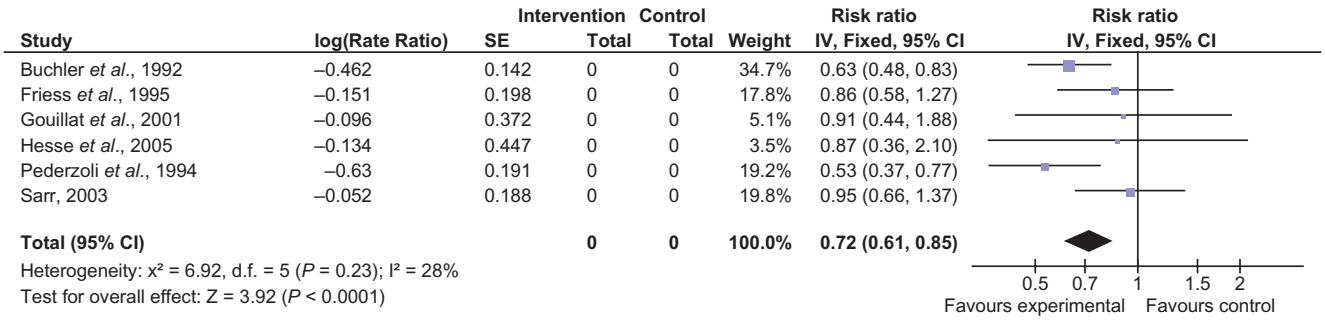
there were no statistically significant outcomes in the main comparison with zero event trials.

Reporting bias

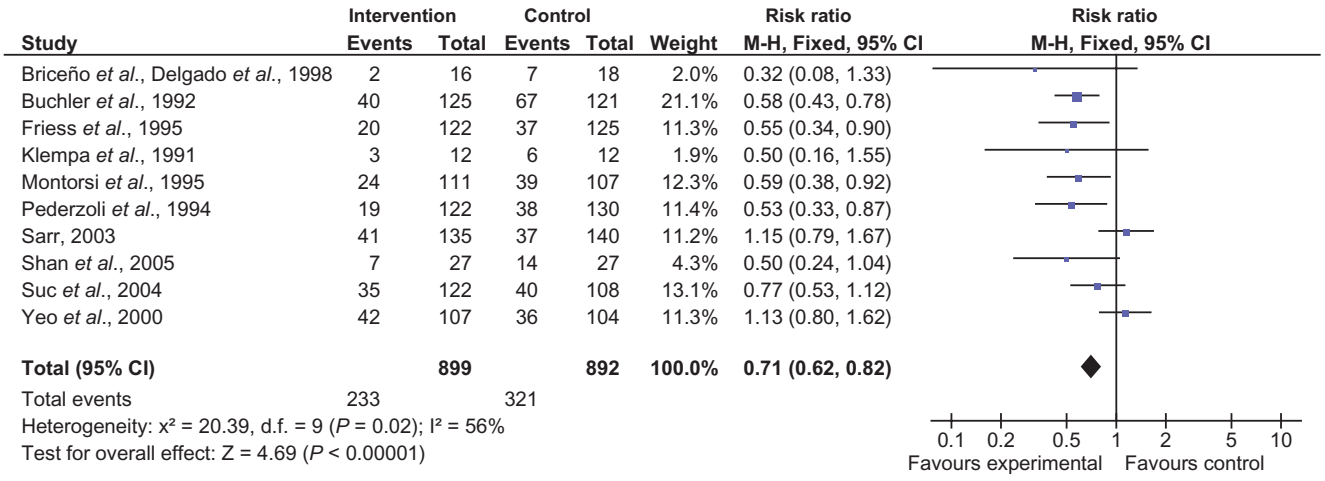
The funnel plot of the primary outcomes did not show any reporting bias (Fig. 6). Egger's linear regression approach to identifying publication bias[24] did not reveal any bias for the outcome perioperative mortality ($P = 0.3199$). This was not calculated for the outcome re-operation because few trials included that outcome.

