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RADIOFREQUENCY ABLATION FOR AMPULLARY NEOPLASIA WITH INTRADUCTAL EXTENSION AFTER ENDOSCOPIC PAPILLECTOMY: SYSTEMATIC REVIEW AND META-ANALYSIS

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Conflict of Interest: Dr. Diogo Turiani Hourneaux De Moura:
BariaTek Medical - Advisory Board Member (Consulting fees). This was not relevant to this study.

Dr. Eduardo Guimaraes Hourneaux De Moura: Olympus - Consultant (Consulting fees) and Boston Scientific - Consultant (Consulting fees). These were not relevant to this study.

The other authors declare no potential conflict of interest.

Abstract:
Background/Aims: Noninvasive ampullary neoplasms may be removed by surgery or endoscopy. However, given the morbidity and mortality associated with surgery, endoscopic papillectomy (EP) is the preferred approach. Radiofrequency ablation (RFA) after EP has emerged as a promising alternative therapy to avoid surgery after incomplete EP. Our goal was to evaluate the efficacy and safety of RFA for residual or recurrent lesions with intraductal extension after endoscopic papillectomy.
Methods: The inclusion criteria include clinical trials, cohort studies, and case series evaluating patients with residual or recurrent lesions with intraductal extension after EP treated with RFA. Case reports, duplicated data, follow-up period of fewer than 10 months were excluded. The metanalysis evaluated adverse events, surgical conversion rate, clinical success and recurrence.
Results: Seven studies were selected, totaling 124 patients. RFA was associated with a clinical success rate of 75.7% (95% CI 65.0-88.0%; I2=23.484) in a mean follow-up period greater than 10 months. However, the biliary stricture rate was 22.2% (95% CI 12.1-28.4%; I2=61.030), 14.3% of pancreatitis (95% CI 8.8-22.3%; I2<0.001), 7.0% of cholangitis (95% CI 3.3-14.5%; I2<0.001), 4.0% of bleeding (95% CI 1.7-9.3%; I2<0.001) and recurrence of 24.3% (95% CI 16.0-35.0%; I2=23.484).
Conclusions: RFA is feasible and appears to be effective for managing residual or recurrent lesions with intraductal extension after EP. However, long-term follow-up and high-quality studies are required to confirm our findings.

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INTRODUCTION

The early diagnosis of papillary neoplasia is challenging since the symptoms usually appear in cases of advanced carcinoma.[1] Most cases are diagnosed incidentally during endoscopy for other indications. In addition, endoscopic biopsies are mandatory for histologic confirmation of adenoma before the therapeutic approach.[2,3]

Surgery is considered the gold standard procedure for therapeutic resection. However, endoscopy can be considered in selected cases because as it is a less invasive approach.[2,3] ESGE guidelines recommend endoscopic papillectomy (EP) in ampullary adenoma without intraductal extension but suggest considering surgical treatment when the endoscopic procedure is not feasible (size > 40 mm and intraductal involvement > 20 mm).[1] Despite the effectiveness of endoscopic resection and the lower morbidity and mortality compared with pancreatoduodenectomy, it determines recurrence in about 30% of cases.[4–9] Given the recurrence rate of endoscopic resection and the risks related to surgery, recent studies have shown the benefits of radiofrequency ablation (RFA) for residual lesions and as a complementary therapy for an intraductal extension.[2,4,5,10–15]

RFA acts directly on residual neoplastic tissue, causing necrosis from the resulting thermal energy, and determines highly immunogenic intracellular components like heat shock proteins.[16–18] To better understand the outcomes of this novel approach, we performed a systematic review and meta-analysis evaluating the efficacy and safety of RFA for residual or recurrent lesions with intraductal extension after EP .

