ARTÍCULOS ORIGINALES

Guide wire-assisted cannulation versus conventional contrast to prevent pancreatitis. A systematic review and meta-analysis based on randomized control trials

Canulación asistida por alambre guía versus contraste convencional para prevenir la pancreatitis. Una revisión sistemática y meta-análisis basados en ensayos aleatorios controlados

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ABSTRACT

Objective: Through this systematic review and meta-analysis, we aim to clarify the differences between these two techniques, thus improving primary success cannulation and reducing complications during endoscopic retrograde cholangiopancreatography, primarily pancreatitis. **Methods:** A comprehensive search was conducted to search for data available up until June 2015 from the most important databases available in the health field: EMBASE, MEDLINE (via PubMed), Cochrane, LILACS and CENTRAL (via BVS), SCOPUS, the CAPES database (Brazil), and gray literature. **Results:** Nine randomized clinical trials including 2583 people were selected from 20,198 studies for meta-analysis. Choledocholithiasis had been diagnosed in mostly (63.8%) of the patients, who were aged an average of 63.15 years. In those patients treated using the guide wire-assisted cannulation technique, provided a significantly lower instance of pancreatitis (RD=0.03; 95% CI: 0.01-0.05; I2= 45%) and greater primary success cannulation (RD=0.07; 95% CI: 0.03-0.12; I^2=12%) than conventional contrast cannulation. **Conclusions:** The guide wire-assisted technique, when compared to the conventional contrast technique, reduces the risk of pancreatitis and increases primary success cannulation rate. Thus, guide wire-assisted cannulation appears to be the most appropriate first-line cannulation technique.

Keywords: Catheterization; Cholangiopancreatography, endoscopic retrograde; Pancreatitis; Meta-analysis (source: MeSH NLM).

RESUMEN

Objetivo: A través de esta revisión sistemática y meta-análisis, nuestro objetivo es aclarar las diferencias entre estas dos técnicas, mejorando así la canulación de éxito primario y reducir las complicaciones durante la colangiopancreatografía retrógrada endoscópica, principalmente la pancreatitis. **Métodos:** Una búsqueda exhaustiva se realizó para buscar datos disponibles hasta junio de 2015, desde las bases de datos más importantes disponibles en el campo de la salud: EMBASE, MEDLINE (vía PubMed), Cochrane, LILACS y CENTRAL (a través de la BVS), SCOPUS, la base de datos CAPES (Brasil), y la literatura gris. **Resultados:** Nueve ensayos clínicos aleatorios incluyendo 2583 personas fueron seleccionados de 20198 estudios de meta-análisis. Coledocolitiasis había sido diagnosticada en su mayoría (63,8%) de los pacientes, que tenían entre un promedio de 63,15 años. En los pacientes tratados con la técnica de canulación guiada, proporcionado una instancia significativamente menor de pancreatitis (RD=0,03; IC del 95%: 0,01-0,05; I^2=45%) y una mayor canalización de éxito primario (RD=0,07; IC del 95%: 0,03-0.12; I^2=12%) que la canulación por contraste. **Conclusiones:** La técnica canulación con alambre guía, en comparación a la técnica de contraste convencional, reduce el riesgo de pancreatitis y aumenta la tasa de canulación con éxito primario. Por lo tanto, canulación con alambre guía parece ser la técnica de canulación de primera línea y la más adecuada.

Palabras clave: Cateterismo; Pancreatocolangiografía retrógrada endoscópica; Pancreatitis; Metanálisis (fuente: DeCS BIREME).

INTRODUCTION

Nowadays, endoscopic retrograde cholangiopancreatography (ERCP) is one of the most important endoscopic procedures. However, cannulation techniques are still controversial [1].

Two types of cannulation techniques are routinely used in current practice: guide wire-assisted (GW) cannulation and conventional contrast (CC) cannulation. Several randomized clinical trials (RCT) had demonstrated that guide wire-assisted cannulation increases the primary success cannulation and reduces the risk of pancreatitis compared to conventional contrast cannulation.

However, some recently papers [2-4] published from Japan suggest that the use of guidewire is a significant risk factor for pancreatitis.

Since its first description in 1968, endoscopic retrograde cholangiopancreatography (ERCP) has become an established modality for the diagnosis and treatment of pancreaticobiliary disorders [5]. Over the years, it has evolved from a purely diagnostic to a primarily therapeutic procedure and is considered one of the most important endoscopic procedures. Nowadays, around 500,000 ERCPs are performed annually in the USA with adverse event rates between 4% and 10%, and mortality between 0.05% and 1% [6].

Acute pancreatitis is one of the most common serious adverse events of ERCP and has an incidence rate between 5% and 10%, except in high-risk populations, where it is up to 25% [7]. Many risks factors for pancreatitis were identified, such as: sphincter of Oddi dysfunction, periampullary diverticulum, recurrent pancreatitis, youth female sex, history of pancreatitis, difficult cannulation, pancreatic sphincterotomy, inadvertently letting the guidewire enter the pancreatic duct, multiple injections of the pancreatic duct, endoscopist's expertise, and trainee involvement in cannulation [8]. To reduce pancreatitis rates, new materials and accessories are being developed daily.

The latest meta-analysis regarding GW and CC cannulation, published in February 2013 of F. Tse *et al*. [9], demonstrated that GW cannulation was associated with a lower pancreatitis rate and a higher initial cannulation success rate. It included twelve randomized controlled trials (RCT).

However, that meta-analysis had some limitations.

Firstly, they used RCT's abstract papers mixing then with RCT's fully text which prevents an appropriate critical evaluation of the studies, for example: randomization and blinding.

Secondly, they mixed non-crossover studies with crossover studies, by mixing different study designs in one meta-analysis reduces the value of the meta-analysis because mixing techniques will cause a loss in statistical power difference in the overall efficacy of the intervention and an inability to distinguish charitable or noxious effects related to the intervention.

In addition, the crossover technique does not preserve the original allocation of patients, preventing a proper comparison between techniques.

Thirdly, the quality of the selected studies is questionable, such as: they used a study which the patient follows up loss was greater than 20%.

Finally, some results shown in his meta-analyses have un acceptable heterogeneities of 85%, which does not support an adequate evidence.

Even though, respecting the last systematic review and meta-analysis of about these theme we performed a new meta-analysis using only RCT's and non-crossover studies to eventually reach a new conclusion comparing techniques for cannulation of the common bile duct, preventing complications such as pancreatitis.

To compare GW cannulation and CC cannulation of the common bile duct during ERCP for the prevention of pancreatitis and primary success cannulation.

METHODS

Protocol and Registration

This meta-analysis has been registered in PROSPERO [10] international prospective register of systematic review by the number CRD42015015445.