Discussion

Somatostatin analogues did not decrease rates of perioperative mortality and re-operation in patients undergoing pancreatic surgery. The main indication for re-operation is the presence of a pancreatic fistula-associated sepsis or organ dysfunction.[13] There is no universal definition of pancreatic fistula or pancreatic leak and incidences vary depending on the definitions used. An international study group of surgeons[13] have graded postoperative pancreatic fistulas by consensus as A, B and C. Grade A fistulas are transient and do not have any clinical impact. Grade B fistulas require alteration in the management of the patient. Grade C fistulas require major alterations in the management of the patient and usually indicate re-operation. Grade B and C fistulas have significant clinical impact and may contribute to increased morbidity and mortality. In this review, only trials in which data on grade B or C fistulas were available separately from grade A were included for the outcome of clinically significant pancreatic fistula (grades B and C). The overall incidence of pancreatic fistula was lower in the SA group. Only three trials distinguished between



(A)



(B)

Figure 4 Comparison of somatostatin analogues vs. no intervention showing effects on perioperative complications. (A) Number of complications. (B) Number with any complications. SE, standard error; M-H, Mantel-Haenszel; 95% CI, 95% confidence interval

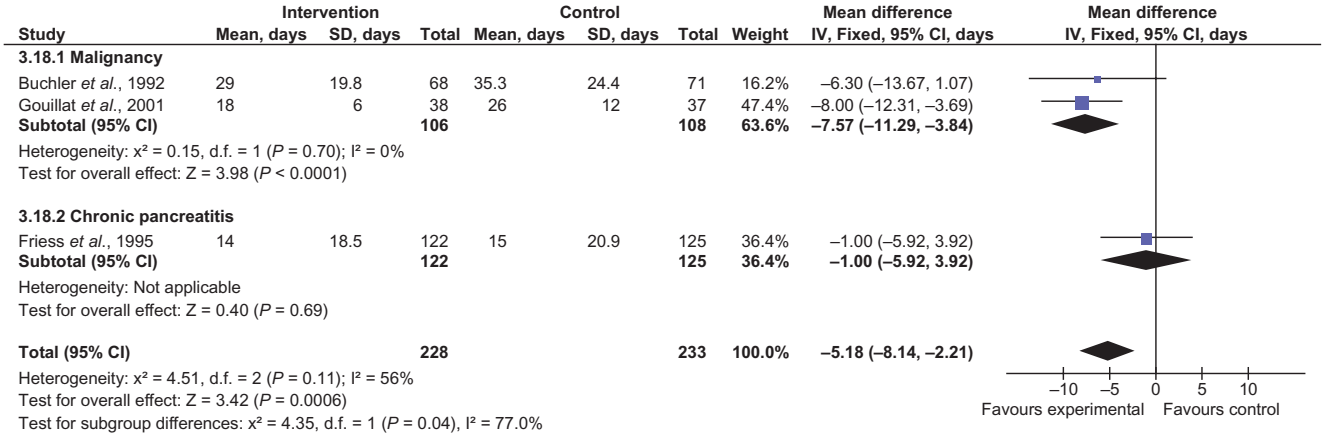


Figure 5 Comparison of somatostatin analogues vs. no intervention. Subgroup analysis stratified by different aetiologies: effects on hospital stay. SD, standard deviation; 95% CI, 95% confidence interval

any pancreatic fistula and clinically significant pancreatic fistula.[26,27,33] There was no difference between the SA and control groups in the incidence of clinically significant pancreatic fistula. It is likely that some of the pancreatic fistulas that were reported in the other trials were clinically significant. However, in the absence of data on the proportion of these fistulas that were clinically significant, such trials could not be included for the outcome 'clinically significant pancreatic fistulas' and could be included