MATERIAL AND METHODS

Protocol and registration

The study was registered in the International Prospective Register of Systematic Reviews (PROSPERO) with the file number (CRD42023395394). This review and meta-analysis were performed under the recommendations of the Cochrane Handbook of Systematic Reviews of Interventions and the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) Guidelines. (Table 1)[19]

Eligibility criteria

The inclusion criteria include clinical trials, cohort studies, and case series that investigate patients with residual or recurrent lesions extending into the pancreatic or biliary duct after EP treated with RFA. Exclusion criteria included case reports, insufficient data, studies from the same authors that had been updated, and follow-up period of fewer than 10 months.

Search and study selection

The studies were identified through a search in electronic databases (MEDLINE, Embase, Cochrane), from inception until October 20, 2023. No date or language restrictions were set. Two reviewers achieved the selection of studies independently, and a third reviewer was consulted in cases of disagreement. The following search strategy was used for the MEDLINE database: (Papillary Adenoma OR Adenomas, Bile Duct OR Ampulla of Vater OR Hepatopancreatic Ampulla OR Major Duodenal Papilla OR Bile Duct) AND (Radiofrequency Catheter Ablation OR Electrical Catheter Ablation OR Catheter Ablation OR Radiofrequency OR Ablation Techniques OR Radiofrequency Therapy OR Electrocoagulation OR Electrocautery OR Thermocoagulation)'.

Data collection process

Data extraction was done by filling out a spreadsheet. The following data were extracted: name and year of the study, number of patients undergoing EP, number of patients undergoing RFA, recurrence rate for evaluation of clinical success, surgical conversion rate, number of AEs, including cholangitis, perforation, stenosis, pancreatitis, bleeding.

Risk of bias and quality of studies

For the analysis of the validity, reliability, and relevance of studies, two independent reviewers assessed the risk of bias using the Joanna Briggs Institute Critical Appraisal Tool (https://jbi.global/critical-

appraisal-tools) (table 3), a specific tool for case series that evaluates the following items: patient demographic characteristics, patient history, current clinical condition on presentation, diagnostic tests or assessment methods and their results, intervention(s) or treatment procedure(s), post-intervention clinical condition, adverse events (harms) or unanticipated events, and takeaway lessons. Additionally, a tool from the Robvis website was employed to create a table summarizing the risk of bias analysis (https://www.riskofbias.info/welcome/robvis-visualization-tool). The risk of bias was graduated in low, high or very high risk.

The quality of evidence was appraised using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) system from the GRADEpro - Guideline Development Tool software (McMaster University, Ontario, Canada). This system considers the following items: design, risk of bias, precision, indirect evidence, inconsistency, publication bias, effect magnitude, dose dependence, and confounding bias (Table 4). The quality of evidence was graded as high, moderate, low, or very low. [20]

Outcomes and definitions

Outcomes evaluated were the clinical success, defined as the rate of patients who did not experience a recurrence during follow-up, surgical conversion rate, recurrence, and number of AEs such as biliary stenosis, pancreatitis, and cholangitis.

Data synthesis and statistical analysis

For continuous variables, the mean difference and standard deviation were calculated using inverse variance. For dichotomous variables, the risk difference (RD) was calculated using Mantel–Haenszel, along with a corresponding 95% confidence interval (CI). When the variance was expressed as a range, the mean and variance of the sample were estimated using the Hozo test.[21] Comprehensive Meta-Analysis V4 software was utilized for data analysis, forest plot generation, and confidence interval calculation.[22] Data heterogeneity was assessed and quantified according to the Higgins Method (I^2). Pooled estimates and the 95% confidence interval (CI) were calculated using a random-effects model.

Radiofrequency Ablation

RFA was conducted after endoscopic papillectomy in all patients who exhibited residual or recurrent lesions. ID-RFA was conducted using RFA catheters (ELRA; STARmed, Goyang, Korea) or (Habib EndoHPB, Boston Scientific, London, U.K). The RFA catheters were inserted into the biliary or pancreatic duct through 0.025- or 0.035-inch guidewires.

