Laparoscopic-endoscopic rendezvous versus preoperative endoscopic sphincterotomy for common bile duct stones in patients undergoing laparoscopic cholecystectomy (Protocol)

Vettoretto N, Arezzo A, Famiglietti F, Cirocchi R, Moja L, Morino M

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Laparoscopic-endoscopic rendezvous versus preoperative endoscopic sphincterotomy for common bile duct stones in patients undergoing laparoscopic cholecystectomy (Protocol)  
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Laparoscopic-endoscopic rendezvous versus preoperative endoscopic sphincterotomy for common bile duct stones in patients undergoing laparoscopic cholecystectomy

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Editorial group: Cochrane Hepato-Biliary Group.


ABSTRACT

This is the protocol for a review and there is no abstract. The objectives are as follows:

This review will compare the classical two-stage approach (endoscopic sphincterotomy followed by laparoscopic cholecystectomy) and the single-stage laparo-endoscopic rendezvous technique and cholecystectomy for the treatment of cholelithiasis and common bile duct stones.

BACKGROUND

Clinical and radiological findings have documented the prevalence of common bile duct stones in patients with gallstones to be between 11% and 20% (Menezes 2000; Videhult 2009; Borzellino 2010). In fact, although there is little knowledge about the natural history of common bile duct stones, it is known that about half of asymptomatic common bile duct stones discovered accidentally at intraoperative cholangiography would pass spontaneously the Papilla of Vater within six weeks (Collins 2004). Nevertheless, the consequences of retained stones may lead to cholangitis, hepatic abscess, and pancreatitis, and thus justify an invasive approach.

In the pre-laparoscopic era, open cholecystectomy, intraoperative cholangiography, and subsequent open common bile duct exploration were the standard of care for common bile duct stones removal during cholecystectomy for cholelithiasis (Neoptolemos 1989). The increasing use of laparoscopic cholecystectomy since the early nineties has changed the surgical management of these patients. Given the large number of possible strategies, the ideal management is still a matter of debate (Martin 2006). Preoperative and postoperative endoscopic sphincterotomy (two-stage intervention) were associated with more procedures undertaken per patient and longer hospital stays when compared with laparoscopic common bile duct exploration (single-stage intervention), without significant differences in terms of morbidity and duct clearance. In fact, laparoscopic transcystic common bile duct exploration should be attempted before laparoscopic common bile duct exploration, having shown a success rate of up to 70% of patients...
and being less harmful than the direct opening of the common bile duct (Wagner 2004). Whichever technique is used, many authors have reported that a single-stage management of choledocholithiasis is the most cost-effective approach when performed in centres highly experienced in laparoscopic common bile duct exploration (Urbach 2001; Poulose 2006; Kharbutli 2008; Topal 2010). Despite these results favouring the single-stage approach over the two-stage approach, pre-operative endoscopic retrograde cholangiopancreatography (ERCP) is still routinely used to treat common bile duct stones in patients scheduled for laparoscopic cholecystectomy (EAES 1998; Williams 2008), while laparoscopic common bile duct exploration is still underutilised for being a highly demanding procedure, requiring an advanced laparoscopic expertise (Poulose 2006).