Eligibility criteria

All RCT's comparing GW and CC cannulation techniques in patients who needed ERCP and who had an intact papilla of Vater. These sources of information and databases were assessed: EMBASE, MEDLINE (via PubMed), Cochrane, LILACS and CENTRAL (via BVS), SCOPUS, CAPES database (Brazil), and gray literature. Any outcome from any date of publication until October 2014, with any number of subjects was considered. Publications were accepted in any format, language, or publication status. The bases were assessed using the Jadad scale [11], and meta-analysis was conducted through the RevMan 5 software [12].

Search strategies

See Appendix 1.

Study selection

Initially, studies were excluded because information in the title or abstract does not allow the comparison between GW and CC cannulation. Furthermore, the abstracts and full articles were assessed and excluded if proven not to be a RCT or if the comparison was not between GW and CC cannulation. Also, some studies were previews of later ones, and were excluded after confirmation.

Data collection process

Data was extracted from all the databases and information sources mentioned by two independent authors, confirming the same eligible final studies. The eligible studies were confronted after both authors completed their searches.

Data items

The pancreatitis outcome was defined as abdominal pain after more than 24 hours post-ERCP

and amylase greater than 3x, except in Lella *et al*. [13], where it was abdominal pain after more than 24 hours. Initial cannulation success was defined as successful cholangiography in selective bile duct cannulation with the cannulation time, pancreatic duct cannulations, and pancreatic duct injections ranging between the studies.

Risk of bias in individual studies

Biases were individually assessed through the Jadad scale [11], a tool used to assess the quality of an RCT through evaluation of blinding, randomization, and losses. We also assessed other biases such as intention to treat analysis (ITT), sample calculation, cross-over, and veiled allocation.

Likewise, we assessed the description of the study (procedure descriptions, techniques used, number of people included, inclusion criteria, exclusion criteria, patient characteristics, comparisons made, patient follow-up, outcomes assessed, size of the effect identified, and whether the study was funded), validity of the study (whether the study followed all the above criteria, whether patient characteristics of different groups were similar, whether the only difference between the groups was the treatment under investigation, whether outcomes were measured in an appropriate and valid way, whether the percentage of loss was lower than 20%, and whether the study was conducted in more than one place, and the overall assessment of the study (if studies were comparable between them and whether it considered if the clinical effect was obtained as a result of intervention).

Summary measure

The difference was calculated in risk differences for dichotomic variables using the Cochrane–Mantel–Haenszel (CMH) test with a 95% confidence interval.

Synthesis of results

RevMan 5 software [12] was used for meta-analysis of initial cannulation success and risk of pancreatitis.

Heterogeneity was evaluated, when possible and necessary, below 50% using a sensitivity analysis. Analyses of all parameters influenced by variability in the data were performed to estimate reliability of results.

The uncertainties derived from sampling errors were analyzed from intervals reliably applied to the result of the study. Sensitivity analyses were used to reduce heterogeneity arising from publication bias, which was used to define the works that result in disparities between effects and sample sizes.

Risk of bias across the studies

The risk of bias was related using a funnel plot (publication bias), heterogeneity, and analysis of the global biases of individual study as shown in the Jadad score (Table 1).

Additional analyses

Sensitivity analyses were evaluated for pancreatitis rate and initial cannulation success.

RESULTS

Study selection

There were 20,872 studies found by the initial search, of which 20,851 were excluded through title, repetition, and/or abstract (Figure 1) [20]. Twenty-one studies were fully assessed, of which twelve were excluded (Table 2).

Study characteristics

Table 3 shows the characteristics of the included studies. All 9 studies were "non-crossover" RCTs. The number of participants per trial ranged from 143 to 413, totaling of 2,583. All studies included patients with intact papilla who required ERCP for pancreatobiliary diseases.

Patient characteristics are shown in Table 4.

Table 1. Jadad scale.

Study	Randomized	Appropriate randomized	Description withdrawals	Double-blind	Described blinding	Jadad score
Lella *et al*. [13], 2004	Yes	Yes	Yes	Yes	Yes	5
Artifon et al. (14), 2007	Yes	Yes	Yes	Yes	Yes	5
Katsinelos *et al*. [15], 2008	Yes	Yes	Yes	Yes	Yes	5
Bailey *et al*. [16], 2008	Yes	Yes	Yes	Yes	Yes	5
Lee *et al*. [17], 2009	Yes	Yes	Yes	Yes	Yes	5
Nambu *et al*. [18], 2011	Yes	Yes	Yes	Yes	Yes	5
Kawakami *et al*. [2], 2012	Yes	Yes	Yes	Yes	Yes	5
Savadkoohi *et al*. [19], 2012	Yes	Yes	Yes	No	No	3
Kobayashi *et al*. [3], 2013	Yes	Yes	Yes	Yes	Yes	5

Figure 1. Prisma flow diagram.
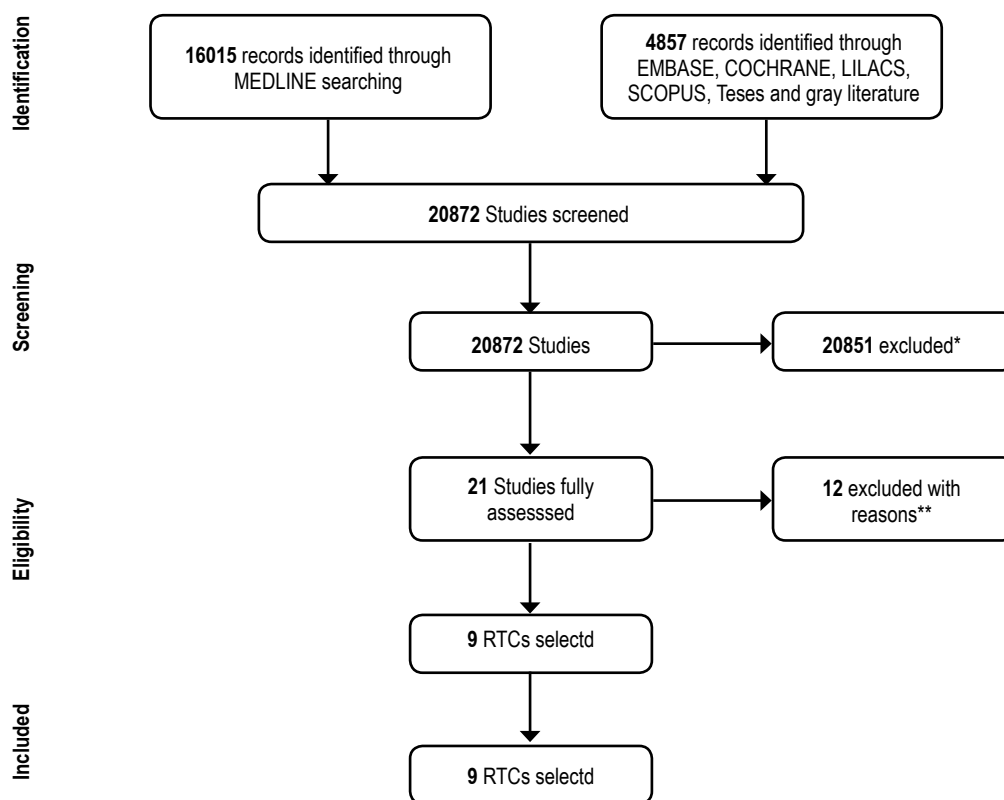
*The title, repetition's studies, or abstract were unrelated to the topic.

