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; I²=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 reduciendo 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 BV), 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; I²=45%) y una mayor canalización de éxito primario (RD=0,07; IC del 95%: 0,03-0,12; I²=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; Metaanálisis (fuente: DeCS BIREME).

INTRODUCTION

Nowadays, endoscopic retrograde cholangiopancreatography (ERCP) is one of the most important endoscopic procedures. However, cannulation techniques are still controversial [10].

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% \(^{(10)}\).

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.

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**Table 1. Jadad scale.**

<table>
<thead>
<tr>
<th>Study</th>
<th>Randomized</th>
<th>Appropriate randomized</th>
<th>Description withdrawals</th>
<th>Double-blind</th>
<th>Described blinding</th>
<th>Jadad score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lella et al. (13), 2004</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>5</td>
</tr>
<tr>
<td>Artifon et al. (14), 2007</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>5</td>
</tr>
<tr>
<td>Katsinelos et al. (15), 2008</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>5</td>
</tr>
<tr>
<td>Bailey et al. (19), 2008</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>5</td>
</tr>
<tr>
<td>Lee et al. (17), 2009</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>5</td>
</tr>
<tr>
<td>Nambu et al. (18), 2011</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>5</td>
</tr>
<tr>
<td>Kawakami et al. (3), 2012</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>5</td>
</tr>
<tr>
<td>Savadkoohi et al. (19), 2012</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>3</td>
</tr>
<tr>
<td>Kobayashi et al. (6), 2013</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>5</td>
</tr>
</tbody>
</table>
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 (12) 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), primary success cannulation was 7% higher in the GW group, and NNT was 14 with a 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
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 (3,14,19) 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 2. Exclusions RCTs.

<table>
<thead>
<tr>
<th>Author</th>
<th>Study</th>
<th>Year</th>
<th>Exclusion reason</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cortas GA et al.</td>
<td>Selective cannulation of the common bile duct: a prospective randomized trial comparing standard catheters with sphincterotomes.</td>
<td>1999</td>
<td>Lost more than 40% on follow-up.</td>
</tr>
<tr>
<td>Nakai Y et al.</td>
<td>Guidewire biliary cannulation does not reduce post-ERCP pancreatitis compared with the contrast injection technique in low-risk and high-risk patients.</td>
<td>2012</td>
<td>Prospective non randomized trial.</td>
</tr>
</tbody>
</table>
Table 3. Study Characteristics.

