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Annual

Advances and Innovations in Endoscopic Oncology and Multidisciplinary Gastrointestinal Cancer Care

Endoscopic Ablation: Now and the Future

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Disclosures

- Consultant for Boston Scientific, Fuji, Mauna Kea Technologies, NanOlogy, Olympus, and Steris.

This presentation and/or comments will be free of any bias toward or promotion of the above referenced companies or their product(s) and/or other business interests.

This presentation and/or comments will provide a balanced, non-promotional, and evidence-based approach to all diagnostic, therapeutic and/or research related content.

This presentation has been peer-reviewed and no conflicts were noted.

Overview

OBJECTIVES

- ERCP and based thermal ablation
- EUS based thermal ablation
- Future applications

Cholangiocarcinoma:

ERCP Based ABLATION

A brief review of Cholangiocarcinoma pathology

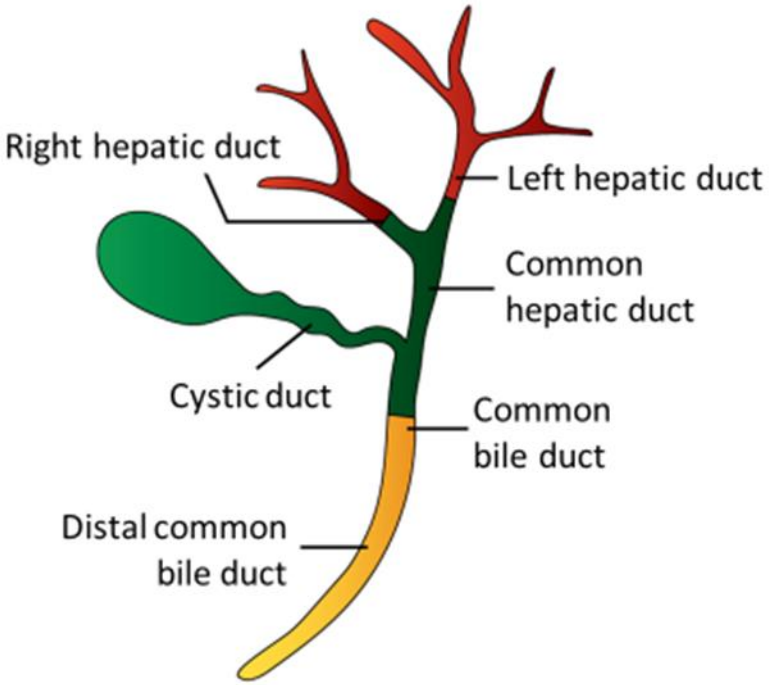
Epidemiology

- **Each year, approximately 8000- 11,00 cases of cholangiocarcinoma** in the United States
  - Less than Gallbladder
  - Less than HCC (Hepatocellular carcinoma)

- **2nd most common primary liver malignancy**
  - HCC is most common
- **Increasing incidence**

- **High mortality – about 11-15% survival at 5 years**
  - **Highly variable survival based on stage and intra vs extrahepatic disease (intrahepatic being worse prognosis)**

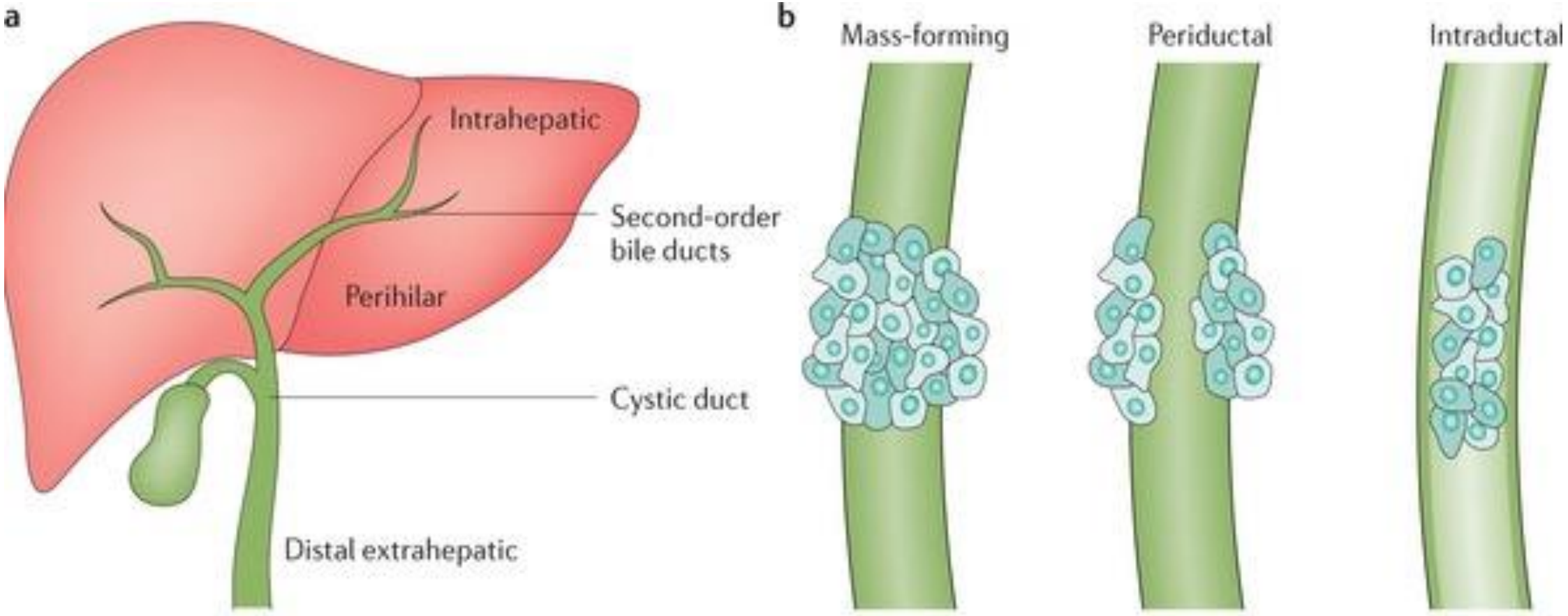
A brief review of Cholangiocarcinoma pathology



Cholangiocarcinomas are cancers which arise from the cells lining the bile ducts.