The so-called laparo-endoscopic rendezvous represents an alternative technique to perform a single-stage treatment for common bile duct stones in patients with symptomatic gallstones disease. This procedure has been described in order to ease bile duct cannulation during endoscopic sphincterotomy, thus reducing failure of endoscopic common bile duct clearance and post-operative pancreatitis due to inadvertent pancreatic duct cannulation. The technique consists in guidewire anterograde transcystic cannulation of the bile duct during laparoscopic cholecystectomy to be retrieved by a duodenoscope, this way facilitating retrograde bile duct cannulation. This is followed by intraoperative endoscopic retrieval of the guide for subsequent over-the-wire sphincterotomy insertion and standard endoscopic bile duct stones clearance. Its feasibility has been proven in several retrospective and prospective patient series (Saccomani 2005). It has been associated with a lower occurrences of acute pancreatitis, shorter hospital stay, and reduced costs compared with pre-operative endoscopic sphincterotomy in randomised clinical trials (Morino 2006; Lella 2006; Rabago 2006). Moreover, such rendezvous seems to be associated with a higher therapeutic success compared with pre-operative endoscopic sphincterotomy and laparoscopic bile duct exploration (La Greca 2009), and the majority of endoscopists consider it easier to do than standard ERCP (La Greca 2008). Despite its advantages, several limitations need to be mentioned. Patients previously treated by total or partial gastric resection are unlikely to be suitable for a rendezvous procedure. In addition, giant impacted stones, Mirizzi syndrome, and preampullary diverticula are other described limitations (Morino 2006; Lella 2006; Williams 2002). Last, but not least, morbidity up to 19% was shown, including post sphincterectomy bleeding, cystic duct leak, and pancreatitis (La Greca 2009), despite the selective bile duct cannulation only. It also requires ERCP team availability, and in any case, it implies approximately 60 minutes longer time than that for laparoscopic cholecystectomy alone (Saccomani 2005).

We think that a systematic review can correctly evaluate the potential advantages of rendezvous shown in previous studies in order to confirm or to deny its role as the procedure of choice if compared to pre-operative endoscopic sphincterotomy. Recently, two systematic reviews (Gurusamy 2011; Alexakis 2012) have compared one-stage versus two-stage approach to cholecysto-choledocholithiasis, but the experimental group summoned different techniques (rendezvous technique, intraoperative “non-aided” endoscopic retrograde cholangiography, laparoscopic clearance of the common bile duct). We acknowledge that the focus on a single technique is important to ascertain its potential advantages over the most common two-stages approach to the problem. For this reason, we will include all randomised clinical trials properly comparing the sole rendezvous technique with the two-staged approach using preoperative endoscopic sphincterotomy and subsequent laparoscopic cholecystectomy.

O B J E C T I V E S

This review will compare the classical two-stage approach (endoscopic sphincterotomy followed by laparoscopic cholecystectomy) and the single-stage laparo-endoscopic rendezvous technique and cholecystectomy for the treatment of cholelithiasis and common bile duct stones.

M E T H O D S

Criteria for considering studies for this review

Types of studies

We will include randomised clinical trials. Quasi-randomised studies that will be retrieved as a result of the searches for randomised clinical trials will only be used to extract data on harm. All randomised trial reports will be eligible regardless of language and publication status (full article, thesis, or abstract).

Types of participants

Only trials enrolling patients with both cholelithiasis and choledocholithiasis will be included, regardless of inflammatory status (cholecystitis, cholangitis, pancreatitis) and grade of biliary obstruction (overt or sub-clinical jaundice). We will not consider limitations based on different diagnostic workouts for the diagnosis of common bile duct stones (i.e., intraoperative cholangiography, magnetic resonance imaging, computed tomography-scan, ultrasounds, laboratory tests). Clinical signs of gallbladder and bile duct stones considered are:
Elevated liver function tests above the normal limits (aspartate amino-transferase, alanine aminotransferase, gamma-glutamyl transpeptidase, alkaline phosphatase, and total bilirubin).
- Cholecystitis and/or cholangitis and/or pancreatitis.
- Abdominal ultrasonography showing possible common bile duct stones or a dilated common bile duct (diameter 8 to 10 mm).
- Magnetic resonance cholangiopancreatography showing common bile duct stones.

Types of interventions
Only patients undergoing laparo-endoscopic rendezvous (as described by Cavina 1998) will be eligible as part of the intervention group. Anterograde sphincterotomy or non-aided intraoperative retrograde cholangiopancreatography will be excluded. Contemporaneous laparoscopic cholecystectomy must have been performed. The patients in the control group should have been randomised to preoperative endoscopic sphincterotomy followed by laparoscopic cholecystectomy. No restriction will be made on the timing of the subsequent operation. We will not consider trials reporting outcomes on patients treated exclusively with post-operative ERCP or with intraoperative common bile duct exploration, neither laparoscopic nor open.

