Thieme

Radiofrequency ablation for ampullary neoplasia with intraductal extension after endoscopic papillectomy: Systematic review and meta-analysis

OPEN ACCESS

Authors

Davi Lucena Landim[1], Diogo Turiani Hourneaux de Moura[1], Bruno Salomao Hirsch[1], Guilherme Henrique Peixoto de Oliveira[1], Matheus de Oliveira Veras[1], Felipe Giacobo Nunes[1], Paulo Ricardo Pavanatto Cavassola[1], Wanderley Marques Bernardo[1], Sultan Mahmood[2], Eduardo Guimarães Hourneaux de Moura[1]

Institutions

1 Gastrointestinal Endoscopy Unit, University of Sao Paulo, Sao Paulo, Brazil
2 Department of Medicine and Division of Gastroenterology, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, United States

Keywords

RFA and ablative methods, Strictures, Endoscopy Upper GI Tract, Pancreatobiliary (ERCP/PTCD)

received 20.7.2023
accepted after revision 6.12.2023
accepted manuscript online 11.12.2023

Bibliography

Endosc Int Open 2024; 12: E440–E447
DOI 10.1055/a-2226-0928
ISSN 2364-3722

© 2024. The Author(s).

This is an open access article published by Thieme under the terms of the Creative Commons Attribution-NonDerivative-NonCommercial License, permitting copying and reproduction so long as the original work is given appropriate credit. Contents may not be used for commercial purposes, or adapted, remixed, transformed or built upon. (https://creativecommons.org/licenses/by-nc-nd/4.0/)

Georg Thieme Verlag KG, Rüdigerstraße 14, 70469 Stuttgart, Germany

Corresponding author

Dr. Davi Lucena Landim, University of Sao Paulo, Gastrointestinal Endoscopy Unit, Sao Paulo, Brazil
davilandimm@gmail.com

ABSTRACT

Background and study 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.

Patients and 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, and studies with follow-up periods <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% confidence interval [CI] 65.0-88.0%; $I^2 = 23.484$) in a mean follow-up period <10 months. However, the biliary stricture rate was 22.2% (95% CI 12.1-28.4%; $I^2 = 61.030$), 14.3% of pancreatitis (95% CI 8.8-22.3%; $I^2 < 0.001$), 7.0% of cholangitis (95% CI 3.3–14.5%; $I^2 < 0.001$), 4.0% of bleeding (95% CI 1.7-9.3%; $I^2 < 0.001$), and recurrence of 24.3% (95% CI 16.0-35.0%; $I^2 = 23.484$).

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.

Introduction

Early diagnosis of papillary neoplasia is challenging because 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]. European Society of Gastrointestinal Endoscopy 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, 5, 6, 7, 8, 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, 11, 12, 13, 14, 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, 17, 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.

Patients 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 [19].

Eligibility criteria

The inclusion criteria included 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 adverse events (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 1**), 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, AEs (harms) or unanticipa-

▶ **Table 1** JBI tool for risk of bias assessment.

Study	D1	D2	D3	D4	D5	D6	D7	D8	D9	D10	Overall
Cho et al.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Include
Dahel et al.	Yes	Unclear	Yes	Yes	Yes	No	Yes	Yes	No	Unclear	Include
Trigali et al.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Include
Choi et al.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Include
Bruwier et al.	Yes	Unclear	Unclear	Yes	Yes	No	Yes	Yes	No	Unclear	Include
Camus et al.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Include
Rustagi et al.	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	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

ted 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 2**). 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 CI calculation [22]. Data heterogeneity was assessed and quantified according to the Higgins Method (I^2). Pooled estimates and the 95% CIs were calculated using a random-effects model.

Radiofrequency ablation

RFA was conducted after EP 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.

▶**Table 2** Quality of evidence by Grading of Recommendations Assessment, Development and Evaluation (GRADE) guidelines [20].

Certainty assessment							No. 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