- **Adenocarcinoma**
- More than 90% of CC are well- to moderately-differentiated adenocarcinomas with tendency to develop desmoplastic reaction and early perineural invasion.
- Sometimes arise from PSC (primary sclerosing cholangitis)
- Major categories:
  1) **ICC: Intrahepatic**
  2) **ECC: Extrahepatic**
  3) **Perihilar**
  4) **Gall Bladder**

American Joint Commission on Cancer (AJCC) has **TNM staging guidelines for Cholangiocarcinoma**



Nature Reviews Gastroenterology & Hepatology 13, 261–280 (2016)

A brief review of Cholanogiocarcinoma pathology

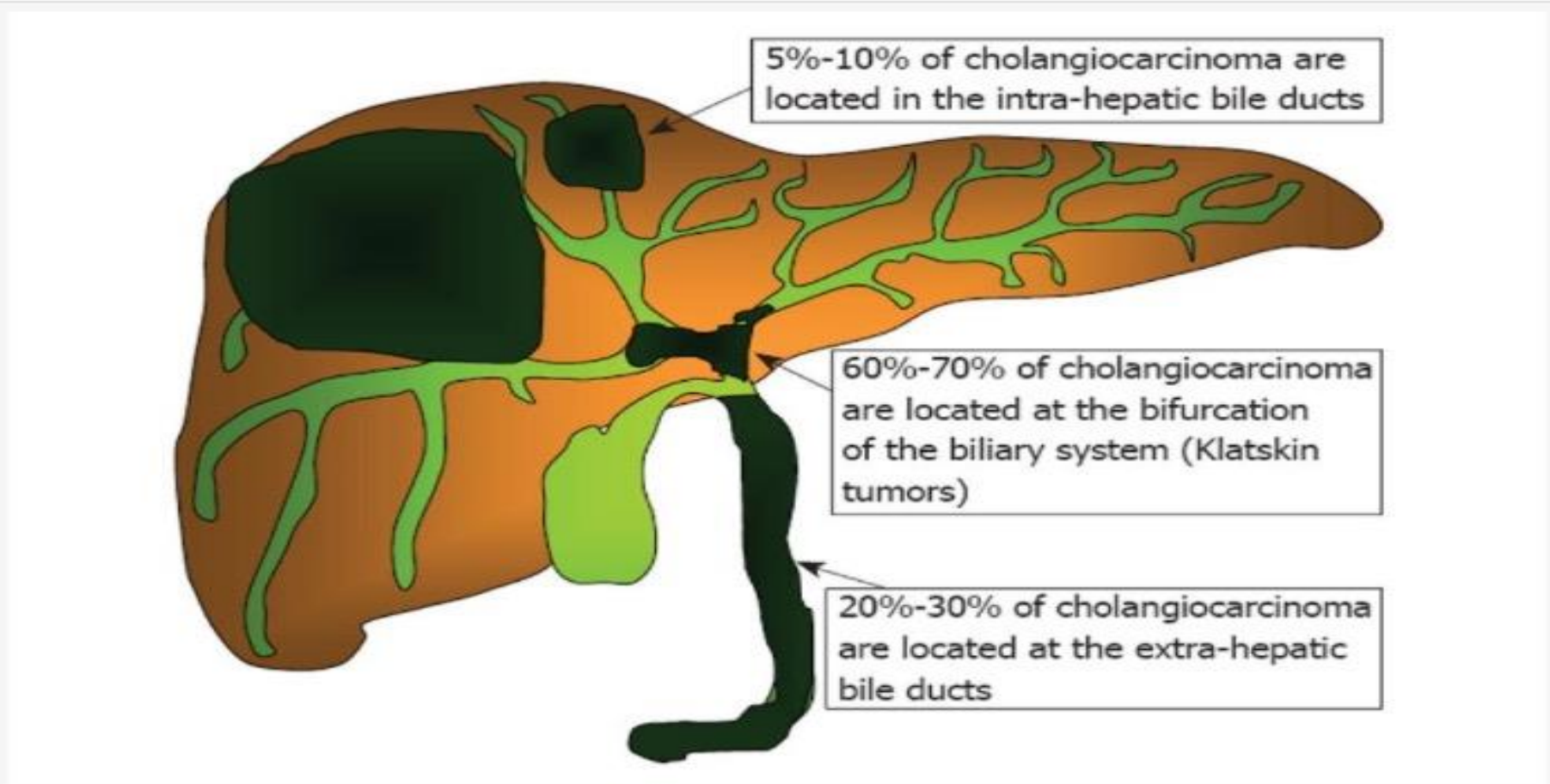


Figure 2 Anatomical presentation of cholangiocarcinomas. The majority of cholangiocarcinomas (60%-70%) present in the area of the biliary duct bifurcation and are called Klatskin tumors. The extra-hepatic bile duct is involved in 20%-30% of cases while intrahepatic cholangiocarcinomas represent 5%-10% of the tumors originating from the biliary system.

Aljiffry et al; World J Gastroenterol. 2009 Sep 14; 15(34): 4240–4262.

Poor prognosis of Cholangiocarcinoma

Cholangiocarcinoma Cancer

Poor Survival despite advances in cancer therapy, these two forms continue to result in some of the worst five-year survival rates

11-15 %
CCA

5-yr survival



Quality of Life pts may develop jaundice, cholangitis, and sepsis, which may adversely impact their quality of life

1. SEER Database 18 2006-2012
2. Intrahepatic, early stage diagnosis. Source American Cancer Society website
3. Wadhwa V. et al. Gastroenterology Report, 5(3), 2017, 213–218

Most Patients are not resectable

5,000-8,000 Cca Patients/Yr, The Vast Majority Are Not Surgical Candidates



Cca non-surgical candidates[2] >60%

Opportunity

1. Cidon, E. Una. "Resectable Cholangiocarcinoma: Reviewing the Role of Adjuvant Strategies." Clinical Medicine Insights. Oncology. Libertas Academica, 12 May 2016. Web. 08 May 2017.
2. "Pancreatic Cancer Surgical Treatment and Whipple Procedure." Pancreatica. Cancer Patients Alliance, n.d. Web. 08 May 2017.