Types of outcome measures

Primary outcomes
- Overall mortality assessed at the latest follow-up.
- Overall morbidity. We will assess surgical morbidity (i.e., pancreatitis, bleeding, intestinal perforations) as well as general morbidity (i.e., pneumonia, wound infection, cardiac complications, deep venous thrombosis etc.)
- Failure of primary clearance (duct clearance as determined by cholangiogram, number of successful common bile duct cannulation).
- Quality of life assessment.

Secondary outcomes
- Operative time.
- Length of hospital stay.

Search methods for identification of studies

Electronic searches

We will search The Cochrane Hepato-Biliary Group Controlled Trials Register (Gluud 2013), The Cochrane Central Register of Controlled Trials (CENTRAL) in The Cochrane Library, MEDLINE, EMBASE, and Science Citation Index Expanded (Royle 2003). We will also search Clinicaltrials.gov (http://clinicaltrials.gov) and the The World Health Organization International Clinical Trials Registry Platform (www.who.int/ictrp/search/en) to identify ongoing and recently completed trials. Because laparoendoscopic rendezvous was first standardised in 1998 (Cavina 1998), searching will be limited to the years following 1995. There will be no limitation based on language. The preliminary search strategies with the expected time spans of the searches are given in Appendix 1.

Searching other resources
Two review authors will screen independently all abstracts retrieved from electronic databases, and the full text publication of each abstract that is deemed relevant by at least one of us will be obtained. The reference lists of potentially relevant articles will be screened for further potentially relevant citations. International meeting proceedings will be handsearched.

Data collection and analysis
We will use both fixed-effect and random-effects model meta-analyses. We will report both results if differences in statistical significance exist when applying the two models. For dichotomous variables, we will use relative risks (RR) with 95% confidence intervals (95% CI). For the analysis of continuous variables, we will use means with their corresponding standard deviations (SDs) to calculate weighted or standardised mean differences with 95% CIs. However, some of the variables, eg, hospital stay or length of surgery, tend to have non-Gaussian distributions. Thus, authors understandably use nonparametric statistics and give their data as medians with ranges. We will present mean and median data separately, but we can use only mean data for statistical analyses. In case a trial failed to report SDs for an outcome, we will assume that the SD is equal to the mean value itself. This approach produces relatively conservative results, since trials without reporting of SDs will tend to receive less weight.

Selection of studies
Two review authors (NV and FF) will independently assess the titles and abstracts of retrieved studies for relevance. After this initial assessment, all studies that seem potentially relevant for the review will be obtained in full. NV and FF will then independently check the full papers for eligibility, with disagreements resolved by discussion, and, where required, the input of another review author will be requested. The review authors will record all reasons for exclusion.
Data extraction and management

We will extract and summarise details of the eligible studies using a data extraction sheet. Two review authors (NV and FF) will extract data independently and will resolve disagreements by discussion. If data are missing from the published reports, review authors will attempt to contact the study authors to obtain the missing information. We will extract the following data from the identified publications:

- Year and language of publication.
- Country.
- Inclusion and exclusion criteria.
- Other co-interventions.
- Outcomes (mentioned above).
- Risk of bias (described below).
- Duration of follow-up.

Assessment of risk of bias in included studies

Two review authors will independently assess the risk of bias of each included trial according to the recommendations in the Cochrane Handbook for Systematic Reviews of Interventions (Higgins 2008), the Cochrane Hepato-Biliary Group Module (Glud 2008), and methodological studies (Schulz 1995; Moher 1998; Kjaergard 2001; Wood 2008; Savovic 2012; Savovic 2012a). We will use the following definitions in the assessment of risk of bias.

Allocation sequence generation

- Low risk of bias: sequence generation was achieved using computer random number generation or a random number table. Drawing lots, tossing a coin, shuffling cards, and throwing dice are adequate if performed by an independent person not otherwise involved in the trial.
- Uncertain risk of bias: the method of sequence generation was not specified.
- High risk of bias: the sequence generation method was not random.