**The reasons for exclusions are displayed in Table 2.

Risk of bias within studies

All the studies scored 5 on the Jadad scale, except Savadkoohi *et al*. [19] which scored 3, because all studies were described as randomized, the randomization methods were described in an appropriate way, all were double-blinded using a described and appropriated method, and all had descriptions about their withdrawals.

The studies [13,14,19] did not always give strict specifications about the cannulation limit criteria and the cannulation device used. Some of them [2,16,18] described trainees starting the procedure, and one study [3] used different sizes of guide-wire in the same study. Kawakami *et al*. [2] used a 15-degree BOAD, which is used only in certain centers in Japan.

Results of individual studies

All studies had extractable information [32] about pancreatitis rates (Table 5) and primary success cannulation (Table 6).

Synthesis of results

Quantitative outcomes:

The pancreatitis rate was 3% lower in the GW group, and NNT was 33. Sensitivity analysis showed heterogeneity of 45%. Figure 2.

Primary success cannulation was 8% higher in the GW group, and NNT was 13, but the sensitivity analysis had an unacceptable heterogeneity of 85%. Figure 3.

Once outliers were removed [3,13,15], (Kobayashi 2013, Lella 2004 and Katsinelos 2008), primary success cannulation, was 7% higher in the GW group, and NNT was 14witha heterogeneity of 12%. Figure 4.

Risk of bias across studies

Pancreatitis definitions varied from study to study, but they always considered, at least, patients with abdominal pain more than 24 hours post-ERCP and

Table 2. Exclusions RCTs.

Author	Study	Year	Exclusion reason
Cortas GA *et al.* [21]	Selective cannulation of the common bile duct: a prospective randomized trial comparing standard catheters with sphincterotomes.	1999	Lost more than 40% on follow-up.
Schwacha H *et al.* [22]	A sphincterotome-based technique for selective transpapillary common bile duct cannulation.	2000	Compared two types of sphincterotome.
Cheung J *et al.* [23]	Guidewire versus conventional contrast cannulation of the common bile duct for the prevention of post-ERCP pancreatitis: a systematic review and meta-analysis.	2009	Systematic review and meta-analysis.
Kouklakis G *et al.* [24]	Evaluation of guide wire cannulation technique in elderly patients with choledocholithiasis.	2009	Retrospectively reviewed.
Shao LM *et al.* [25]	Can wire-guided cannulation reduce the risk of post-endoscopic retrograde cholangiopancreatography pancreatitis? A meta-analysis of randomized controlled trials.	2009	Meta-analysis of randomized trials.
Trifan A *et al.* [26]	Guide-wire versus conventional contrast cannulation of the common bile duct for the prevention of post-ERCP pancreatitis in patients with choledocholithiasis.	2011	Retrospectively reviewed.
Nakai Y *et al.* [27].	Impact of introduction of wire-guided cannulation in therapeutic biliary endoscopic retrograde cholangiopancreatography.	2011	Retrospectively reviewed.
Cennamo V *et al.* [28]	Can a wire-guided cannulation technique increase bile duct cannulation rate and prevent post-ERCP pancreatitis? A meta-analysis of randomized controlled trials.	2011	Meta-analysis of randomized trials.
Mariani A *et al.* [29]	Guidewire biliary cannulation does not reduce post-ERCP pancreatitis compared with the contrast injection technique in low-risk and high-risk patients.	2012	Prospective non randomized trial.
Mohammad Alizadeh AH *et al.* [30]	Preventive role of wire-guided cannulation to reduce hyperamylasemia and pancreatitis following ERCP.	2012	Retrospectively reviewed.
Tse F *et al.* [9]	Guide wire-assisted cannulation for the prevention of post-ERCP pancreatitis: a systematic review and meta-analysis.	2013	Systematic review and meta-analysis.
Nakai Y, *et al.* [31]	Risk factors for post-ERCP pancreatitis in wire-guided cannulation for therapeutic biliary ERCP.	2015	Retrospective study.

amylase greater than 3x. The definitions of initial cannulation success also varied between the studies. There was also bias regarding the different types of guide-wires (0.0035 inch soft tipped, 0.035 inch soft hydrophilic, with a loop in the tip, 0.035 angle-tipped, or 0.025 inch soft tipped), sphincterotomes, catheters, and duodenoscopes (with 15-degree BOAD or standard duodenoscopes) used in the studies.

Therefore, the pancreatitis rate, seen in the funnel plot, shows that Lee *et al.* [17] is outside the curve. This is explained by the population presence in the study; it was a low-risk cohort. Just 7/300 (2.33%) of the patients had suspected dysfunction of the sphincter of Oddy and 217/300 (72.3%) had choledocholithiasis.

Furthermore, initial cannulation success, seen in the funnel plot, shows that three RCT's [3,13,15], were outside the curve, causing a heterogeneity of 85%. This can be explained because two of them [13,15] are extremely favored GW, and one [3] extremely favored CC, with significant discrepancies compared to other studies. Because of these huge discrepancies and losing

a significant statistical difference, we withdrew these studies to have an acceptable heterogeneity, assuring that all studies remaining had homogeneous and reliable data.

Some bias across the studies [13,14,19] was introduced in that strict specifications about the cannulation limit criteria and the cannulation devices were not always given. Some of them [2,16,18] allowed a trainee to start the procedure. One study [3] used different sizes of guide-wire in the same study, and in another study [2] a 15-degree BOAD that is only used in some centers in Japan were used.

DISCUSSION

Over the years, several mechanisms have been postulated to explain why GW prevents pancreatitis. For example: inadvertent contrast injection into the pancreatic duct, facilitating selective biliary cannulation and limiting papillary trauma [33]. Although, inadvertent guide wire insertion into the pancreatic duct can cause an increase in pancreatitis rate.

Table 3. Study Characteristics.