Pancreatic Cancer & Cholangiocarcinoma:

Some of These Patients May Outlive Their Stents

6[1] -12[2] mo

mean **survival**

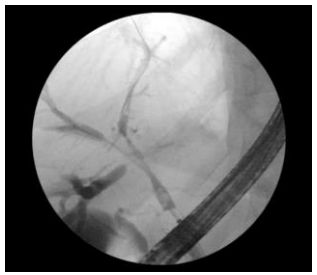
3.4 mo

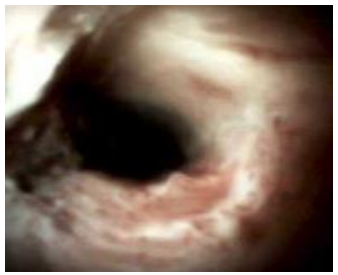
mean patency **plastic** stent[3] (Cca)

2.4 - 8.9 mo [4,5]

mean patency **SEMS** (Panc Ca & Cca)



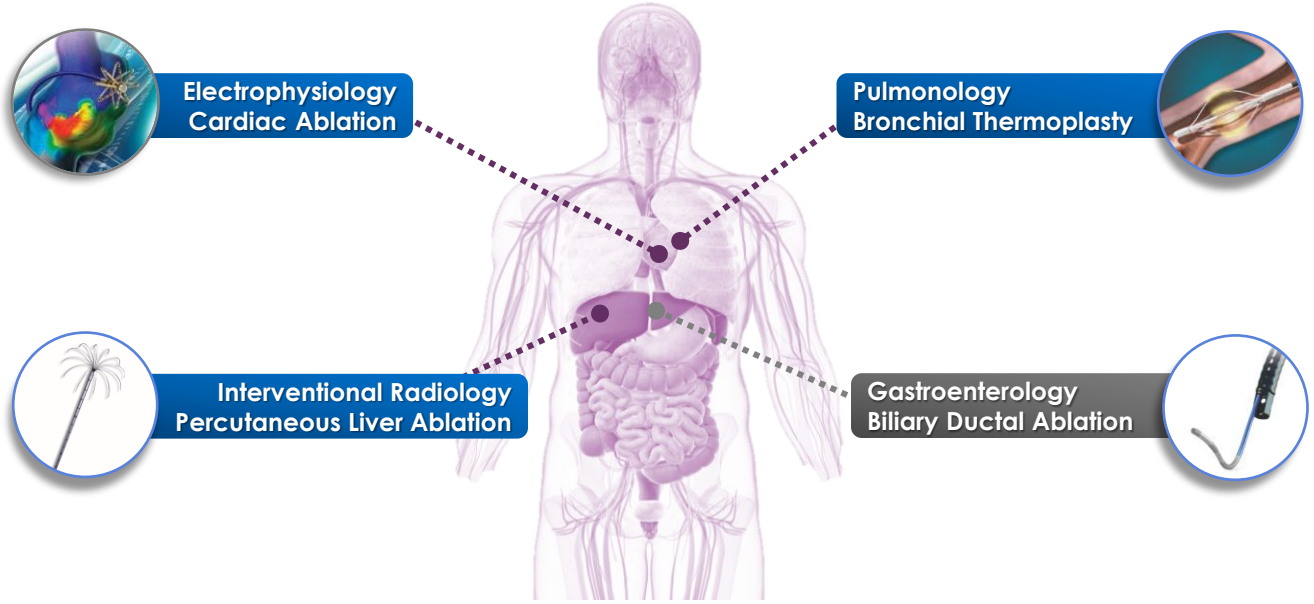




1. Sharaiha, R et al, " Comparison of Metal Stenting with Radiofrequency Ablation Versus Stenting Alone for Treating Malignant Biliary Strictures: Is There an Added Benefit?", Dig Dis Sci, June 2014
2. pancreatica.org
3. Yang J., et al, "Efficacy and safety of endoscopic radiofrequency ablation for unresectable extrahepatic cholangiocarcinoma: a randomized trial", GIE, January 2018
4. Kadayifci, *Radiofrequency ablation for the management of occluded biliary metal stents*, Endoscopy, 2016
5. Liang, H. et al, "Metal Stenting with or without Endobiliary Radiofrequency Ablation for Unresectable Extrahepatic Cholangiocarcinoma", Journal of Cancer Therapy, Oct 2017.

All images are property of Boston Scientific Corporation

Ablation: *RFA has been used for years*



Endo Biliary Ductal Ablation Has Not Demonstrated Clinical Outcomes

ERCP Catheter based ablation





What is RFA – Radiofrequency Ablation

- Radiofrequency ablation is the application of thermal energy to create tissue necrosis via the conduction of heat.

- Energy is deployed via a electrical current delivered be a probe coupled to an electrode.
  - When deployed through the skin this is monopolar
  - For intraductal RFA the probe is bipolar
  - The current alternates between probes at the frequency of radio waves, typically 400-600 hertz (Hz)
  - The tissue nearest to the probe garners the most heat with target tissue heating up to 50-100 degrees Celsius.