The ELRA catheter had a diameter of 7 French and a length of 175 cm, equipped with bipolar probes consisting of electrodes of various lengths (11 mm, 18 mm, 22 mm, and 33 mm), employed to accommodate diverse anatomical and geometric variations at the target ablation site. The VIVA Combo generator (STARmed, Seoul, South Korea) was employed for intraductal RFA delivery, providing precise control over power settings, target temperature, and impedance.[14,15,23]

The Habib catheter it is an 8 French (2.7 mm) sizable bipolar RFA probe, extending 180 cm in length, and is equipped with two ring electrodes that are spaced 8 mm apart, and the distal electrode is positioned 5 mm from the front edge. The catheter was attached to an electrosurgical generator, with options including the RITA 1500X from Angiodynamics in Latham, NY, the Erbe system from Surgical Technology Group in Hampshire, England, U.K., or the Beamer from ConMed.[12,13]

Results

Result of searches and characteristics of the included studies

The initial search found a total of 4,546 studies. After removing duplicate articles and reviewing titles and abstracts, 20 case series were found eligible for full-text analysis. We excluded eight case reports. (Figure 1) A total of 12 were utilized for qualitative synthesis and 7 for quantitative synthesis, totaling 124 patients.[12–15,23–25] Five studies were excluded from the quantitative analysis due to duplicate data (Table 2).

Clinical Success

All included studies assessed clinical success. RFA after EP revealed a clinical success rate of 75.7% (95% CI 65.0-88.0%; I^2=23.484). (Figure 2)

Recurrence

All studies reported this outcome. The meta-analysis resulted in a recurrence of 24.3% (95% CI 16.0-35.0%; I^2 <0.001). (Figure 2)

Surgical conversion rate

All studies reported this outcome. The meta-analysis resulted in a surgical conversion rate of 6.7% (95% CI 3.2-13.4%; I^2 <0.001). (Figure 2)

Total adverse events

All included studies reported the rate of adverse events during the follow-up period. The rate of total adverse events of 41.1% (95% CI 30.7-52.4%; I^2=27.541). (Figure 2)

Biliary stricture

All included studies reported the incidence of RFA-related biliary stricture. The incidence of biliary stricture was 22.2% (95% CI 12.1-28.4%; I^2=61.030). (Figure 3)

Pancreatitis

All included studies reported the incidence of RFA-related pancreatitis. The incidence of pancreatitis was 14.3% (95% CI 8.8-22.3%; I^2<0.001). (Figure 3)

Cholangitis

All included studies reported the incidence of RFA-related cholangitis. The incidence of cholangitis was 7.0% (95% CI 3.3-14.5%; I^2<0.001). (Figure 3)

Bleeding

All included studies reported the incidence of RFA-related bleeding. The incidence of bleeding was 4.0% (95% CI 1.7-9.3%; I^2<0.001). (Figure 3)

Perforation

No perforations were related to endoscopic resection and RFA in any of the evaluated studies.

Discussion

This is the first systematic review and meta-analysis evaluating the outcomes of RFA for residual lesions after EP, showing that this technique may be effective in managing this challenging condition but with a very high rate of AEs.

This meta-analysis revealed a high clinical success rate; however, this should be evaluated cautiously due to the short follow-up period of patients and the heterogeneity of the sample. The minimum follow-up period of 10 months and the maximum of 36 months do not allow for an adequate assessment of the recurrence rate. Recent data suggest that recurrence can occur even after 5 years, therefore, follow-up for this period is necessary to assess the recurrence rate properly.[26,27] The heterogeneity of our meta-analysis is demonstrated by including patients with intramucosal ADCs in some studies because adenomas have a lower recurrence rate than ADCs. Furthermore, the included ADCs were not classified by their histological type, and it is well known that the pancreaticobiliary-type is more aggressive than the intestinal-type. Pancreaticobiliary-type and other undifferentiated cancers have a high capacity for local dissemination and a high recurrence rate, deserving a multidisciplinary approach to management.[3,28,29] All guidelines recommend referring the patient for surgery in case of papillary adenocarcinoma.[1–3] However, some authors advocate less invasive procedures for early-stage adenocarcinoma, and it is essential to differentiate Tis carcinoma, which does not invade the lamina propria and is associated with a lower incidence of lymph node invasion, and T1a carcinoma, which invades a lamina propria and is associated with more than 20% lymph node invasion.[1,3,30] ESGE recommends that endoscopic papillectomy for Tis ampullary cancer might be considered sufficient when there is no residual disease.[1] Thus, some studies have reported that EP alone may achieve curative resection in cases of Tis and T1a carcinoma without lymphatic invasion.[30–32] Moreover, despite the absence of studies evaluating the use of RFA for neuroendocrine tumors (NET), the study published by Dahel et al. included a single patient with this neoplasm.[24] There are no available studies