Allocation concealment

- Low risk of bias: the participant allocations could not have been foreseen in advance of, or during, enrolment. Allocation was controlled by a central and independent randomisation unit. The allocation sequence was unknown to the investigators (for example, if the allocation sequence was hidden in sequentially numbered, opaque, and sealed envelopes).
- Uncertain risk of bias: the method used to conceal the allocation was not described so that intervention allocations may have been foreseen in advance of, or during, enrolment.
- High risk of bias: the allocation sequence was likely to be known to the investigators who assigned the participants.

Blinding of participants, personnel, and outcome assessors

- Low risk of bias: blinding was performed adequately, or the assessment of outcomes was not likely to be influenced by lack of blinding.
- Uncertain risk of bias: there was insufficient information to assess whether blinding was likely to induce bias on the results.
- High risk of bias: no blinding or incomplete blinding, and the assessment of outcomes were likely to be influenced by lack of blinding.

Incomplete outcome data

- Low risk of bias: missing data were unlikely to make treatment effects depart from plausible values. Sufficient methods, such as multiple imputation, has been employed to handle missing data.
- Uncertain risk of bias: there was insufficient information to assess whether missing data in combination with the method used to handle missing data were likely to induce bias on the results.
- High risk of bias: the results were likely to be biased due to missing data.

Selective outcome reporting

- Low risk of bias: all outcomes were pre-defined and reported, or all clinically relevant and reasonably expected outcomes were reported.
- Uncertain risk of bias: it is unclear whether all pre-defined and clinically relevant and reasonably expected outcomes were reported.
- High risk of bias: one or more clinically relevant and reasonably expected outcomes were not reported, and data on these outcomes were likely to have been recorded.

For-profit bias

- Low risk of bias: the trial appears to be free of industry sponsorship or other kind of for-profit support that may manipulate the trial design, conductance, or results of the trial.
- Uncertain risk of bias: the trial may or may not be free of for-profit bias as no information on clinical trial support or sponsorship is provided.
- High risk of bias: the trial is sponsored by the industry or has received other kind of for-profit support.

Other biases

- Low risk of bias (the trial appears to be free of other sources of bias).
- Uncertain risk of bias (there is insufficient information to assess
whether other sources of bias are present).
- High risk of bias (it is likely that potential sources of bias related to the specific trial design used, or other bias risks are present).

We will resolve any differences in opinion through discussion, and in the case of unsettled disagreements, the third author will adjudicate.

Trials judged with low risk of bias in all domains will be considered as trials with low risk of bias. In all the other remaining cases, the trials will be considered with high risk of bias. We will present our assessment of risk of bias findings using a ‘Risk of bias’ summary figure, which presents all of the judgements in a cross-tabulation of study by entry. This display of internal validity indicates the weight the reader may give the results of each trial. We will also aim to present this assessment in the narrative review.

In addition, in the quasi-randomised trials we will examine whether patient groups have been similar at baseline in terms of demographic and laboratory findings.

Measures of treatment effect

For dichotomous variables, we will calculate the risk ratio (RR) with 95% CI. We will also calculate the risk difference with 95% CI. We will report the risk difference only if the results were different from the risk ratio. Risk difference includes ‘zero event trials’ (trials in which both groups have no events); such trials will not be taken into account in calculating the summary treatment effect in the case of risk ratio. When analysing continuous variables, we will calculate the mean difference (MD) with 95% CI (for outcomes such as total hospital stay) or the standardised mean difference (SMD) with 95% CI (for outcomes such as pain whenever different authors use different pain scales). Generally, in the analysis of continuous variables, means with their corresponding standard deviations (SDs) are needed to calculate weights or standardized mean differences with 95% CIs. However, some of the variables, i.e., hospital stay or length of surgery, tend to have non-Gaussian distribution. Thus, authors understandably use non-parametric statistics and give their data as medians with ranges. We will present mean and median data separately, but we can use only mean data for the meta-analyses. In case a trial fails to report SDs for an outcome measure, we will assume that the SDs equal to the mean value itself. This approach produces relatively conservative results, since trials without reporting of SDs will tend to receive less weight.