<table>
<thead>
<tr>
<th>Study</th>
<th>Endoscopist</th>
<th>Trainee</th>
<th>Cannulation device</th>
<th>Guide wire</th>
<th>Guide wire technique</th>
<th>Cannulation limit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lelia et al. (1), 2004</td>
<td>Single center</td>
<td>1</td>
<td>Sphincterotome</td>
<td>0.035-inch soft tipped Teflon Tracer</td>
<td>Sphincterotome inserted into papilla then guide wire advanced</td>
<td>Unclear</td>
</tr>
<tr>
<td>Artifon et al. (14), 2007</td>
<td>Multi-center</td>
<td>1</td>
<td>Sphincterotome</td>
<td>0.035-inch soft tipped Teflon Tracer</td>
<td>Sphincterotome inserted into papilla then guide wire advanced</td>
<td>Unclear</td>
</tr>
<tr>
<td>Katsinelos et al. (15), 2008</td>
<td>Multi-center</td>
<td>2</td>
<td>Catheter</td>
<td>0.035-inch soft hydrophilic tipped Jagwire</td>
<td>Guide wire directly advanced into the CBD</td>
<td>10 min</td>
</tr>
<tr>
<td>Bailey et al. (16), 2008</td>
<td>Single center</td>
<td>2</td>
<td>Sphincterotome</td>
<td>0.035-inch soft hydrophilic tipped Jagwire</td>
<td>Guide wire directly advanced into the CBD</td>
<td>10 min (5 min trainee)</td>
</tr>
<tr>
<td>Lee et al. (17), 2009</td>
<td>Single center</td>
<td>1</td>
<td>Sphincterotome</td>
<td>0.035-inch soft hydrophilic tipped Jagwire</td>
<td>Sphincterotome inserted into papilla then guide wire advanced</td>
<td>10 min or 5 PD cannulations or 2 PD injections</td>
</tr>
<tr>
<td>Nambu et al. (18), 2011</td>
<td>Single center</td>
<td>Multiple</td>
<td>Sphincterotome/Catheter</td>
<td>0.035-inch soft hydrophilic angle-tipped Jagwire</td>
<td>Guide wire directly advanced into the CBD</td>
<td>10 min (5 min trainee)</td>
</tr>
<tr>
<td>Kawakami et al. (19), 2012</td>
<td>Multi-center</td>
<td>Multiple</td>
<td>Sphincterotome/Catheter</td>
<td>0.035-inch soft hydrophilic tipped Jagwire</td>
<td>Guide wire directly advanced into the CBD under fluoroscopy</td>
<td>10 min (5 min trainee)</td>
</tr>
<tr>
<td>Savadkoohi et al. (20), 2012</td>
<td>Multi-center</td>
<td>Multiple</td>
<td>Sphincterotome/Catheter</td>
<td>0.035-inch soft hydrophilic tipped Jagwire</td>
<td>Unclear</td>
<td>Unclear</td>
</tr>
<tr>
<td>Kobayashi et al. (21), 2013</td>
<td>Multi-center</td>
<td>Multiple</td>
<td>Discretion of the endoscopist</td>
<td>0.025 or 0.035 inches soft hydrophilic tipped Teflon</td>
<td>Sphincterotome or catheter inserted into papilla then guide wire advanced</td>
<td>20 min</td>
</tr>
</tbody>
</table>

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

Firstly, we must not forget that primary success cannulations is 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. (16), 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
decisions about which new techniques of cannulation (i.e., double-guidewire cannulation, placement of a pancreatic stent, precut sphincterotomy, 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>
<thead>
<tr>
<th>Study</th>
<th>Number of patients</th>
<th>Sex (Female%)</th>
<th>Age (Average)</th>
<th>Choledocholithiasis</th>
<th>Malignancy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Study</strong></td>
<td><strong>GW events</strong></td>
<td><strong>GW total (%)</strong></td>
<td><strong>RA</strong></td>
<td><strong>CC events</strong></td>
<td><strong>CC total (%)</strong></td>
</tr>
<tr>
<td>Lella et al. (13), 2004</td>
<td>0</td>
<td>0/200 (0%)</td>
<td>8</td>
<td>8/200 (4%)</td>
<td>0.04</td>
</tr>
<tr>
<td>Artifon et al. (14), 2007</td>
<td>13</td>
<td>13/150 (8.7%)</td>
<td>25</td>
<td>25/150 (16.7%)</td>
<td>0.14</td>
</tr>
<tr>
<td>Katsinelos et al. (15), 2008</td>
<td>9</td>
<td>9/167 (5.4%)</td>
<td>13</td>
<td>13/165 (7.9%)</td>
<td>0.07</td>
</tr>
<tr>
<td>Bailey et al. (16), 2008</td>
<td>16</td>
<td>16/202 (7.9%)</td>
<td>13</td>
<td>13/211 (6.2%)</td>
<td>0.06</td>
</tr>
<tr>
<td>Lee et al. (17), 2009</td>
<td>3</td>
<td>3/150 (2%)</td>
<td>17</td>
<td>17/150 (11.3%)</td>
<td>0.10</td>
</tr>
<tr>
<td>Nambu et al. (18), 2011</td>
<td>2</td>
<td>2/86 (2.3%)</td>
<td>5</td>
<td>5/84 (6%)</td>
<td>0.05</td>
</tr>
<tr>
<td>Kawakami et al. (3), 2012</td>
<td>6</td>
<td>6/102 (5.9%)</td>
<td>4</td>
<td>4/101 (4%)</td>
<td>0.04</td>
</tr>
<tr>
<td>Savadkoohi et al. (19), 2012</td>
<td>6</td>
<td>6/65 (9.2%)</td>
<td>12</td>
<td>12/78 (15.4%)</td>
<td>0.13</td>
</tr>
<tr>
<td>Kobayashi et al. (3), 2013</td>
<td>10</td>
<td>10/163 (6.1%)</td>
<td>10</td>
<td>10/159 (6.3%)</td>
<td>0.06</td>
</tr>
</tbody>
</table>