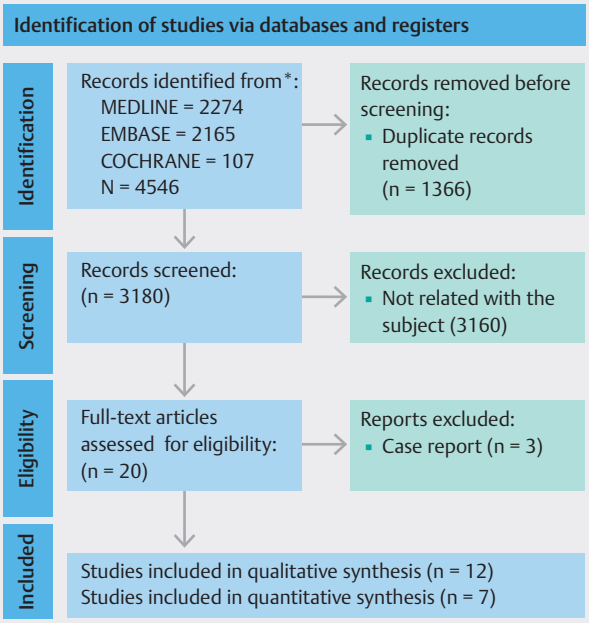
The ELRA catheter had a diameter of 7F and a length of 175 cm, equipped with bipolar probes consisting of electrodes of various lengths (11 mm, 18 mm, 22 mm, and 33 mm), employed to accommodate diverse anatomical and geometric variations at the target ablation site. The VIVA Combo generator (STARmed, 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 8F (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, New York, United States the Erbe system from Surgical Technology Group in Hampshire, England, UK, 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 (▶ **Fig. 1**). A total of 12 were utilized for qualitative synthesis and seven for quantitative synthesis, totaling 124 patients [12, 13, 14, 15, 23, 24, 25]. Five studies were excluded from the quantitative analysis due to duplicate data (▶ **Table 3**).