Unit of analysis issues

The units of analysis will be the patients who are about to undergo bile duct clearance and laparoscopic cholecystectomy, either in one or two stages.

Dealing with missing data

We will perform an intention-to-treat analysis (Newell 1992) as far as possible. Otherwise, we will perform the ‘available-case analysis’ (Higgins 2011). For continuous variables, if the mean value was missing from the report and author communications (either as numbers or graphs), we will use the median for the meta-analysis. If the standard deviation was missing from the report and author communications, we will impute the standard deviation from the standard error, confidence intervals, and P values. If it is not possible to impute standard deviation from any of these measures, we will impute the standard deviation as the largest standard deviation from other trials included in the outcome.

Assessment of heterogeneity

We will consider both clinical and statistical heterogeneity. If appropriate, we will analyse data using meta-analyses, that is where trials appear similar in terms of level of participants, intervention type, duration, and outcome type. We will assess statistical heterogeneity using the I² test (Higgins 2002). The I² test examines the percentage of total variation across trials due to heterogeneity rather than chance.

We will classify heterogeneity using the following I² values:
- 0% to 40%: might not be important;
- 30% to 60%: may represent moderate heterogeneity;
- 50% to 90%: may represent substantial heterogeneity;
- 75% to 100%: considerable heterogeneity.

Values of I² over 50% indicate a high level of heterogeneity. In the absence of clinical heterogeneity and in the presence of statistical heterogeneity (I² over 50%), we plan to use a random-effects model. However, we will not use trials for analyses where heterogeneity is substantial. Where there is no clinical or statistical heterogeneity, we plan to use a fixed-effect model meta-analyses.

Assessment of reporting biases

We will use a funnel plot to explore bias in the presence of at least 10 trials for our primary outcome (Egger 1997; Macaskill 2001). Asymmetry in funnel plot of trial size against treatment effect will be used to assess this bias. We will perform linear regression analysis described by Egger 1997 to determine the funnel plot asymmetry in the presence of at least 10 trials for the outcome.

Data synthesis

Meta-analyses

We will perform the meta-analyses according to the recommendations of The Cochrane Collaboration (Higgins 2011) and the Cochrane Hepato-Biliary Group Module (Gluud 2013) if there are at least two trials to perform a meta-analysis. If there is no substantial statistical heterogeneity and if there is not clinical heterogeneity between the trials, we will combine the results in a meta-analysis, using both fixed- and random-effects models. We will
report results using the random-effects model when heterogeneity between the trials is substantial ($I^2 > 50\%$), or using the fixed-effect model when heterogeneity between the trials is unimportant or moderate ($I^2 < 50\%$). We will report both results when differences in statistical significance exist when applying the two models. If substantial statistical heterogeneity is detected (i.e., a high $I^2$ value), we will meta-analyse the results of the trials, provided that the majority of individual trials results are consistent with the direction of the effect (i.e., the RR and CI largely fall on one side of the null line) from the examination of the forest plot. In case of substantial clinical heterogeneity or in case of forest-plot with inconsistent direction of the effect across studies, we will not combine study results but present a narrative or tabulated summary. We will conduct meta-analyses using Review Manager 5 (RevMan 2011).

We will exclude quasi-randomised trials from the analysis of benefits and consider them only to describe harm, without meta-analysing data from these together with the identified randomised trials.

Trials sequential analyses

Trial sequential analysis (TSA) is a tool for quantifying the statistical reliability of the data in a cumulative meta-analysis (CTU 2011; Thorlund 2011), adjusting alpha and beta values for sparse data and repetitive testing on accumulating data (Brok 2008; Wetterslev 2008; Brok 2009; Thorlund 2009, Wetterslev 2009; Thorlund 2010; Thorlund 2011). TSA is a methodology that combines a required information size calculation (cumulated sample sizes of included trials) with the threshold of statistical significance. In order to control for the risks of random errors due to sparse data and multiplicity, we will perform TSA for the dichotomous outcomes as well as for the continuous outcomes (Brok 2008; Wetterslev 2008; Brok 2009; Thorlund 2009, Wetterslev 2009; Thorlund 2010; Thorlund 2011). We will base our calculations on the required information size on the proportion of patients with the outcome in the conventional group, a relative risk reduction of 20\%, an alpha (type I error) of 5\%, a beta (type II error) of 20\%, and the diversity of the meta-analysis (Wetterslev 2009).