assessing its use for duodenal NET; however, two meta-analyses published in 2023 demonstrated positive outcomes in the use of RFA for pancreatic NET.[33,34]

Additionally, the rate of AEs was higher than evidenced in studies that analyze RFA for malignant biliary strictures.[35,36] The most common AE was biliary stenosis, but we couldn't evaluate the correlation with the absence of a prophylactic biliary stent. ESGE suggests using a temporary biliary stent with a complementary technique, such as RFA for ampullary adenoma with ≤ 20 mm intraductal extension. The Expert Consensus mentioned that stent placement in case of residual tissue after EP can facilitate the inspection of the distal CBD, but no consensus was achieved about this matter.(2) Additionally, ablation with higher power and longer time may be associated with a higher incidence of biliary stricture. Most studies have applied energy of 7 to 10 W for 90 to 120 seconds for each intrabiliary RFA application. Although, it was also not possible to evaluate this correlation based on the data available, further research can identify the optimal settings for these parameters for treating ampullary adenomas.[15,23,37]

In this meta-analysis, the second most significant AEs was pancreatitis. Unfortunately, it was not possible to classify the severity of the AEs evaluated due to the scarcity of data provided. In the updated ESGE Guideline on ERCP-related AEs, pancreatic duct stenting, rectal nonsteroidal anti-inflammatory drugs, and high-volume hydration were recommended to prevent post-ERCP pancreatitis.[1,38] These recommendations can also be applied to patients after EP to decrease the risk of post-ERCP pancreatitis. In a subgroup analysis, including 3 studies involved in the meta-analysis, there were 6 (13%) cases of pancreatitis among the 44 patients who used prophylactic stents, representing a significant rate of events. However, it was not possible to carry out a comparative analysis with the group of patients who did not use a stent due to the lack of data.

In addition to the limitations already discussed, our study has other relevant limitations. The most important is the small number of studies and patients included in the analysis. However, the reason for that is the lack of large studies on this subject, and we performed the analysis with the available data. Also, as it is an approach that has emerged in recent years, no randomized clinical trials and cohort studies are available, contributing to the high risk of bias in all the included studies.

Furthermore, while some studies conduct RFA for patients with residual lesions shortly after papillectomy, others address patients with either residual or recurrent lesions. However, the lack of standardization in defining recurrence across these studies presents another limitation. This inconsistency impedes a thorough assessment of RFA efficacy for each specific situation separately. Relevant data such as the number of radiofrequency sessions performed on each patient, the use of combined therapy involving argon plasma coagulation (APC), and the correlation between the type of stent and incidence of pancreatitis or bile duct narrowing were only reported in some studies, which precludes a more detailed analysis.

In summary, this study showed that using RFA for residual lesions after EP has a significant clinical success rate, although it reveals a high rate of AEs. These events may be associated with factors such as the absence of prophylactic biliary or pancreatic stents. With our results, we believe this method may become the gold standard technique to avoid complex surgeries with a high rate of complications, such as pancreaticoduodenectomy. Despite the high rate of AEs revealed in our meta-analysis, most of them were mild and self-limited, and they become less relevant when comparing surgery-related complications.