What is RFA – Radiofrequency Ablation

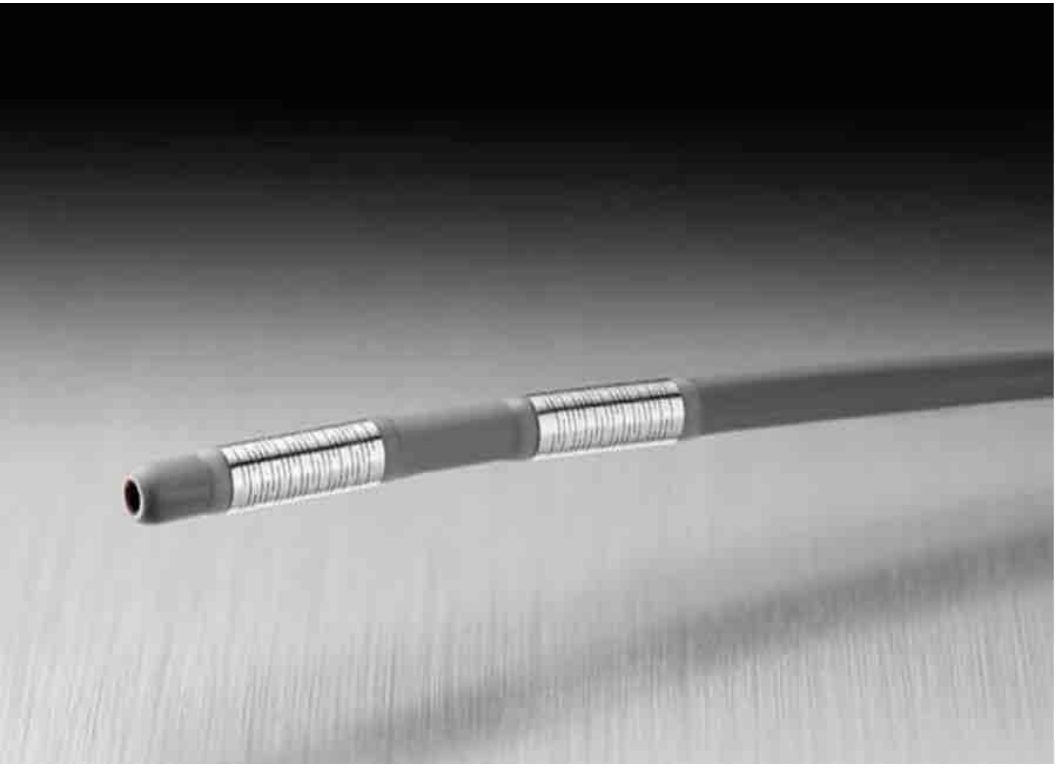
- Ablation is performed at 7 W for intrahepatic and 10 W for extrahepatic disease
- Ablation is performed for 90seconds
- 1minute cool off period
- The probe can then be moved to provide overlapping coverage over an extended area via an additional 90 seconds of ablation for long strictures.

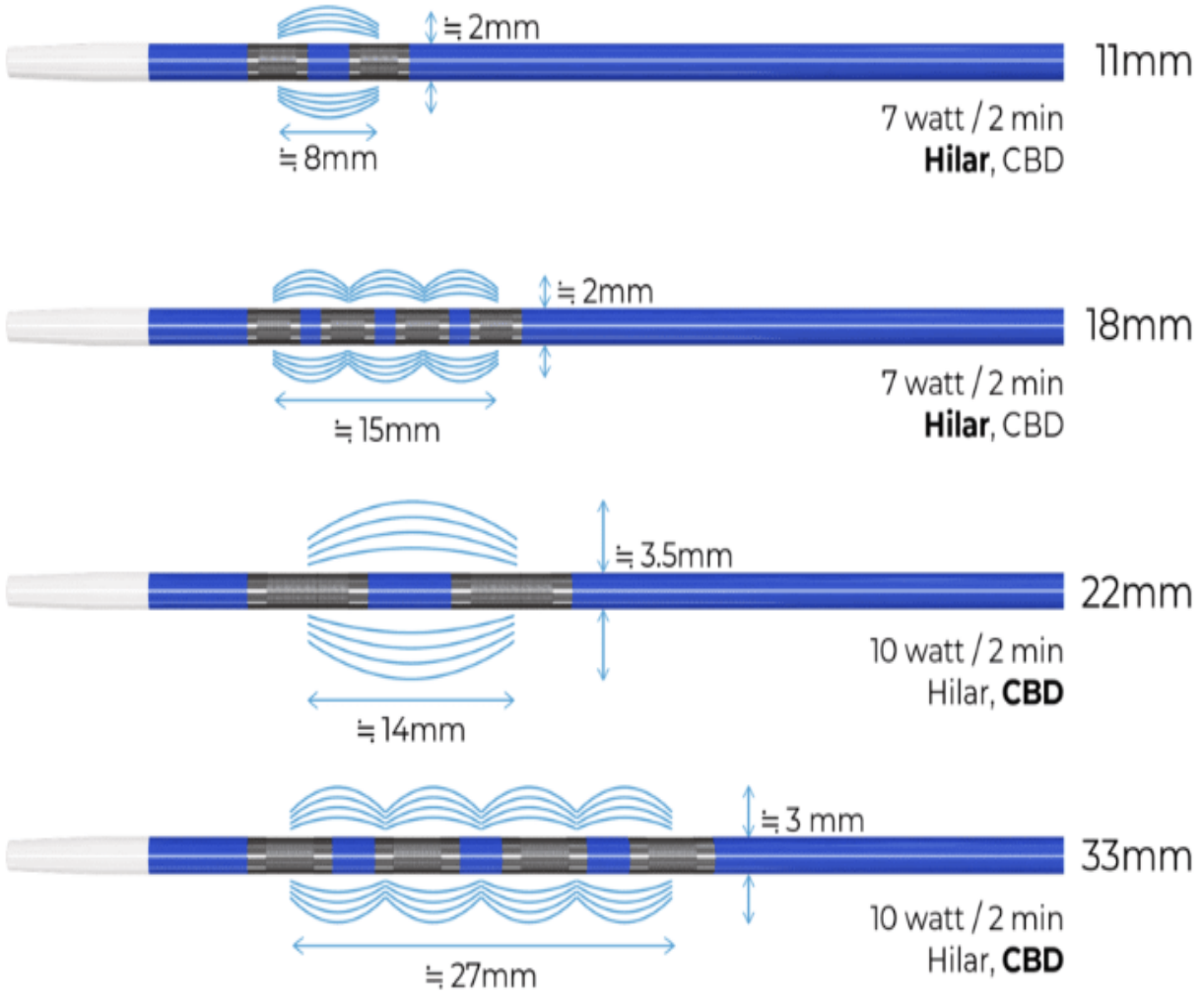
What is RFA – Radiofrequency Ablation

- After cells adjacent to the probe have undergone necrosis, they will char and cause resistance to the passage of electrical current.
- The current is needed to continue to heat tissue and cause cell death.
- This resistance is called “impedance” and can be seen to rise on electrical generators. This limits the passage of current to depth tissues which limits depth of penetration of RFA.
  - Limits depth of penetrance to1-2m or 3-4mm