Study	Endoscopist	Trainee	Cannulation device	Guide wire	Guide wire technique	Cannulation limit
Lella *et al.* [13], 2004 Single center	1	None	Sphincterotome	0.035-inch soft tipped Teflon Tracer	Sphincterotome inserted into papilla then guide wire advanced	Unclear
Artifon *et al.* [14], 2007 Multi-center	1	None	Sphincterotome	0.035-inch soft tipped Teflon Tracer	Sphincterotome inserted into papilla then guide wire advanced	Unclear
Katsinelos *et al.* [15], 2008 Multi-center	2	None	Catheter	0.035-inch soft hydrophilic tipped Jagwire	Guide wire directly advanced into the CBD	10 min
Bailey *et al.* [16], 2008 Single center	2	Started procedure	Sphincterotome	0.035-inch soft hydrophilic tipped Jagwire	Guide wire directly advanced into the CBD	10 min (5 min trainee)
Lee *et al.* [17], 2009 Single center	1	None	Sphincterotome	0.035-inch soft hydrophilic tipped Jagwire	Sphincterotome inserted into papilla then guide wire advanced	10 min or 5 PD cannulations or 2 PD injections
Nambu *et al.* [18], 2011 Single center	Multiple	Started procedure	Sphincterotome/ Catheter	0.035-inch soft hydrophilic angle-tipped Jagwire	Guide wire directly advanced into the CBD	10 min (5 min trainee)
Kawakami *et al.* [2], 2012 Multi-center	Multiple	Started procedure	Sphincterotome/ Catheter	0.035-inch soft hydrophilic tipped Jagwire	Guide wire directly advanced into the CBD under fluoroscopy	10 min (5 min trainee)
Savadkoohi *et al.* [19], 2012 Multi-center	Multiple	None	Sphincterotome/ Catheter	0.035-inch soft hydrophilic tipped Jagwire	Unclear	Unclear
Kobayashi *et al.* [3], 2013 Multi-center	Multiple	None	Discretion of the endoscopist	0.025 or 0.035 inches soft hydrophilic tipped Teflon	Sphincterotome or catheter inserted into papilla then guide wire advanced	20 min

This meta-analysis shows that GW reduced PEP and increased initial cannulation success compared to CC.

Firstly, we must not forget that primary success cannulationis probably the most important step in ERCP because this will reduce cannulation attempts, precut sphincterotomy, use of fistulation, and inadvertent insertion into the pancreatic duct, preventing injury to the papilla.

Secondly, preventing contact to the papilla will not cause a lot of edema in the papilla, which a lot of papers affirm is the main cause of pancreatitis's development in ERCP.

However, some recent Japanese center's RCTs [2,3,4], suggests that introduction of the guidewire in the pancreatic duct is a risk factor for pancreatitis and that opacification of the pancreatic duct is not a risk factor for pancreatitis. This may lead some to conclude that the use, in general, of the guidewire can be a risk factor for pancreatitis.

Japanese centers result differ in that they have 15-degree BOAD duodenoscopes, and they believe that the angulation of the duodenoscope did not require the bow-up function of the sphincterotome, making it easy to adjust to the axis of the bile duct, not requiring the guidewire to facilitate primary success cannulation [34].

Unfortunately, these duodenoscopes are found only in Japan, and it is not possible to perform RCTs with them and also to use in our clinical practice or elsewhere in the world [35].

In addition, we disagree when F. Tse *et al.* [9], categorized these RCT's, such as: Bailey AA *et al.* [16], Katsinelos P *et al.* [15], Kobayashi G *et al.* [3], Nambu T *et al.* [18] and Kawakami H *et al.* [2], such as crossover studies, because they clearly have database to be categorized as non-crossover studies and we also find a new RCT's Savadkoohi *et al.* [19] that they did not select.

Differently, from the last systematic review and meta-analysis about these theme, we did not select abstract's papers Mangiavillano B *et al.* [36], Apostolopoulos P *et al.* [37] and Mangiavillano B *et al.* [38] just fully text and we did not use RCT's Cortas GA *et al.* [21], which the patient follow up loss was greater than 20%.

Beyond the vast equipment and materials available these days, new devices and methods are still necessary for further improvements in ERCP. Our objective of providing decision support in performing routine ERCP's, should improve initial cannulation success and reduce pancreatitis. However, we believe new RCT's and meta-analyses should be performed so that

Table 4. Patient characteristics.

Study	Number of patients (GW/CC)	Sex (Female%)	Age (Average)	Choledocholitiasis	Malignancy
Lella *et al.* [13], 2004 Single center	200/200	54.5% total	61.2 total	89.8% total	6% total
Artifon *et al.* [14], 2007 Multi-center	150/150	39.3% / 27.3%	52.7 (+- 17.7) / 54.05 (+-17.5)	54.7% / 61.3%	23.3% / 32.7%
Katsinelos *et al.* [15], 2008 Multi-center	167/165	57.5% / 58.8%	70.17 (+- 14.09) / 67.79 (+- 13.88)	62.3% / 61.2%	18.6% / 18.8%
Bailey *et al.* [16], 2008 Single center	202/211	61.9% / 59.7%	60.2 (+-18.9) / 58.6 (+- 18.6)	52.2% / 50.5%	2% / 5.3%
Lee *et al.* [17], 2009 Single center	150/150	44.7% / 52%	63.6 (+-16.2) / 62.7 (+- 16)	68% / 76.7%	26.7% / 22.7%
Nambu *et al.* [18], 2011 Single center	86/84	59.3% / 50%	69.8 (+- 14.4) / 71.3 (+- 14.1)	53.5% / 58.3%	23.2% / 27.3%
Kawakami *et al.* [2], 2012 Multi-center	102/101	31.3% / 44.5%	67.4 / 68.2	39,2%/ 57.4%	30.3% 21.7%
Savadkoohi *et al.* [19], 2012 Multi-center	65/78	82.5% total	56.5 (+- 16.8) total	NA	NA
Kobayashi *et al.* [3], 2013 Multi-center	163/159	43.5% / 37.1%	69.6 (+- 13.0) / 69.6 (+- 11.7)	50% / 58%	35% / 29%

GW: guide-wire; CC: conventional cannulation; NA: not avaliable; Total: no distinction between GW/CC.

decisions about which new techniques of cannulation (i.e., double-guidewire cannulation, placement of a pancreatic stent, precut sphincterotome, or kindle knife access) should be used in cases of difficult cannulation.

Finally, we believe that the use of the guidewire to start ERCP should be encouraged to reduce the morbidity of the procedure and to reach primary cannulation success, but it is unacceptable to suppose that the procedure should be performed with either technique alone.

Limitations

Only pancreatitis rates and initial cannulation success rates were meta-analyzed because there

Table 5. Pancreatitis rates.