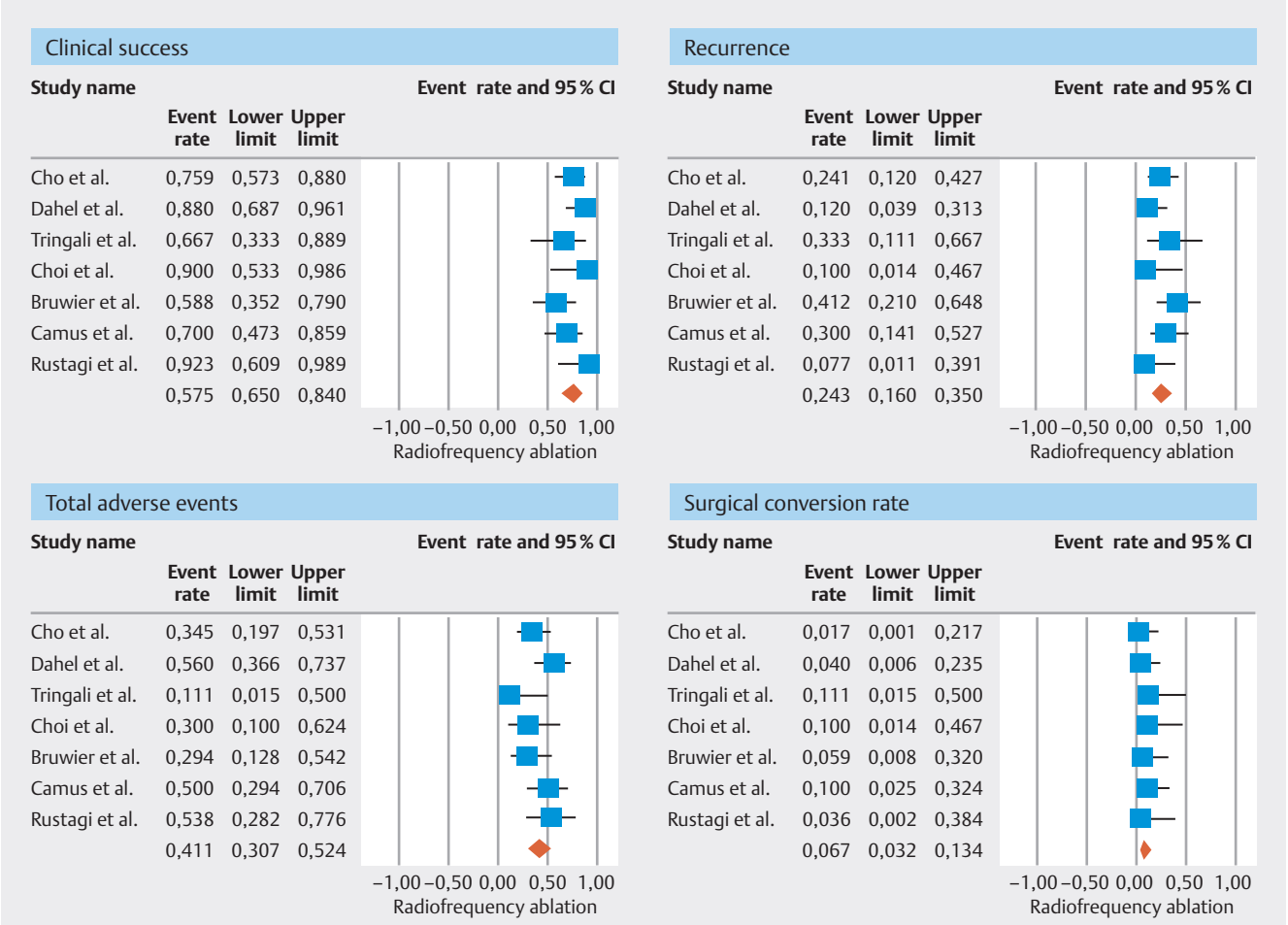


▶ **Fig. 1** PRISMA flow chart [19].

▶ **Table 3** Summary of the included studies.

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)	120 s (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)	65 s (CBD) 15 s (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; CBD, common bile duct; PD, pancreatic duct; NET, neuroendocrine tumor.



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

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) (▶ **Fig. 2**).

Recurrence

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

Total adverse events

All included studies reported the rate of AEs during the follow-up period. The rate of total AEs of 41.1% (95% CI 30.7–52.4%; I^2 = 27.541) (▶ **Fig. 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) (▶ **Fig. 3**).

Pancreatitis

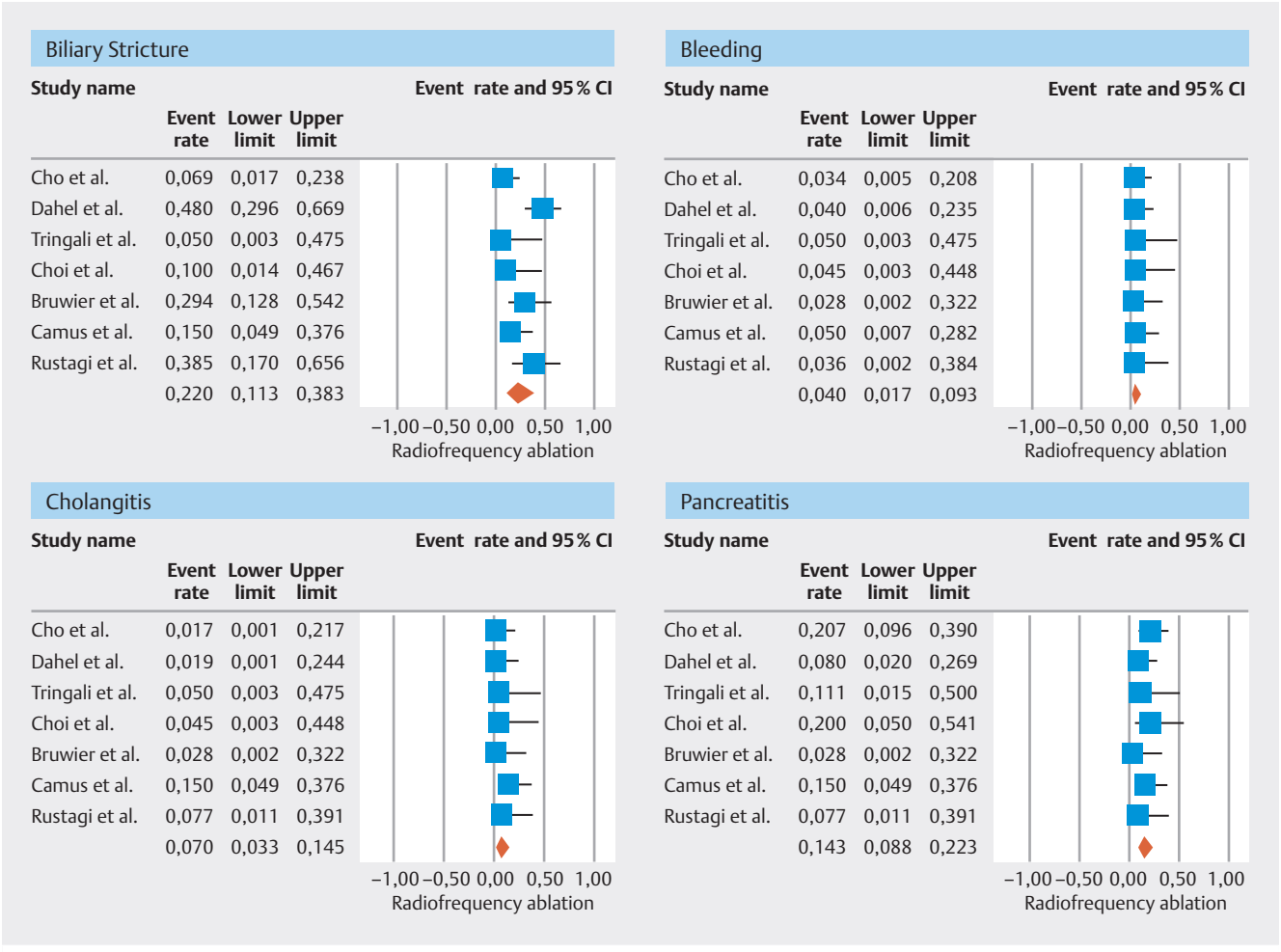
All included studies reported the incidence of RFA-related pancreatitis. The incidence of pancreatitis was 14.3% (95% CI 8.8–22.3%; $I^2 < 0.001$) (▶ **Fig. 3**).