What is RFA – Radiofrequency Ablation

Produce ablation depths 3-4mm from the wall of the catheter. Resulting ablation zone is 25mm ± 3mm long by 9mm ± 2mm wide





Endoscopic Biliary Ductal Ablation:
Clinical Patency

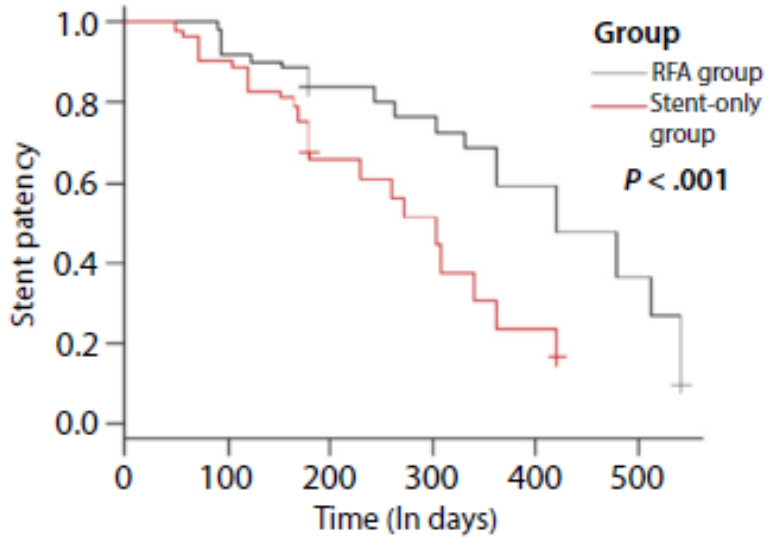
Studies Suggest Improved Stent Patency For Ablation + Stenting, Vs. Stenting Alone

SYSTEMATIC REVIEW AND META-ANALYSIS

Radiofrequency ablation combined with biliary stent placement versus stent placement alone for malignant biliary strictures: a systematic review and meta-analysis

Aijaz Ahmed Sofi, MD,[1] Muhammad Ali Khan, MD,[2] Ananya Das, MD,[1] Mankanwal Sachdev, MD,[1] Sadik Khuder, PhD,[3] Ali Nawras, MD, FACG,[3] Wade Lee, MLS, BS[3]

Gilbert, Arizona; Memphis, Tennessee; Toledo, Ohio, USA



Results: *Note the pooled weighted mean difference in stent patency (95% confidence interval)*

Ductal Ablation: *complication rated*

Study Did Not Show Statistically Significant Differences For Key Complications Compared to ERCP & Stenting

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- **Pain (24hrs post procedure), showed a difference**
- **Other complications (red circle) did not show statistically significant differences**

TABLE 3. Adverse events in RFA study group and control group

	RFA + biliary stent placement (n = 239)	Biliary stent placement only (n = 266)	*P* value
Abdominal pain	31	20	.003
Cholangitis	6.2	5.2	.87
Acute cholecystitis	3.3	0	.4
Acute pancreatitis	2.09	1.5	.2
Hemobilia	3.76	1.88	.19

Values are percents.
RFA, Radiofrequency ablation.

ERCP RFA for Unresectable Disease

Efficacy and safety of endoscopic radiofrequency ablation for unresectable extrahepatic cholangiocarcinoma: a randomized Trial

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1 Department of Gastroenterology, Hangzhou First People's Hospital, Nanjing Medical University,Hangzhou, China

2 Hangzhou Geriatric Hospital, Hangzhou First People'sHospital Group, Hangzhou, China

Published online: 2018 | Endoscopy

Background: Endoscopic placement of biliary stents to relieve jaundice is the main palliative treatment for unresectable extrahepatic cholangiocarcinoma. Endoscopic biliary radiofrequency ablation (RFA) has been reported to prolong stent patency, which may be beneficial in improving patient survival. However, available evidence is still insufficient, as most reported studies are retrospective case series. The aim of this study was to explore the clinical effect and safety of RFA in patients with unresectable extrahepatic cholangiocarcinoma.

Methods: 65 patients with unresectable extrahepatic cholangiocarcinoma, except Bismuth type III and IV hilar cholangiocarcinoma, were enrolled and randomly underwent either RFA combined with biliary stenting (RFA+ stent group; n = 32) or biliary stent only (stent-only group; n = 33). Overall survival time, stent patency period, and postoperative adverse events were recorded.

Results: In the 21-month follow-up period, the overall mean survival time was significantly longer in the RFA+ stent group than in the stent-only group (13.2 ± 0.6 vs. 8.3 ± 0.5 months; $P < 0.001$). The mean stent patency period of the RFA+ stent group was also significantly longer than that of the stent-only group (6.8 vs. 3.4 months; $P = 0.02$). There was no significant difference in the incidence of postoperative adverse events between the two groups (6.3% [2/32] vs. 9.1% [3/33]; $P = 0.67$).

Conclusion: Endoscopic RFA combined with stenting can significantly prolong survival and the stent patency period without increasing the incidence of adverse events in patients with extrahepatic cholangiocarcinoma patient, except Bismuth type III and IV hilar cholangiocarcinoma. This approach can be considered as a safe and effective palliative treatment for these patients.

Stent vs Stent + RFA

Radiofrequency ablation combined with biliary stent placement versus stent placement alone for malignant biliary strictures: a systematic review and meta-analysis

Aijaz Ahmed Sofi, MD,1 Muhammad Ali Khan, MD,2 Ananya Das, MD,1 Mankanwal Sachdev, MD,1 Sadik Khuder, PhD,3 Ali Nawras, MD, FACG,3 Wade Lee, MLS, BS3 Gilbert, Arizona; Memphis, Tennessee; Toledo, Ohio, USA

Background and Aims: Unresectable malignant biliary strictures are generally managed by palliative stent placement for drainage of biliary tree. Recently, radiofrequency ablation (RFA) has been used to improve the patency of biliary stents in these patients. Several studies have evaluated the effectiveness of biliary stent placement with RFA on stent patency and patient survival with variable results. We performed this meta-analysis to evaluate the efficacy and safety of biliary stent placement with RFA compared with stent placement alone in patients with malignant biliary strictures.