Study	GW events	GW total (%)	RA	CC events	CC total (%)	RA	RRA/ARA	IC 95%	NNT/NNH
Lella *et al.* [13], 2004	0	0/200 (0%)	0	8	8/200 (4%)	0.04	0.04	[-0.07, -0.01]	25
Artifon *et al.* [14], 2007	13	13/150 (8.7%)	0.08	25	25/150 (16.7%)	0.14	0.06	[-0.15, -0.01]	17
Katsinelos *et al.* [15], 2008	9	9/167 (5.4%)	0.05	13	13/165 (7.9%)	0.07	0.02	NS	NS
Bailey *et al.* [16], 2008	16	16/202 (7.9%)	0.07	13	13/211 (6.2%)	0.06	-0.01	NS	NS
Lee *et al.* [17], 2009	3	3/150 (2%)	0.02	17	17/150 (11.3%)	0.10	0.08	[-0.15, -0.04]	13
Nambu *et al.* [18], 2011	2	2/86 (2.3%)	0.02	5	5/84 (6%)	0.05	0.03	NS	NS
Kawakami *et al.* [2], 2012	6	6/102 (5.9%)	0.05	4	4/101 (4%)	0.04	-0.01	NS	NS
Savadkoohi *et al.* [19], 2012	6	6/65 (9.2%)	0.08	12	12/78 (15.4%)	0.13	0.05	NS	NS
Kobayashi *et al.* [3], 2013	10	10/163 (6.1%)	0.06	10	10/159 (6.3%)	0.06	0	NS	NS

GW = guide-wire; RA= absolute risk; CC= conventional cannulation; RRA= absolute risk reduction; ARA= absolute risk increase; NNT= number needed to treat; NNH= number needed to harm; NS= not statistically significant; CI= confidence interval.

Table 6. Primary success cannulation.

Study	GW events	GW total (%)	RA	CC events	CC total (%)	RA	RRA/ARA	IC	NNT/NNH
Lella *et al.* [13], 2004	197	197/200 (98.5%)	0.50	195	195/200 (97.5%)	0.50	0	NS	NS
Artifon *et al.* [14], 2007	132	150 (88%)	0.46	108	108/150 (72%)	0.42	-0.04	[0.07, 0.25]	25
Katsinelos *et al.* [15], 2008	136	136/167 (81.4%)	0.45	89	89/165 (54%)	0.35	-0.10	[0.18, 0.37]	10
Bailey *et al.* [16], 2008	167	167/202 (82.6%)	0.45	156	156/211 (74%)	0.42	-0.03	[0.01, 0.17]	33
Lee *et al.* [17], 2009	120	120/150 (80%)	0.44	111	111/150 (74%)	0.42	-0.02	NS	NS
Nambu *et al.* [18], 2011	67	67/86 (78%)	0.44	62	62/84 (74%)	0.42	-0.02	NS	NS
Kawakami *et al.* [2], 2012	75	75/102 (73.5%)	0.42	72	72/101 (71%)	0.42	0	NS	NS
Savadkoohi *et al.* [19], 2012	44	44/65 (68%)	0.40	53	53/78 (68%)	0.40	0	NS	NS
Kobayashi *et al.* [3], 2013	136	136/163 (83.4%)	0.45	138	138/159 (87%)	0.46	0.01	NS	NS

GW = guide-wire; RA= absolute risk; CC= conventional cannulation; RRA= absolute risk reduction; ARA= absolute risk increase; NNT= number needed to treat; NNH= number needed to harm; NS= not statistically significant; CI= confidence interval.
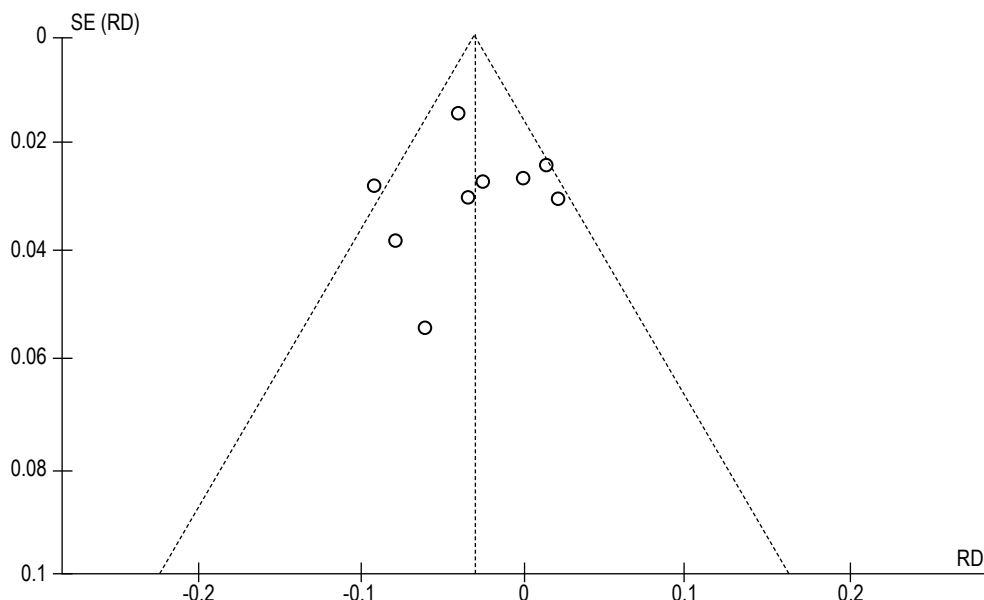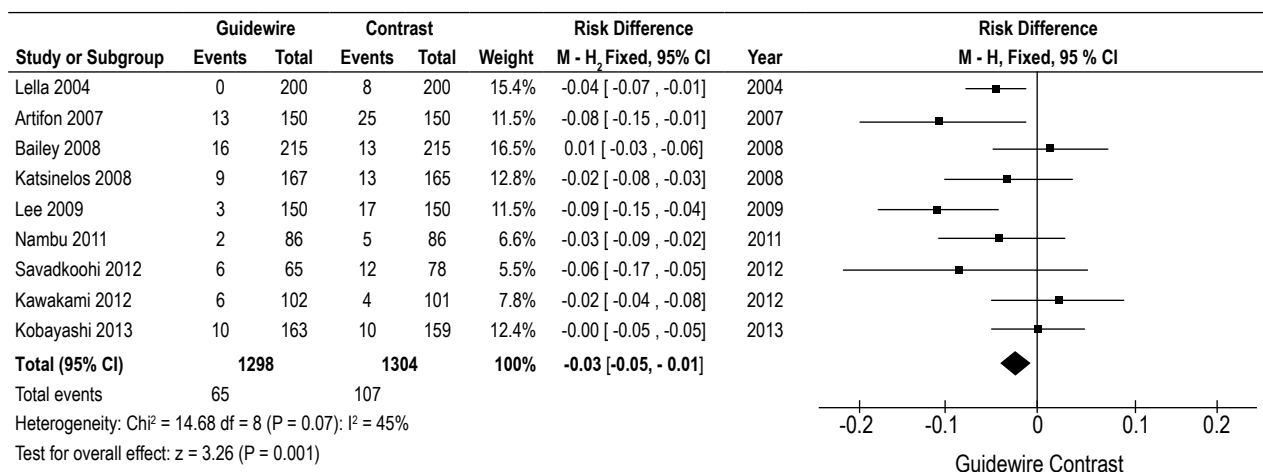

Figura 2. After ERCP patients rate.