Subgroup analysis and investigation of heterogeneity

We will perform the following subgroup analyses:

- Trials with low risk of bias compared to trials with high risk of bias.
- Patients with or without pancreatitis at debut.

We will use the 'test for interaction' to identify the differences between subgroups. We will only conduct subgroup analyses if there are two or more trials in each subgroup. We will also use meta-regression (in the presence of at least 10 trials) to determine the influence of different factors (i.e. age) on the primary outcome effect estimate.

Sensitivity analysis

Sensitivity analyses will be defined at the review stage.

Summary of findings tables

We will display results on all primary and secondary outcomes using Summary of findings tables (GRADE Pro).

ACKNOWLEDGEMENTS

Cochrane Hepato-Biliary Group, in particular Dimitrinka Nikolova for the editing and Sarah Louise Klingenberg for the search strategy, Saboor Khan and Luit Penninga for the review protocol.

Peer reviewers: Luit Penninga, Denmark; Olaf J Bakker, The Netherlands.

Contact editor: Saboor A Khan, UK.

REFERENCES

Additional references

Alexakis 2012


Borzellino 2010


Brok 2008


Brok 2009

Brok J, Thorlund K, Wetterslev J, Gluud C. Apparently conclusive meta-analyses may be inconclusive - Trial sequential analysis adjustment of random error risk due to repetitive testing of accumulating data in apparently
Laparoscopic-endoscopic rendezvous versus preoperative endoscopic sphincterotomy for common bile duct stones in patients undergoing laparoscopic cholecystectomy (Protocol)

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Cavina 1998

Collins 2004

CTU 2011

EAES 1998

Egger 1997

Gluud 2013

GRADE Pro

Gurusamy 2011

Higgins 2011

Kharbutli 2008

Kjaergard 2001

La Greca 2008

La Greca 2009

Lella 2006

Macaskill 2001

Martin 2006

Menezes 2000

Moher 1998

Morino 2006
undergoing laparoscopic cholecystectomy (Protocol)

Rabago 2006

Newell 1992

Neoptolemos 1989

Poulose 2006

Rabago 2006
Rábago LR, Vicente C, Soler F, Delgado M, Moral I, Guerra I, et al. Two-stage treatment with preoperative endoscopic retrograde cholangiopancreatography (ERCP) compared with single-stage treatment with intraoperative ERCP for patients with symptomatic cholecystitis with possible choledocholithiasis. Endoscopy 2006; Vol. 38, issue 8:779–86. [0013–726X: (Print)]

Royle 2003

Saccomani 2005

Savovic 2012

Savovic 2012a

Schulz 1995

Thorlund 2009

Thorlund 2010

Thorlund 2011

Topal 2010

Urbach 2001

Videhult 2009

Wagner 2004

Wetserslev 2008

Wetserslev 2009

Williams 2002
Williams GL, Vellacott KD. Selective operative cholangiography and Perioperative endoscopic retrograde cholangiopancreatography (ERCP) during laparoscopic cholecystectomy: a viable option for choledocholithiasis.
Williams 2008
[1468–3288: (Electronic)]

Wood 2008
* Indicates the major publication for the study

APPENDICES

Appendix 1. Search strategies

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<td>Date will be given at review stage.</td>
<td>('endoscopic sphincterotom*' OR EST) AND rendezvous AND (cholelihiasis OR gallstone* OR 'gallbladder stone') AND ('common bile duct' OR choledoch*) AND (stone* OR calcul*)</td>
</tr>
</tbody>
</table>

Cochrane Central Register of Controlled Trials (CENTRAL) in The Cochrane Library

Latest issue.