Conclusion

RFA is feasible and appears to be effective for managing residual lesions after endoscopic papillectomy. However, long-term follow-up and high-quality studies are required to confirm our findings. In addition, to improve safety before disseminating this therapy, we should carefully assess the high rate of AEs related to RFA after EP.

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Figures and Tables Legends

Figure 1. PRISMA flow chart.[19]

Figure 2. Forest plot for rate of clinical success, total adverse rates, surgical conversion rate and recurrence using the random-effect model. CI, confidence interval.

Figure 3. Forest plot for rate of adverse events, using the random-effect model. CI, confidence interval.

Table 1. Prisma Checklist.[19]

Table 2. Summary of the included studies.

CS: Case Series; HGD: High-Grade Dysplasia; LGD: Low-Grade Dysplasia; Tis Carcinoma in-situ; ADC: Adenocarcinoma; IMC: Intramucosal Carcinoma; mo: Months; NM: Not Mentioned; s: seconds; CDB: Common Biliary Duct; PD: Pancreatic Duct; NET: Neuroendocrine Tumor;

Table 3. JBI tool for risk of bias assessment.

No	
Unclear	
Yes	
Include	

D1: Inclusion Criteria
D2: Condition Evaluation
D3: Condition Identification
D4: Consecutive inclusion
D5: Complete Inclusion
D6: Study Demographic report
D7: Clinical Information
D8: Outcomes and Follow-up
D9: Site demographic information
D10: Statistical Analysis

Table 4. Quality of evidence by Grading of Recommendations Assessment, Development and Evaluation (GRADE) guidelines.[20]

Tables

Table 1

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	Page 1
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	Page 3
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	Page 4
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	Page 4
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	Page 5
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	Page 5
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Page 5*
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	Page 5
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	Page 5
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	Page 6
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	Page 6
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	Page 6
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	Page 6
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	Page 6
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	Page 6
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	Page 6
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	Page 6

Section and Topic	Item #	Checklist item	Location where item is reported
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	Page 6
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	Page 6
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	Page 6
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	Page 6
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	Page 6
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Page 6
Study characteristics	17	Cite each included study and present its characteristics.	Page 6
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Page 7
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Page 7
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	Page 7
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	Page 7
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	Page 7
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	Page 7
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	Page 7
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	Page 7
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	Page 8
	23b	Discuss any limitations of the evidence included in the review.	Page 9
	23c	Discuss any limitations of the review processes used.	Page 9
	23d	Discuss implications of the results for practice, policy, and future research.	Page 8
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	Page 2
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	Page 2
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	Page 2
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	Page 2
Competing interests	26	Declare any competing interests of review authors.	Page 2
Availability of data, code and other	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for	Page 5

Section and Topic	Item #	Checklist item	Location where item is reported
materials		all analyses; analytic code; any other materials used in the review.	

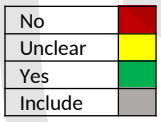
Table 2

Study	Study Design	Age (Mean)	Number of Patients (RFA)	Neoplasia	Devices	Duration (RFA)	Power Setting (RFA)	Number of Sessions (mean)	Follow up (mean)
Cho et al. 2023[15]	Prospective Series	61.2	29	21(LGD); 8 (HGD);	ELRA (STARmed)	120s (CBD) 30 (PD)	7w	1.5	25 mo
Dahel et al. 2023[24]	Retrospective Series	NM	25	10(LGD);5(HGD); 3(CIS); 1(ADC);1(NET)	NM	NM	NM	1.3	36 mo
Trigali et al. 2021[14]	Prospective Series	73	9	4(LGD); 4(HGD); 1(CIM)	ELRA (STARmed)	120s	10w	1.6	26.2 mo
Choi et al. 2021[23]	Retrospective Series	56.7	10	8(LGD); 2(HGD);	ELRA (STARmed)	65s (CBD) 15s (PD)	7w	1	10 mo
Bruwier et al.2020[25]	Prospective Series	73	17	14(LGD); 3(HGD);	ELRA (STARmed)	30-240s	7-10w	1.8	12 mo
Camus et al.2018[12]	Prospective Series	67	20	15(LGD); 5(HGD)	Habib (Boston)	30s	10w	1	12 mo
Rustagi et al.2016[13]	Retrospective Series	68	14	08(LGD); 4(HG); 1 (ADC)	Habib (Boston)	90s	7-10w	1.6	16 mo