Study or Subgroup	Guidewire Events	Total	Contrast Events	Total	Weight	Risk Difference M - H, Fixed, 95% CI	Year	Risk Difference M - H, Fixed, 95 % CI
Lella 2004	197	200	195	200	15.5%	0.01 [-0.02 , 0.04]	2004	
Artifon 2007	132	150	108	150	11.6%	0.16 [0.07 , 0.25]	2007	
Katsinelos 2008	136	167	89	215	12.9%	0.27 [0.18 , 0.37]	2008	
Bailey 2008	167	202	156	165	16.0%	0.09 [0.01 , 0.17]	2008	
Lee 2009	120	150	111	150	11.6%	0.06 [-0.03 , 0.15]	2009	
Nambu 2011	67	86	62	86	6.6%	0.04 [-0.09 , 0.17]	2011	
Savadkoohi 2012	44	65	53	78	5.5%	-0.00 [-0.16 , 0.15]	2012	
Kawakami 2012	75	102	72	101	7.9%	0.02 [-0.10 , 0.15]	2012	
Kobayashi 2013	136	163	138	159	12.5%	-0.03 [-0.11 , 0.04]	2013	
Total (95% CI)		**1285**		**1298**	**100%**	**0.08 [0.05, 0.11]**		
Total events	1074		107					

Heterogeneity: Chi^2 = 52,35 df = 8 (P < 0.00001): I^2 = 85%

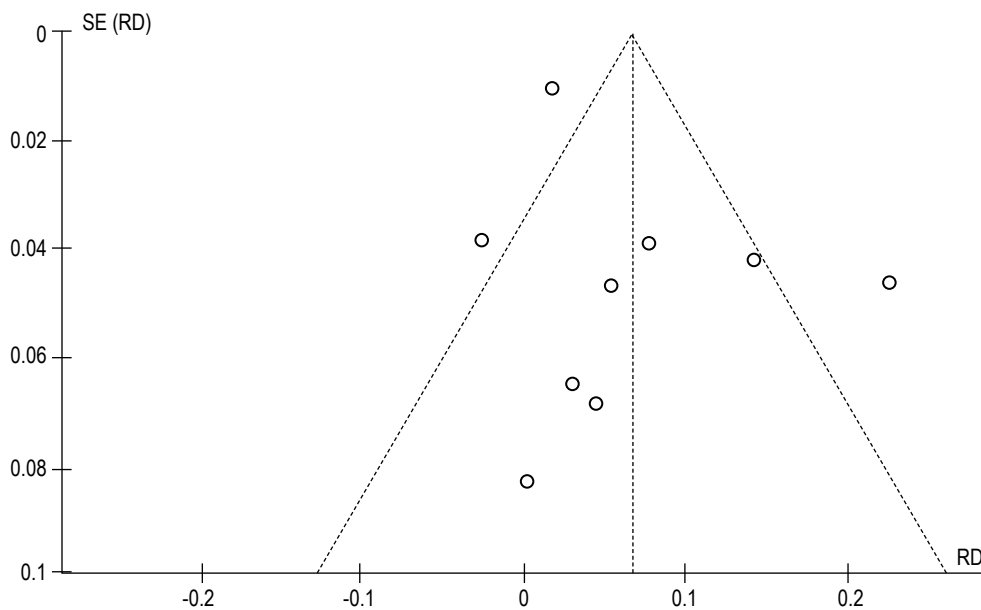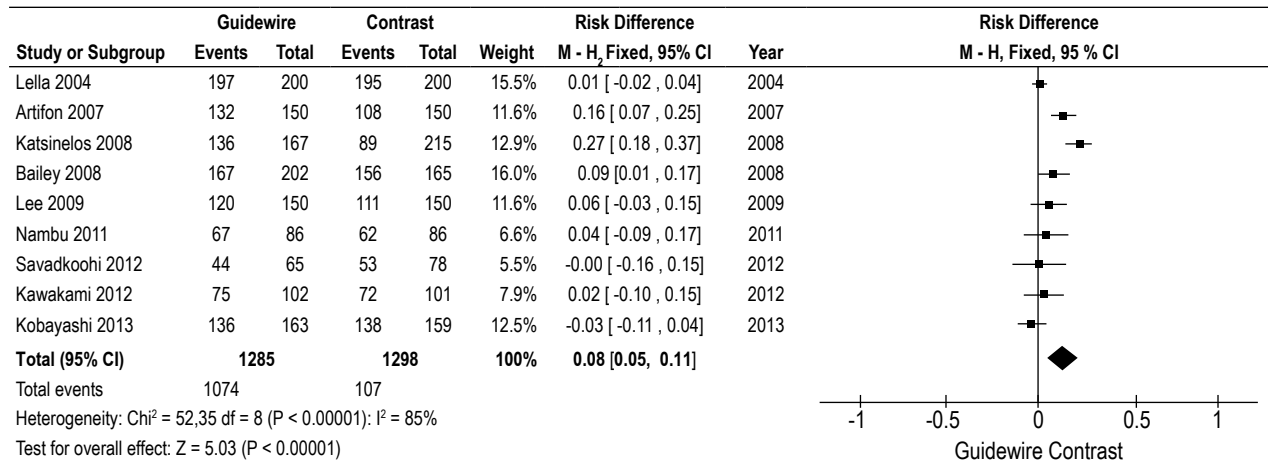Test for overall effect: Z = 5.03 (P < 0.00001)

Figura 3. Primary success canulation rate.

were insufficient data in the studies about precut sphincterotomy, inadvertent pancreatic duct manipulation, pancreatic duct stent, and use of medications to prevent pancreatitis. The number of patients included varied greatly between studies, and some studies used only an experienced endoscopist for performing the procedures while others involved trainees.

Other complications such as bleeding, perforation, and infections had similar rates between the studies. Unfortunately, there were insufficient data to perform meta-analyses. Moreover, various types of guide-wires were used in single studies and various duodenoscopes were used between studies.

Another important limitation is the way and velocity in which the contrasts were injected during a CC cannulation. In some studies, doctors were the only ones injecting the contrast. In others, trainees and nurses injected the contrast with variable speeds.

Conclusions

Guide wire-assisted cannulation was associated with a significantly lower pancreatitis rates and higher primary success cannulation rates compared to CC.