#1 MeSH descriptor Sphincterotomy, Endoscopic explode all trees  
#2 endoscopic sphincterotom* OR EST  
#3 (#1 OR #2)  
#4 MeSH descriptor Cholecystectomy, Laparoscopic explode all trees  
#5 rendezvous  
#6 (#4 OR #5)  
#7 MeSH descriptor Cholelithiasis explode all trees  
#8 cholelithiasis OR gallstone* OR gallbladder stone  
#9 (#7 OR #8)  
#10 MeSH descriptor Gallstones explode all trees  
#11 (common bile duct OR choledoch*) AND (stone* OR calcul*)  
#12 (#10 OR #11)  
#13 (#3 AND #6 AND #9 AND #12)
| MEDLINE (Ovid SP) | 1995 to the date of search. | 1. exp Sphincterotomy, Endoscopic/
2. (endoscopic sphincterotomy* or EST).mp. [mp=
protocol supplementary concept, rare disease sup-
plementary concept, title, original title, abstract,
name of substance word, subject heading word, unique identifier]
3. 1 or 2
4. exp Cholecystectomy, Laparoscopic/
5. rendezvous.mp. [mp=protocol supplementary
concept, rare disease supplementary concept, title,
original title, abstract, name of substance word,
subject heading word, unique identifier]
6. 4 or 5
7. exp Cholelithiasis/
8. (cholelithiasis or gallstone* or gallbladder stone)
.mp. [mp=protocol supplementary concept, rare
disease supplementary concept, title, original title,
abstract, name of substance word, subject heading
word, unique identifier]
9. 7 or 8
10. exp Gallstones/
11. ((common bile duct or choledoch*) and (stone*
or calcul*)).mp. [mp=protocol supplementary con-
cept, rare disease supplementary concept, title, original
title, abstract, name of substance word, subject heading
word, unique identifier]
12. 10 or 11
13. 3 and 6 and 9 and 12
14. (random* or blind* or placebo* or meta-anal-
ysis).mp. [mp=protocol supplementary concept, rare
disease supplementary concept, title, original
title, abstract, name of substance word, subject heading
word, unique identifier]
15. 13 and 14

| EMBASE (Ovid SP) | 1995 to the date of search. | 1. exp endoscopic sphincterotomy/
2. (endoscopic sphincterotomy* or EST).mp. [mp=
title, abstract, subject headings, heading word, drug
trade name, original title, device manufacturer,
drug manufacturer]
3. 1 or 2
4. exp CHOLECYSTECTOMY/
5. rendezvous.mp. [mp=title, abstract, subject
headings, heading word, drug trade name, original
title, device manufacturer, drug manufacturer]
6. 4 or 5
7. exp CHOLELITHIASIS/
8. (cholelithiasis or gallstone* or gallbladder stone)
.mp. [mp=title, abstract, subject headings, heading
9. 7 or 8
10. exp gallstone/
11. ((common bile duct or choledoch*) and (stone* or calcul*)).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer]
12. 10 or 11
13. 3 and 6 and 9 and 12
14. (random* or blind* or placebo* or meta-analysis).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer]
15. 13 and 14

Science Citation Index Expanded

1995 to the date of search.

#1 TS=(endoscopic sphincterotomy* or EST)
#2 TS=(rendezvous)
#3 TS=(cholelithiasis or gallstone* or gallbladder stone)
#4 TS=((common bile duct or choledoch*) and (stone* or calcul*))
#5 #4 AND #3 AND #2 AND #1

CONTRIBUTIONS OF AUTHORS

Alberto Arezzo, Nereo Vettoretto, and Federico Famiglietti generated the idea for the review. Lorenzo Moja has defined the methodology, Roberto Cirocchi has helped in the protocol and review process and Mario Morino has defined the review strategy and is in control of the review process.

DECLARATIONS OF INTEREST

None known.

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Internal sources

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External sources

- No sources of support supplied