Methods: We performed a comprehensive search of electronic databases for all studies comparing RFA with biliary stent placement versus stent placement only. Measured outcomes included patient survival, stent patency, and procedure-related adverse events. An inverse variance method was used to pool data on stent patency into a random-effects model. Cox-regression analysis was used to calculate hazard ratio for survival analysis. We used the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) framework to interpret our findings.

Results: Nine studies (including 2 abstracts) with a total of 505 patients were included in the meta-analysis. The pooled weighted mean difference in stent patency was 50.6 days (95% confidence interval [CI], 32.83-68.48), favoring patients receiving RFA. Pooled survival analysis of the reconstructed Kaplan-Meier data showed improved survival in patients treated with RFA (hazard ratio, 1.395; 95% CI, 1.145-1.7; P < .001). However, RFA was associated with a higher risk of postprocedural abdominal pain (31% vs 20%, P Z .003). Our analysis did not show significant difference between the RFA and stent placement–only groups with regard to the risk of cholangitis, acute cholecystitis, pancreatitis, and hemobilia.

Conclusions: In the light of this limited data based on observational studies, RFA was found to be safe and was associated with improved stent patency in patients with malignant biliary strictures. In addition, RFA may be associated with improved survival in these patients. (Gastrointest Endosc 2018;87:944-51.)

Comparative Data for RFA: RCT and Observational Studies

References	Design	% SEMS Stents: RFA/ No RFA	CCA/Non-CCA	Number of RFA Sessions (mean)	Patency (Days) RFA/No RFA	Cholangitis Rates, % RFA/No RFA	Survival RFA/No RFA
Gao 2018 GIE Ab*	RS, Obs **RFA v.PDT**	"Plastic Stents Preferred"	**31**/16 (66%)	>=2 (88%)	NR	55/54% P=0.977	491/333 dys (p=0.149)
Yang 2018 Endoscopy	RCT	0/0 **Plastic Only**	**65**,/0 **(100%)** BI-II only	2.6 Sessions, Mean	6.8/3.4mnt p=0.02	6/3% P=0.67	13.2/8.3mths p=<0.001
Sampath 2016 GIE Ab*	Obs	20%/33%	**25**/0 **(100%)**	3 Sessions, Mean	NR	**30**/0% p=0.052	357 /141dys, p=0.01
Hu 2016 GIE Ab*	RCT	0/0 **Plastic Only**	**63**/0 **(100%)**	Q 3mnth	150/117dys p=0.701	50/44% p=0.701	311/172dys p=0.012
Strand 2014 GIE	RS, Obs **RFA v.PDT**	81/34%	**48**/0 16 RFA/32PDT	1.2	0.06/0.02 occ ep mnth P=0.008	**0.13**/0.5 ep per mnth P=0.008	9.6/7.5mnths P=0.799
Sharaiha R 2014 DDS	Pro, Obs	30%cov/98%cov **SEMS Only**	**37**/29 (56%)	1 Session	NR	Rate NR, "no difference"	HR-0.26 P=0.012

Obs= Observational, Pro= Prospective registry, RS= retrospective review, RCT= randomized control trial
Cov=cSEMS,

Jeffrey J Easler, M.D.
&
N.R. Sharma, M.D.

Stent vs Stent + RFA – *negative RCT*

Endoscopy
Original research

Endoluminal radiofrequency ablation in patients with malignant biliary obstruction: a randomised trial

PDF

PDF + Supplementary Material

Jana Jarosova [1], Lea Zarivnijova [2], Ivana Cibulkova [3], Jan Mares [4], Peter Macinga [1], Alzbeta Hujova [1], Premysl Falt [2], Ondrej Urban [2], Jan Hajer [3], Julius Spicak [1], Tomas Hucl [1]

Correspondence to Professor Tomas Hucl, Department of Gastroenterology and Hepatology, Institute of Clinical and Experimental medicine, Praha 14021, Czech Republic; tomas.hucl@ikem.cz

Abstract

Background Endoluminal radiofrequency ablation (RFA) has been promoted as palliative treatment for patients with cholangiocarcinoma (CCA) and pancreatic ductal adenocarcinoma (PDAC) in order to improve biliary drainage and eventually prolong survival. No high level evidence is, however, available on this technique.

Design In this randomised controlled study, we compared endoluminal RFA plus stenting with stenting alone (control group) in patients with malignant biliary obstruction; metal stents were primarily placed. Primary outcome was overall survival; secondary outcomes were stent patency, quality of life and adverse events. In a superiority design, survival was assumed to be doubled by RFA as compared with 6.4 months in the control group (n=280).

Results A total of 161 patients (male:female 90:71, mean age 71±9 years) were randomised before recruitment was terminated for futility after an interim analysis. Eighty-five patients had CCA (73 hilar, 12 distal) and 76 had pancreatic cancer. There was no difference in survival in both subgroups: for patients with CCA, median survival was 10.5 months (95% CI 6.7 to 18.3) in the RFA group vs 10.6 months (95% CI 9.0 to 24.8), p=0.58)) in the control group. In the subgroup with pancreatic cancer, median survival was 6.4 months (95% CI 4.3 to 9.7) for the RFA vs 7.7 months (95% CI 5.6 to 11.3), p=0.73) for the control group. No benefit was seen in the RFA group with regard to stent patency (at 12 months 40% vs 36% in CCA and 66% vs 65% in PDAC), and quality of life was unchanged by either treatment and comparable between the groups. Adverse events occurred in seven patients in each groups.

Conclusion A combination of endoluminal RFA and stenting was not superior to stenting alone in prolonging survival or improving stent patency in patients with malignant biliary obstruction.

Stent vs Stent + RFA

Open Access | Systematic Review

The Impact of Radiofrequency Ablation on Survival Outcomes and Stent Patency in Patients with Unresectable Cholangiocarcinoma: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

by Daniele Balducci [1], Michele Montori [1], Francesco Martini [1], Marco Valvano [2,3], Federico De Blasio [1], Maria Eva Argenziano [1], Giuseppe Tarantino [1], Antonio Benedetti [1], Emanuele Bendia [4], Marco Marzioni [1] and Luca Maroni [1,*]

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Cancers **2024**, *16*(7), 1372; https://doi.org/10.3390/cancers16071372

Out of 275 results, 5 randomized trials and 370 patients were included. While overall survival was not different between the groups (HR 0.62; 95% CI 0.36–1.07; $p = 0.09$; $I^2 = 80\%$;),

The subgroup analysis of studies employing plastic stents showed a trend toward better survival in the RFA-treated group (HR 0.42; 95% CI 0.22–0.80; $p = 0.009$; $I^2 = 72\%$).