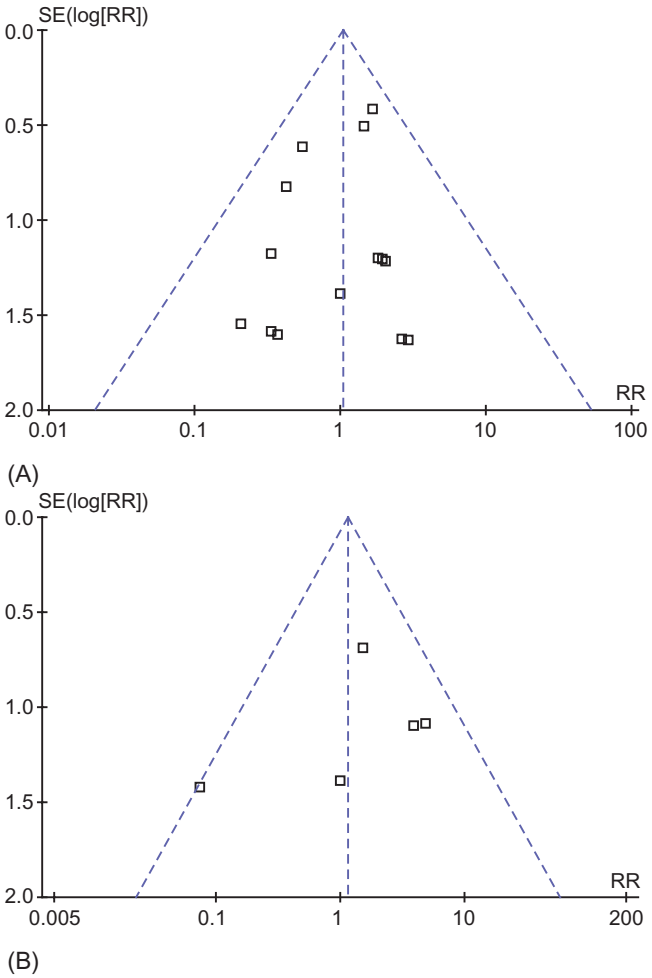


Figure 6 Funnel plots of comparison of somatostatin analogues vs. no intervention for outcomes (A) perioperative mortality and (B) re-operation. SE, standard error; RR, risk ratio

only for the outcome 'all pancreatic fistulas'. That only a few trials were included under the outcome 'clinically significant pancreatic fistulas' may explain the lack of any statistically significant difference between the SA and control groups. Alternatively, the lack of a statistically significant difference may reflect the lack of effect. In patients undergoing pancreatic surgery for malignancy, a decrease in hospital stay was noted in the SA group. This suggests that SAs decreased clinically significant fistulas in patients undergoing pancreatic surgery for cancer.

Overall postoperative complications were lower in the intervention group than the control group. However, there was no difference between the two groups in length of hospital stay in the main analysis. The possible reasons for the absence of difference in total hospital stay include a lack of effect of SAs with regard to incidence of re-operation, anastomotic leak or clinically significant pancreatic fistulas and the fact that pancreatic fistulas are often managed at the patient's home (as community-based treatment). Pancreatic fistulas that are amenable to community-based treatment may decrease the quality of life of the patients concerned during the time they take to close, increase the length of the convalescence period, thus causing a later return to work and resulting in major cost implications for patients, patients' carers and patients' employers, and increase the costs associated with the provision of community-based treatment, despite the fact that SAs do not appear to reduce hospital stay.

As far as the interventions were concerned, somatostatin must be administered by continuous i.v. infusion for approximately 1 week. This can decrease the patient's mobility. By contrast, octreotide is administered subcutaneously thrice per day, allowing good patient mobility. Its other advantage is that it can be administered even in patients with difficult venous access, thereby increasing compliance. The adverse effects associated with the intervention were mainly minor, such as pain at the injection site. No serious adverse effects were reported in any of the trials. Of the trials that reported the withdrawal of intervention, the treatment was stopped in about 1.5% of the 540 patients. In high-income countries, the cost of an entire course of octreotide is less than the cost of 1 day in hospital. There was no difference in length of hospital stay between the two groups in the main analysis. However, the subgroup analysis revealed a shorter hospital stay in the intervention group in the somatostatin ($P = 0.0006$) and malignancy ($P < 0.0001$) subgroups. Only three trials were included in each of these subgroups,[27,28,34] one of which featured in both subgroups.[27] It is not clear whether the lower hospital stay in the intervention group in these subgroups is because of the intervention effect or because of the numerous subgroup analyses that were performed. The lack of information on pancreatic fistula (i.e. whether it was clinically significant or not) does not help us to reach a conclusion. Patients with chronic pancreatitis have a lower risk of postoperative complications than those with malignancy and this may be because the tissue fibrosis usually seen in patients with chronic pancreatitis facilitates the anastomotic procedure.[34] This logical reasoning combined with the very low *P*-value obtained suggests that the decrease in hospital stay in patients undergoing pancreatic surgery for malignancy reflects the true effect of SAs. Further evaluation of the cost-effectiveness of SAs in pancreatic surgery is necessary.

Somatostatin analogues reduce perioperative complications but do not reduce perioperative mortality. In patients undergoing pancreatic surgery for malignancy, they shorten hospital stay. Further adequately powered trials of low risk of bias are necessary.

Statement

This paper is a shortened version of a review submitted to the Cochrane Upper Gastrointestinal and Pancreatic Diseases Group. Cochrane reviews are regularly updated as new evidence emerges and in response to comments and criticisms. The Cochrane Library should be consulted for the most recent version of the review. The results of a Cochrane review can be interpreted

differently, depending on the reader's perspectives and circumstances. Please consider the conclusions presented carefully. They are the opinions of the review authors and are not necessarily shared by the Cochrane Collaboration.

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Conflicts of interest

None declared.

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