Cholangitis

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



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

Perforation

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

Discussion

This was 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, 2, 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 EP 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, 31, 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].

In addition, 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 could not 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 common bile duct, but no consensus was achieved about this matter [2]. In addition, 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 three studies involved in the meta-analysis, there were six cases (13%) 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, 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.

Conclusions

RFA is feasible and appears to be effective for managing residual lesions after EP. 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.

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.

References

[1] Vanbiervliet G, Strijker M, Arvanitakis M et al. Endoscopic management of ampullary tumors: European Society of Gastrointestinal Endoscopy (ESGE) Guideline. Endoscopy 2021; 53: 429–448

[2] Fritzsche JA, Fockens P, Barthet M et al. Expert consensus on endoscopic papillectomy using a Delphi process. Gastrointest Endosc 2021; 94: 760–773.e18

[3] Itoi T, Ryozawa S, Katanuma A et al. Clinical practice guidelines for endoscopic papillectomy. Digest Endosc 2022; 34: 394–411

[4] Yang J, Han S, Zhou H et al. The efficacy and safety of endoscopic papillectomy combined with endobiliary radiofrequency ablation for ampullary neoplasms with intraductal biliary extension. Techniq Innovations Gastrointest Endosc 2022; 24: 240–245

[5] Binmoeller KF, Boaventura S, Ramsperger K et al. Endoscopic snare excision of benign adenomas of the papilla of Vater. Gastrointest Endosc 1993; 39: 127–131

[6] Jordan P. Treatment of ampullary villous adenomas that may harbor carcinoma. J Gastrointest Surg 2002; 6: 770–775

[7] TranTin C, Vitale GC et al. Ampullary tumors: endoscopic versus operative management. Surg Innovation 2004; 11: 255–263

[8] Ceppa EP, Burbridge RA, Rialon KL et al. Endoscopic versus surgical ampullectomy. Annals Surgery 2013; 257: 315–322

[9] Gracient A, Delcenserie R, Chatelain D et al. Endoscopic or surgical ampullectomy for intramucosal ampullary tumor: the patient populations are not the same. J Visceral Surgery 2020; 157: 183–191

[10] Norton ID, Gostout CJ, Baron TH et al. Safety and outcome of endoscopic snare excision of the major duodenal papilla. Gastrointest Endosc 2002; 56: 239–243

[11] Nam K, Song TJ, Kim RE et al. Usefulness of argon plasma coagulation ablation subsequent to endoscopic snare papillectomy for ampullary adenoma. Digest Endosc 2018; 30: 485–492

[12] Camus M, Napoléon B, Vienne A et al. Efficacy and safety of endobiliary radiofrequency ablation for the eradication of residual neoplasia after endoscopic papillectomy: a multicenter prospective study. Gastrointest Endosc 2018; 88: 511–518

[13] Rustagi T, Irani S, Reddy DN et al. Radiofrequency ablation for intraductal extension of ampullary neoplasms. Gastrointest Endosc 2017; 86: 170–176

[14] Tringali A, Matteo MV, Orlandini B et al. Radiofrequency ablation for intraductal extension of ampullary adenomatous lesions: proposal for a standardized protocol. Endosc Int Open 2021; 09: E749–E755

[15] Cho SH, Oh D, Song TJ et al. Long-term outcomes of endoscopic intraductal radiofrequency ablation for ampullary adenoma with intraductal extension after endoscopic snare papillectomy. Gut Liver 2023; 17: 638–646

[16] Haen SP, Pereira PL, Salih HR et al. More than just tumor destruction: immunomodulation by thermal ablation of cancer. Clin Develop Immunol 2011; 2011: 1–19

[17] Ali MY, Grimm CF, Ritter M et al. Activation of dendritic cells by local ablation of hepatocellular carcinoma. J Hepatol 2005; 43: 817–822

[18] Weismüller TJ. Role of intraductal RFA: A novel tool in the palliative care of perihilar cholangiocarcinoma. Visceral Mede 2021; 37: 39–47

[19] Page MJ, Moher D, Bossuyt PM et al. PRISMA 2020 explanation and elaboration: updated guidance and exemplars for reporting systematic reviews. BMJ 2021: doi:10.1136/bmj.n160

[20] GRADEpro GDT: GRADEpro Guideline Development Tool Software. McMaster University and Evidence Prime, 2023. Available from gradepro.org.