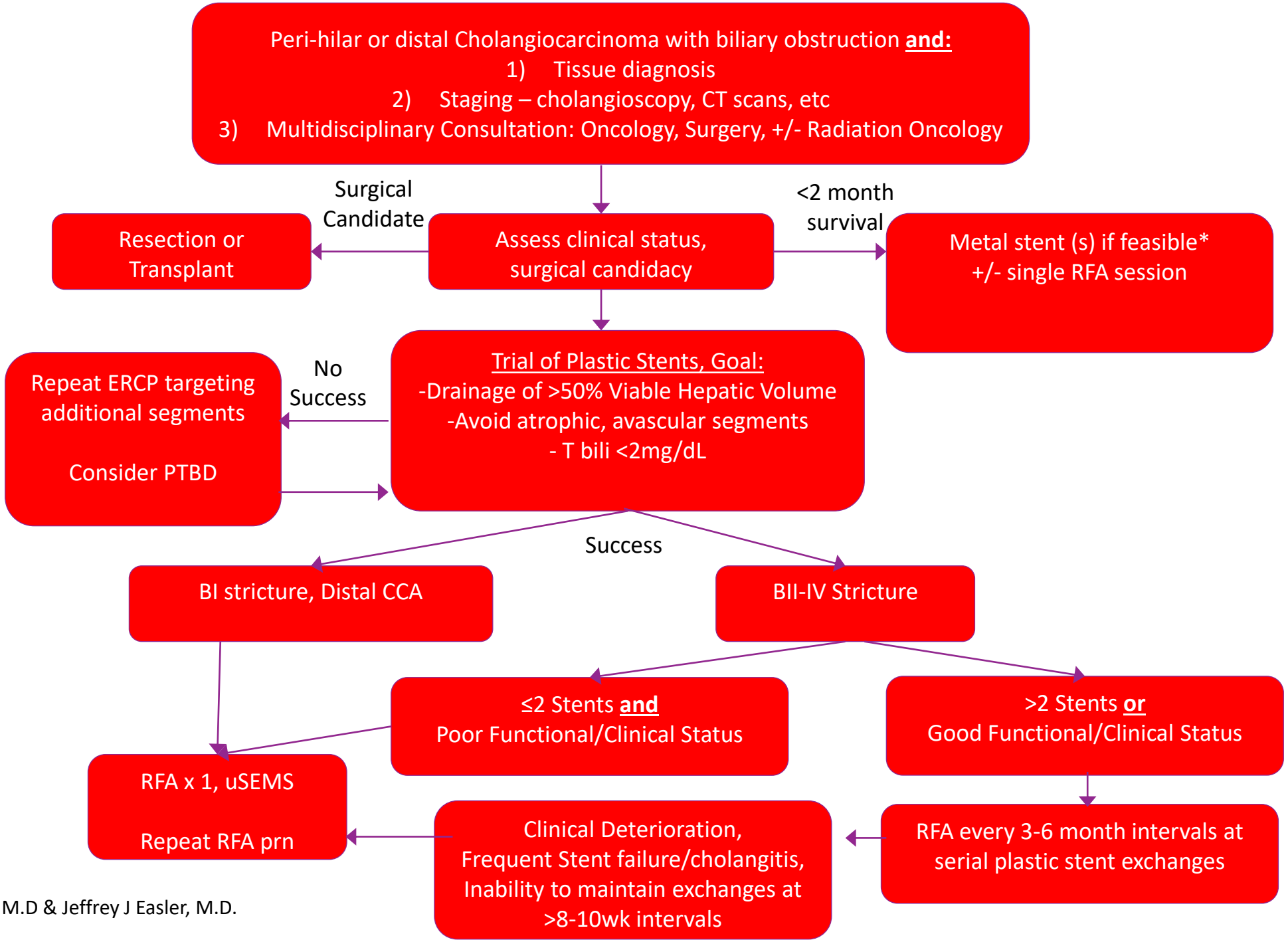
Stent patency was improved in patients receiving RFA (HR 0.64; 95% CI 0.45–0.90; $p = 0.01$; $I^2 = 23\%$).

Adverse events were not different between the groups

RFA & Stent Approach

Clinical Scenario	ERCP-RFA Approach	Stent approach
Resectable / Possible transplant candidate	None	Plastic stents
Borderline candidate for surgery	”Neo adjuvant RFA” plus chemotherapy	Plastic stents
Unresectable/metastatic CCA & >4-6 months expected survival	RFA serial or single session as adjunct to palliative chemotherapy	Plastic stents or SEMS
Advanced/metastatic disease, poor clinical status, & <4-6 months expected survival	Maybe, single session prior to SEMS placement	Strongly, consider conversion to SEMS. -uncovered if hilar or intrahepatic

Jeffrey J Easler, M.D. & Neil R. Sharma, M.D.