Study or Subgroup	Guidewire Events	Guidewire Total	Contrast Events	Contrast Total	Weight	Risk Difference M - H, Fixed, 95% CI	Year
Lella 2004	197	200	195	200	0.0%	0.01 [-0.02 , 0.04]	2004
Artifon 2007	132	150	108	150	19.6%	0.16 [0.07 , 0.25]	2007
Bailey 2008	167	202	156	211	27.0%	0.09 [0.01 , 0.17]	2008
Katsinelos 2008	136	167	89	165	0.0%	0.27 [0.18 , 0.37]	2008
Lee 2009	120	150	111	150	19.6%	0.06 [-0.03 , 0.15]	2009
Nambu 2011	67	86	62	84	11.1%	0.04 [-0.09 , 0.17]	2011
Kawakami 2012	75	102	72	101	13.3%	0.02 [-0.10 , 0.15]	2012
Savadkoohi 2012	44	65	53	78	9.3%	-0.00 [-0.16 , 0.15]	2012
Kobayashi 2013	136	163	138	159	0.0%	-0.03 [-0.11 , 0.04]	2013
Total (95% CI)		**755**		**774**	**100%**	**0.07 [0.03, 0.12]**	
Total events	605		652				

Heterogeneity: Chi^2 = 5.68 df = 5 (P < 0.34): I^2 = 12%
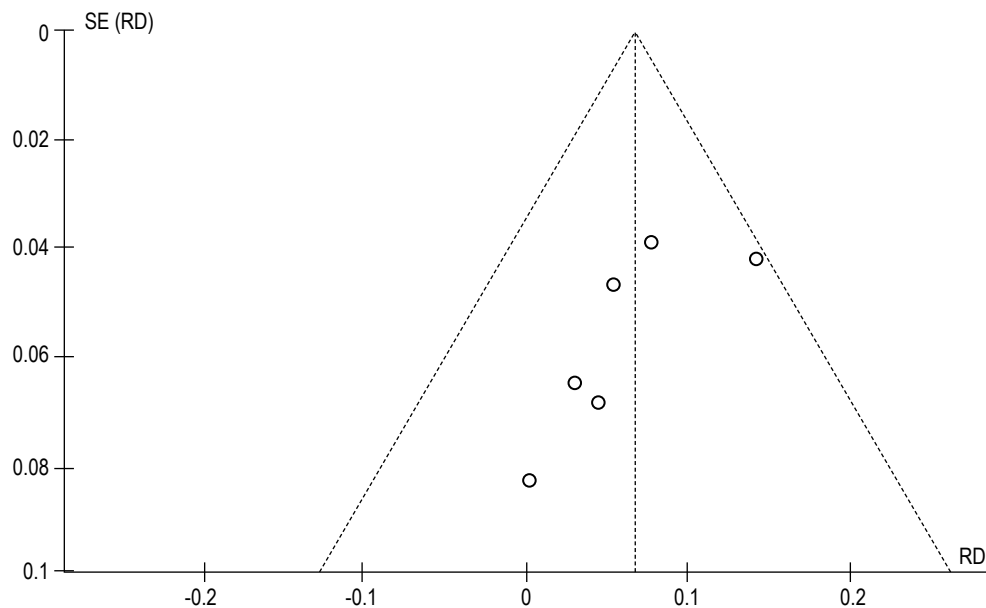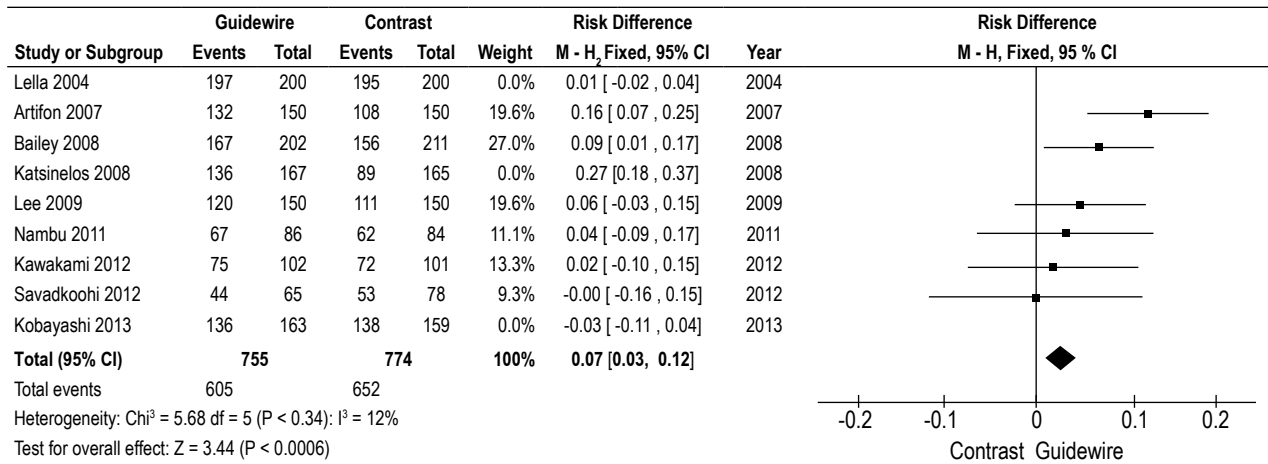
Test for overall effect: Z = 3.44 (P < 0.0006)

Figura 4. Primary success canulation rate (without outliers).