[21] Hozo SP, Djulbegovic B, Hozo I. Estimating the mean and variance from the median, range, and the size of a sample. BMC Med Res Method 2005; 5: 13

[22] Borenstein M, Hedges L, Higgins J et al. Comprehensive Meta-Analysis Version 4. Englewood, NJ: Biostat; 2022

[23] Choi YH, Yoon SB, Chang JH et al. The safety of radiofrequency ablation using a novel temperature-controlled probe for the treatment of residual intraductal lesions after endoscopic papillectomy. Gut Liver 2021; 15: 307–314

[24] Dahel Y, Giovannini M, Pesenti C et al. Efficacy of biliary radiofrequency ablation for the treatment of residual and recurrence neoplasia after endoscopic papillectomy. Endoscopy 2023; 55: 51–52

[25] Bruwier L, Meunier C, Leuhg-Ki E et al. Can we ameliorate the safety of intraductal radiofrequency ablation for persistent dysplasia after endoscopic ampullectomy? Endoscopy 2020; 52: 133–134

[26] Fritzsche JA, Klein A, Beekman MJ et al. Endoscopic papillectomy; a retrospective international multicenter cohort study with long-term follow-up. Surg Endosc 2021; 35: 6259–6267

[27] Sahar N, Krishnamoorthi R, Kozarek RA et al. Long-term outcomes of endoscopic papillectomy for ampullary adenomas. Digest Dis Sci 2020; 65: 260–268

[28] Alvarez-Sanchez M-V, Oria I, Luna OB et al. Can endoscopic papillectomy be curative for early ampullary adenocarcinoma of the ampulla of Vater? Surg Endosc 2017; 31: 1564–1572

[29] Fernández Moro C, Fernandez-Woodbridge A, Alistair D'souza M et al. Immunohistochemical typing of adenocarcinomas of the pancreatobiliary system improves diagnosis and prognostic stratification. PLoS One 2016; 11: e0166067

[30] Yamamoto K, Itoi T, Sofuni A et al. Expanding the indication of endoscopic papillectomy for T1a ampullary carcinoma. Digest Endosc 2019; 31: 188–196

[31] Salmi S, Ezzedine S, Vitton V et al. Can papillary carcinomas be treated by endoscopic ampullectomy? Surg Endosc 2012; 26: 920–925

[32] Yoon SM, Kim M-H, Kim MJ et al. Focal early stage cancer in ampullary adenoma: surgery or endoscopic papillectomy? Gastrointest Endosc 2007; 66: 701–707

[33] Khoury T, Sbeit W, Fusaroli P et al. Safety and efficacy of endoscopic ultrasound-guided radiofrequency ablation for pancreatic neuroendocrine neoplasms: Systematic review and meta-analysis. Digest Endosc 2023: doi:10.1111/den.14681

[34] Armellini E, Facciorusso A, Crinò SF. Efficacy and safety of endoscopic ultrasound-guided radiofrequency ablation for pancreatic neuroendocrine tumors: a systematic review and metanalysis. Medicina (B Aires) 2023; 59: 359

[35] Sofi AA, Khan MA, Das A et al. Radiofrequency ablation combined with biliary stent placement versus stent placement alone for malignant biliary strictures: a systematic review and meta-analysis. Gastrointest Endosc 2018; 87: 944–951.e1

[36] Yoon SM, Kim M-H, Kim MJ et al. Focal early stage cancer in ampullary adenoma: surgery or endoscopic papillectomy? Gastrointest Endosc 2007; 66: 701–707

[37] Lee YN, Jeong S, Choi HJ et al. The safety of newly developed automatic temperature-controlled endobiliary radiofrequency ablation system for malignant biliary strictures: A prospective multicenter study. J Gastroenterol Hepatol 2019: doi:10.1111/jgh.14657

[38] Dumonceau J-M, Kapral C, Aabakken L et al. ERCP-related adverse events: European Society of Gastrointestinal Endoscopy (ESGE) Guideline. Endoscopy 2020; 52: 127–149