CS: Case Series; HGD: High-Grade Dysplasia; LGD: Low-Grade Dysplasia; Tis Carcinoma in-situ; ADC: Adenocarcinoma; IMC: Intramucosal Carcinoma; mo: Months; NM: Not Mentioned; s: seconds; CDB: Common Biliary Duct; PD: Pancreatic Duct; NET: Neuroendocrine Tumor;

Table 3

Study	D1	D2	D3	D4	D5	D6	D7	D8	D9	D10	Over
Cho et al.											
Dahel et al.											
Trigali et al.											
Choi et al.											
Bruwier et al.											
Camus et al.											
Rustagi et al.											



D1: Inclusion Criteria
D2: Condition Evaluation
D3: Condition Identification
D4: Consecutive inclusion
D5: Complete Inclusion
D6: Study Demographic report
D7: Clinical Information
D8: Outcomes and Follow-up
D9: Site demographic information
D10: Statistical Analysis

Table 4

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Radioablation		Relative (95% CI)	Absolute (95% CI)	
7	observational studies	not serious	not serious	not serious	not serious	none	50/124 (40.3%)	-	-	-	⨁⨁◯◯ Low
7	observational studies	not serious	not serious	not serious	not serious	none	95/124 (76.6%)	-	-	-	⨁⨁◯◯ Low
7	observational studies	not serious	not serious	not serious	not serious	none	3/124 (2.4%)	-	-	-	⨁⨁◯◯ Low
7	observational studies	not serious	not serious	not serious	not serious	none	4/124 (3.2%)	-	-	-	⨁⨁◯◯ Low
7	observational studies	not serious	not serious	not serious	not serious	none	15/124 (12.1%)	-	-	-	⨁⨁◯◯ Low
7	observational studies	not serious	not serious	not serious	not serious	none	28/124 (22.6%)	-	-	-	⨁⨁◯◯ Low
7	observational studies	not serious	not serious	not serious	not serious	none	6/124 (4.8%)	-	-	-	⨁⨁◯◯ Low