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APPENDIX 1

<u>Search strategies:</u> appendix 1MEDLINE strategy [stratified by Population (P), Intervention (I) and Comparison (C)]: P: (Disease, Biliary Tract OR Diseases, Biliary Tract OR Bile Duct Disease OR Diseases, Bile Duct OR Bile Duct Neoplasm OR Neoplasms, Bile Duct OR Bile Duct Cancer OR Bile Duct Cancers OR Cancer of the Bile Duct OR Cancer of Bile Duct OR Common Bile Duct OR Common Bile Duct Neoplasms OR Biliary Atresia, Extrahepatic OR Biliary Atresias, Extrahepatic OR Atresia, Biliary OR Familial Extrahepatic Biliary Atresia OR Idiopathic Extrahepatic Biliary Atresia OR Bile Ducts OR abnormalities OR Cholangitides OR Cholangitis OR SclerosingCholangitides OR Sclerosing Cholangitis OR SclerosingCholangiitides OR SclerosingCholangiitis OR Primary Sclerosing Cholangitis OR Primary SclerosingCholangitides OR Cholangitis OR Sclerosis OR Choledochal Cysts OR Cyst, Choledochal OR Bile Duct Cysts OR Bile Duct Cyst OR Choledochocele OR Choledochoceles OR Congenital Choledochal Cyst OR Choledochal Cysts, Congenital OR Choledochal Cyst, Type V OR Choledochal Cyst, Intrahepatic OR Choledochal Cysts, Intrahepatic OR Choledochal Cyst, Type III OR Choledochal Cyst, Type IV OR Multiple Choledochal Cysts OR Multiple Choledochal Cyst OR Choledochal Cyst, Type I OR Cyst, Common Bile Duct OR Cysts, Common Bile Duct OR Choledochal Cyst, Type II OR Choledochal Diverticulum OR CholedochalDiverticulums OR Choledochal Cyst, Diverticulum OR Choledochal Cysts, Diverticulum OR Biliary Tract Diseases OR Cysts OR Disease, Caroli OR Caroli's Syndrome OR Caroli Syndrome OR Carolis Syndrome OR Caroli's Disease OR Carolis Disease OR Bile Duct Diseases OR congenital OR Biliary Dyskinesia OR Cholestases OR Biliary Stasis OR Biliary Stases OR Bile Duct Obstruction OR Bile Duct Obstructions OR Extrahepatic Biliary Stasis OR Extrahepatic Cholestasis OR Bile Duct Obstruction, Extrahepatic OR Bile Ducts Cholestasis OR specific extrahepatic bile duct OR Cholestases, Intrahepatic OR Bile Duct Obstruction, Intrahepatic OR Intrahepatic Cholestasis OR Biliary Stasis, Intrahepatic OR Biliary Stases, Intrahepatic OR Bile Ducts, Intrahepatic OR Liver OR Syndrome, Alagille OR Alagille's Syndrome OR Alagilles Syndrome OR Alagille-Watson Syndrome OR Arteriohepatic Dysplasia OR Cardiovertebral Syndrome OR Hepatic Ductular Hypoplasia, Syndromatic OR Hepatofacioneurocardiovertebral Syndrome OR Watson Alagille Syndrome OR Watson Miller Syndrome OR Watson-Miller syndrome OR Cholestasis with Peripheral Pulmonary Stenosis OR Alagille Syndrome 2 OR Paucity of Interlobular Bile Ducts OR Hepatic Ductular Hypoplasia OR Alagille Syndrome 1 OR Bile Ducts, Intrahepatic OR Cholestasis, Intrahepatic OR Liver Cirrhoses, Biliary OR Biliary Cirrhosis OR Obstructive Liver Cirrhosis OR Secondary Biliary Cirrhosis OR Cholangitis, Chronic Nonsuppurative Destructive OR Primary Biliary Cirrhosis OR Liver Cirrhosis, Biliary OR Mirizzi's Syndrome OR Mirizzis Syndrome OR Mirizzi Syndrome OR Biliary Tract Diseases OR Common Bile Duct Diseases OR Biliary Dyskinesias OR Dyskinesia, Biliary OR Gallbladder Dyskinesia OR Gallbladder Dyskinesias OR Sphincter of Oddi Stenosis OR Sphincter of Oddi Dyskinesia OR Sphincter of Oddi Dysfunction OR Choledocholithiasis OR Common Bile Duct OR Bile Reflux OR Biliary Tract Neoplasm OR Biliary Tract Cancer OR Biliary Tract Cancers OR Cancer of Biliary Tract OR Cancer of the Biliary Tract OR Biliary Tract Neoplasms OR Bile Duct Neoplasm OR Bile Duct Cancer OR Bile Duct Cancers OR Cancer of the Bile Duct OR Cancer of Bile Duct OR Bile Duct Neoplasms OR Common Bile Duct Neoplasms OR Cholelithiases OR Cholelithiasis OR Cholecystolithiasis OR Gallstone OR Gall Stones OR Biliary Calculi OR Gall Stone OR Common Bile Duct Calculi OR Common Bile Duct Gallstones OR Gall Stones, Common Bile Duct OR Biliary Calculi, Common Bile Duct OR Common Bile Duct Gall Stones OR Gallstones OR Cholelithiasis, Common Bile Duct OR Gallbladder Diseases OR Disease, Gallbladder OR Gall Bladder Diseases OR Bladder Disease, Gall OR Bladder Diseases, Gall OR Disease, Gall Bladder OR Gallbladder Inflammation OR Gallbladder Empyema OR Gall Bladder Empyema OR Cholecystitis OR Cholecystitis, Acalculous OR Acalculous Gallbladder Inflammation OR Acute Cholecystitis OR Cholecystitis, Emphysematous OR Cholecystolithiasis OR Gallbladder Neoplasm OR Neoplasms, Gallbladder OR Cancer of Gallbladder OR Gallbladder Cancers OR Cancer, Gallbladder OR Gall Bladder Cancer OR Bladder Cancers, Gall OR Cancer of the Gallbladder OR Postcholecystectomy Syndromes OR Syndrome, Postcholecystectomy OR Post-Cholecystectomy Syndrome OR Post-Cholecystectomy Syndromes OR Sump Syndrome OR Sump Syndromes OR Postcholedochostomy Syndrome OR Postcholedochostomy Syndromes OR Post-Choledochostomy Syndrome OR Post-Choledochostomy Syndromes OR Postcholedochoduodenostomy Syndromes OR Syndrome, Postcholedochoduodenostomy OR Post-Choledochoduodenostomy Syndrome OR Post Choledochoduodenostomy Syndrome OR Post-Choledochoduodenostomy Syndromes OR Postcholedochojejunostomy Syndrome OR Postcholedochojejunostomy Syndromes OR Syndrome, Post-Choledochojejunostomy OR Syndromes, Post-Choledochojejunostomy OR Postcholecystectomy Syndrome OR Cholecystectomy OR Postoperative Complications) AND I: (cholangiopancreatography, endoscopic retrograde OR cholangiopancreatographies, endoscopic retrograde OR ERCP OR Cholangiography) AND C: (Catheterization OR Cannulation OR Catheterizations OR Cannulations OR Catheterization* OR Catheters OR Catheters* OR Stents OR Stents* OR instrumentation* OR Drainage OR methods).

Brazilian masters and doctorate theses (CAPES) strategy: ERCP and guide-wire.

EMBASE strategy: cholangiopancreatography, AND endoscopic AND retrograde OR cholangiopancreatographies, AND endoscopic AND retrograde OR ercp OR cholangiography AND (catheterization OR cannulation OR catheterizations OR cannulations OR catheterization* OR catheters OR catheters* OR stents OR stents* OR instrumentation* OR drainage OR methods), (filter: [controlled clinical trial]/lim OR [randomized controlled trial]/lim).

Cochrane strategy: 'cholangiopancreatography, AND endoscopic AND retrograde OR cholangiopancreatographies AND endoscopic AND retrograde OR ercp OR cholangiography AND (catheterization OR cannulation OR catheterizations OR cannulations OR catheterization* OR catheters OR catheters* OR stents OR stents* OR instrumentation* OR drainage OR methods) - (filter: randomized controlled trials).

LILACS or CENTRAL strategy: cholangiopancreatography retrograde endoscopy (filter- randomized controlled trials).

SCOPUS strategy: (cholangiopancreatography AND endoscopic AND retrograde OR cholangiopancreatographies AND endoscopic AND retrograde OR ERCP OR cholangiography AND (catheterization OR cannulation or catheterizations OR cannulations OR catheterization)) AND (LIMIT-TO (DOCTYPE, "ar") OR LIMIT-TO (DOCTYPE, "re")) AND (LIMIT-TO (LANGUAGE, "English") OR LIMIT-TO (LANGUAGE, "Spanish")) AND (LIMIT-TO (SUBJAREA, "MEDI")).