GW = guide-wire; RA = absolute risk; CC = conventional cannulation; RRA = absolute risk reduction; ARA = absolute risk increase; IC 95% = confidence interval.
### Table 6. Primary success cannulation.

<table>
<thead>
<tr>
<th>Study</th>
<th>GW events</th>
<th>GW total (%)</th>
<th>RA</th>
<th>CC events</th>
<th>CC total (%)</th>
<th>RA</th>
<th>RRA/ARA</th>
<th>IC</th>
<th>NNT/NNH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lella et al. (13), 2004</td>
<td>197</td>
<td>197/200 (98.5%)</td>
<td>0.50</td>
<td>195</td>
<td>195/200 (97.5%)</td>
<td>0.50</td>
<td>0</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Artifon et al. (14), 2007</td>
<td>132</td>
<td>150 (88%)</td>
<td>0.46</td>
<td>108</td>
<td>108/150 (72%)</td>
<td>0.42</td>
<td>-0.04</td>
<td>[0.07, 0.25]</td>
<td>25</td>
</tr>
<tr>
<td>Katsinelos et al. (15), 2008</td>
<td>136</td>
<td>136/167 (81.4%)</td>
<td>0.45</td>
<td>89</td>
<td>89/165 (54%)</td>
<td>0.35</td>
<td>-0.10</td>
<td>[0.18, 0.37]</td>
<td>10</td>
</tr>
<tr>
<td>Bailey et al. (16), 2008</td>
<td>167</td>
<td>167/202 (82.6%)</td>
<td>0.45</td>
<td>156</td>
<td>156/211 (74%)</td>
<td>0.42</td>
<td>-0.03</td>
<td>[0.01, 0.17]</td>
<td>33</td>
</tr>
<tr>
<td>Lee et al. (17), 2009</td>
<td>120</td>
<td>120/150 (80%)</td>
<td>0.44</td>
<td>111</td>
<td>111/150 (74%)</td>
<td>0.42</td>
<td>-0.02</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Nambu et al. (18), 2011</td>
<td>67</td>
<td>67/86 (78%)</td>
<td>0.44</td>
<td>62</td>
<td>62/84 (74%)</td>
<td>0.42</td>
<td>-0.02</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Kawakami et al. (19), 2012</td>
<td>75</td>
<td>75/102 (73.5%)</td>
<td>0.42</td>
<td>72</td>
<td>72/101 (71%)</td>
<td>0.42</td>
<td>0</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Savadkoohi et al. (19), 2012</td>
<td>44</td>
<td>44/65 (68%)</td>
<td>0.40</td>
<td>53</td>
<td>53/78 (68%)</td>
<td>0.40</td>
<td>0</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Kobayashi et al. (20), 2013</td>
<td>136</td>
<td>136/163 (83.4%)</td>
<td>0.45</td>
<td>138</td>
<td>138/159 (87%)</td>
<td>0.46</td>
<td>0.01</td>
<td>NS</td>
<td>NS</td>
</tr>
</tbody>
</table>

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.

### Figure 2.

Figura 2. After ERCP patients 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.

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## REFERENCES


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**Figura 4.** Primary success cannulation rate (without outliers).