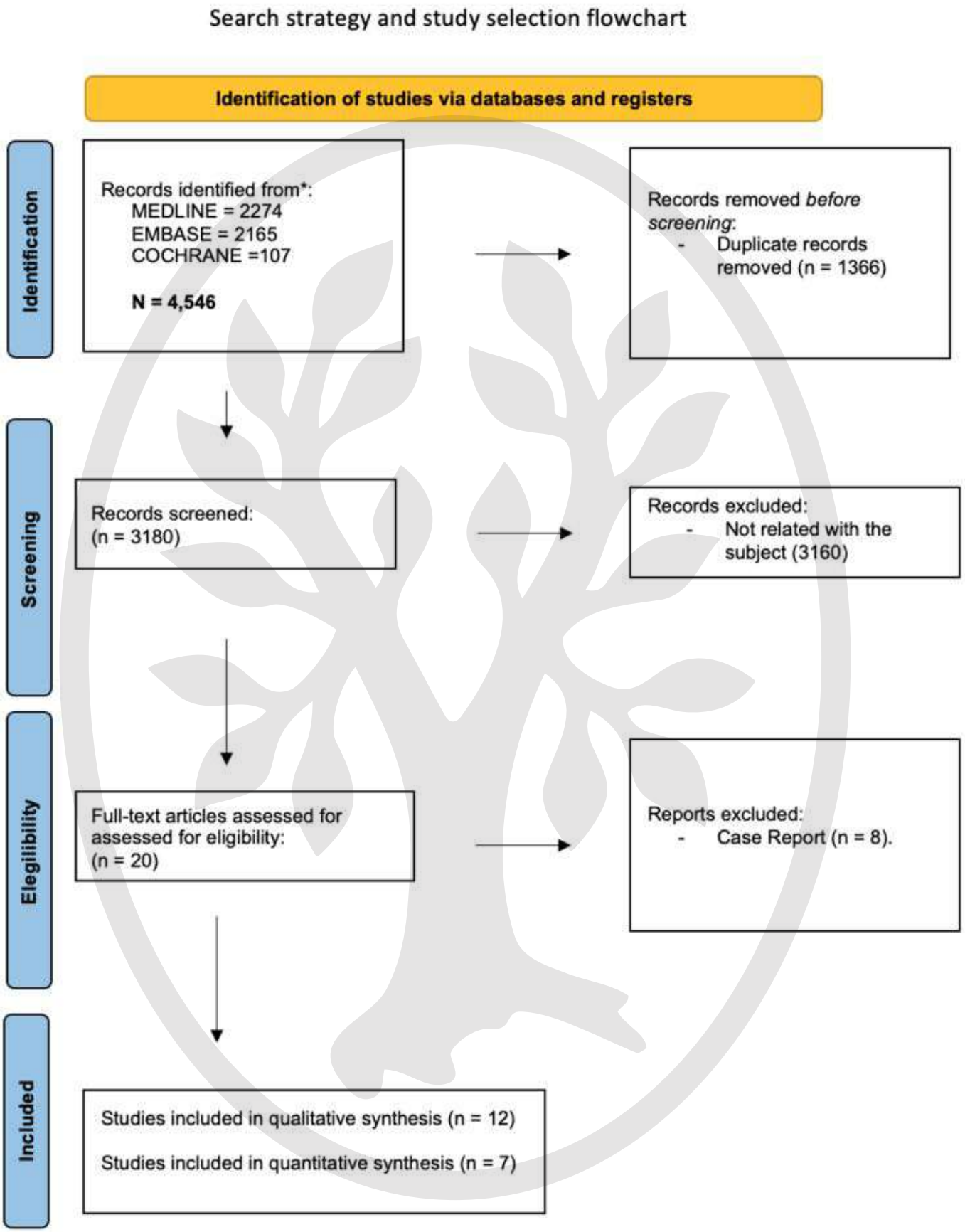
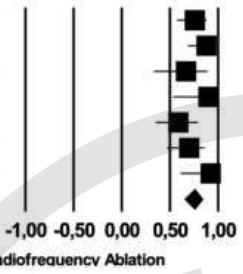


Figure 1.

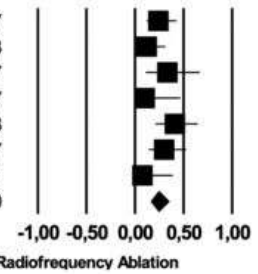
Clinical Success

Study name	Event rate	Lower limit	Upper limit
Cho et al.	0,759	0,573	0,880
Dahel et al.	0,880	0,687	0,961
Tringali et al.	0,667	0,333	0,889
Choi et al.	0,900	0,533	0,986
Bruwier et al.	0,588	0,352	0,790
Camus et al.	0,700	0,473	0,859
Rustagi et al.	0,923	0,609	0,989
	0,757	0,650	0,840



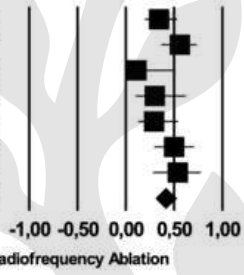
Recurrence

Study name	Event rate	Lower limit	Upper limit
Cho et al.	0,241	0,120	0,427
Dahel et al.	0,120	0,039	0,313
Tringali et al.	0,333	0,111	0,667
Choi et al.	0,100	0,014	0,467
Bruwier et al.	0,412	0,210	0,648
Camus et al.	0,300	0,141	0,527
Rustagi et al.	0,077	0,011	0,391
	0,243	0,160	0,350



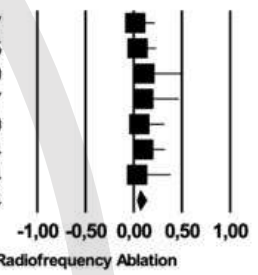
Total Adverse Events

Study name	Event rate	Lower limit	Upper limit
Cho et al.	0,345	0,197	0,531
Dahel et al.	0,560	0,366	0,737
Tringali et al.	0,111	0,015	0,500
Choi et al.	0,300	0,100	0,624
Bruwier et al.	0,294	0,128	0,542
Camus et al.	0,500	0,294	0,706
Rustagi et al.	0,538	0,282	0,776
	0,411	0,307	0,524



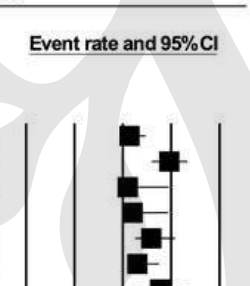
Surgical Conversion Rate

Study name	Event rate	Lower limit	Upper limit
Cho et al.	0,017	0,001	0,217
Dahel et al.	0,040	0,006	0,235
Tringali et al.	0,111	0,015	0,500
Choi et al.	0,100	0,014	0,467
Bruwier et al.	0,059	0,008	0,320
Camus et al.	0,100	0,025	0,324
Rustagi et al.	0,036	0,002	0,384
	0,067	0,032	0,134



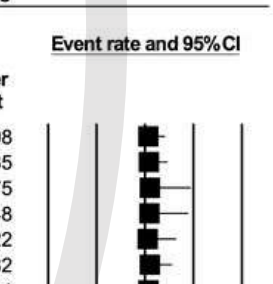
Biliary Stricture

Study name	Event rate	Lower limit	Upper limit
Cho et al.	0,069	0,017	0,238
Dahel et al.	0,480	0,296	0,669
Tringali et al.	0,050	0,003	0,475
Choi et al.	0,100	0,014	0,467
Bruwier et al.	0,294	0,128	0,542
Camus et al.	0,150	0,049	0,376
Rustagi et al.	0,385	0,170	0,656
	0,220	0,113	0,383



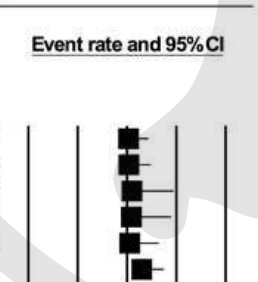
Bleeding

Study name	Event rate	Lower limit	Upper limit
Cho et al.	0,034	0,005	0,208
Dahel et al.	0,040	0,006	0,235
Tringali et al.	0,050	0,003	0,475
Choi et al.	0,045	0,003	0,448
Bruwier et al.	0,028	0,002	0,322
Camus et al.	0,050	0,007	0,282
Rustagi et al.	0,036	0,002	0,384
	0,040	0,017	0,093



Cholangitis

Study name	Event rate	Lower limit	Upper limit
Cho et al.	0,017	0,001	0,217
Dahel et al.	0,019	0,001	0,244
Tringali et al.	0,050	0,003	0,475
Choi et al.	0,045	0,003	0,448
Bruwier et al.	0,028	0,002	0,322
Camus et al.	0,150	0,049	0,376
Rustagi et al.	0,077	0,011	0,391
	0,070	0,033	0,145



Pancreatitis

Study name	Event rate	Lower limit	Upper limit
Cho et al.	0,207	0,096	0,390
Dahel et al.	0,080	0,020	0,269
Tringali et al.	0,111	0,015	0,500
Choi et al.	0,200	0,050	0,541
Bruwier et al.	0,028	0,002	0,322
Camus et al.	0,150	0,049	0,376
Rustagi et al.	0,077	0,011	0,391
	0,143	0,088	0,223