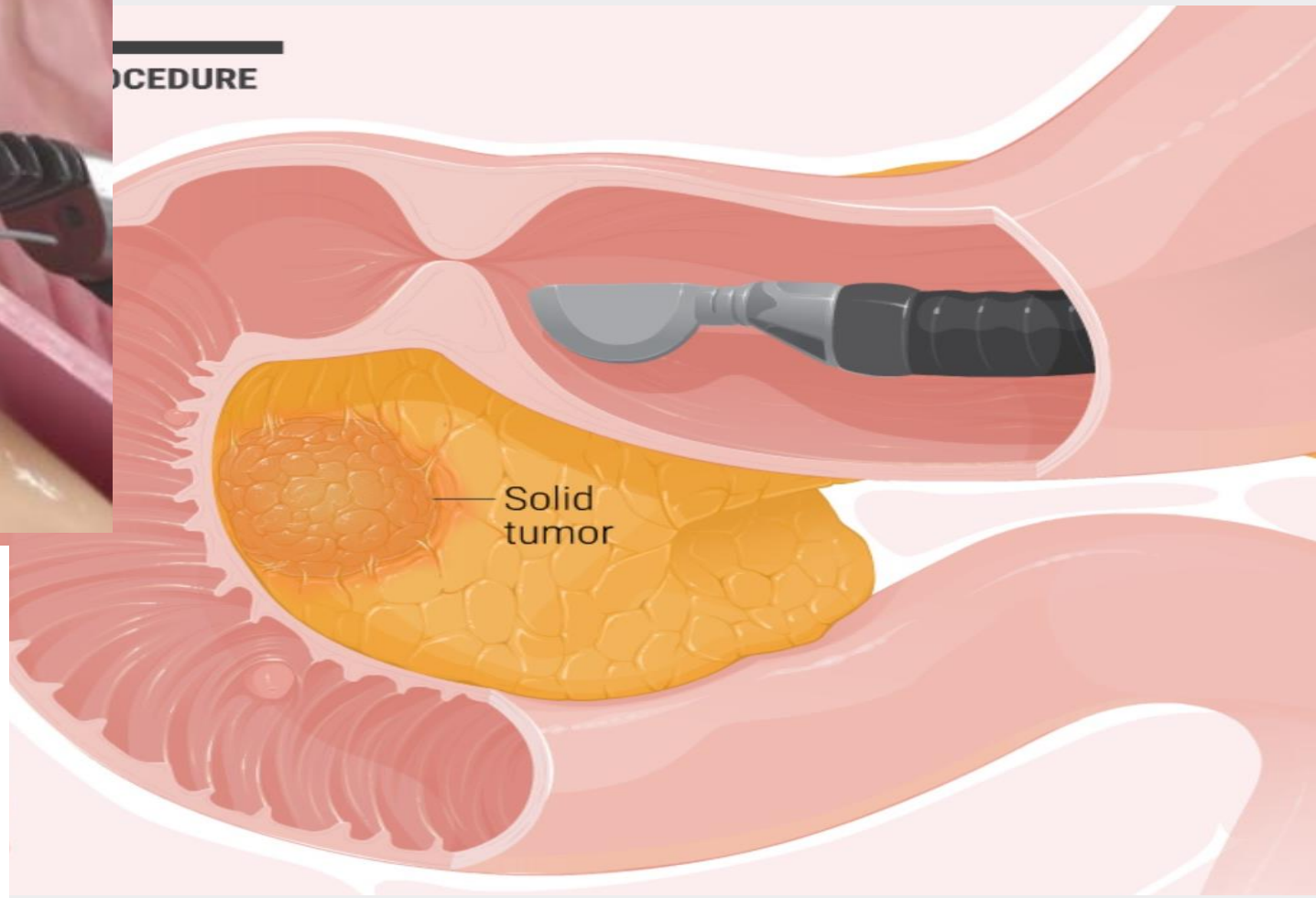
Neil R Sharma, M.D & Jeffrey J Easler, M.D.

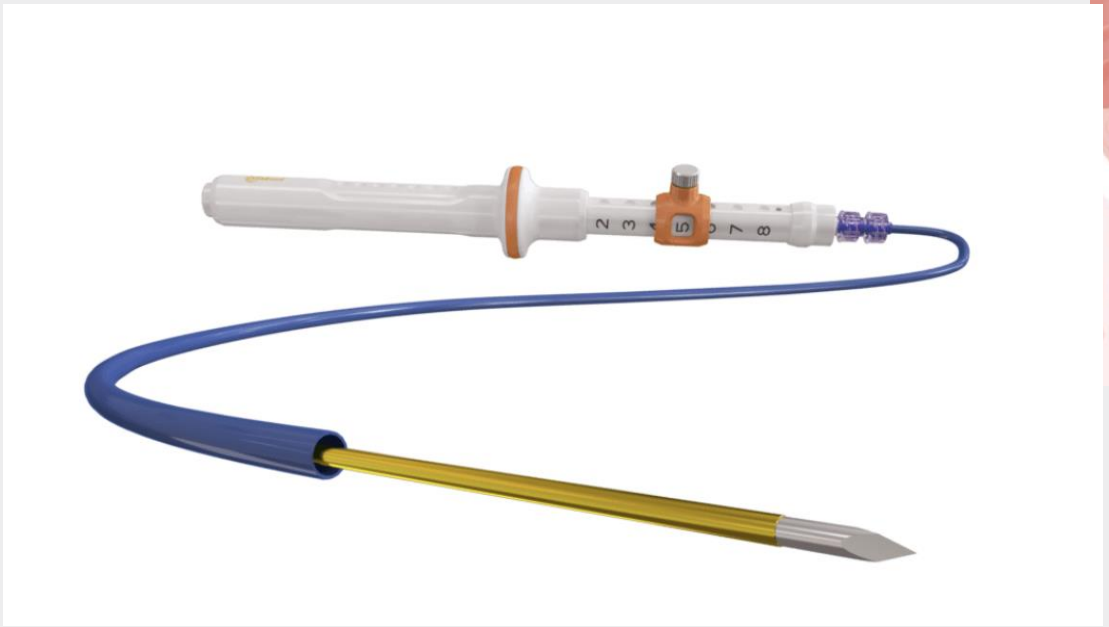
EUS Based THERMAL ABLATION: RFA & MICROWAVE

Banner Health

EUS Thermal Ablation –RFA & Microwave







EUS Thermal Ablation –RFA & Microwave

EUS Thermal ablation:

- **RFA – Radiofrequency**
  - More data in EUS application
  - Has greater issues with impedance
  - Device more user friendly

- **Microwave**
  - Less heat sinking
  - More potential for uniform ablations
  - Less Data in EUS
  - Gen 1.0 device

Pancreatic Cancer – Epidemiology

- Most Pancreatic cancer cases are adenocarcinomas (90%)
  - 5-10% are PNET (pancreatic neuroendocrine tumors)
- 7-12 % 5 year survival for pancreatic cancer
- High percentage of cases detected in late stage disease

Pancreatic Cancer

- **Staging in Pancreatic Cancer is paramount to optimal treatment**
    - Only R-0 resection has survival value for surgery
    - Often there are large vessels preventing complete resection
    - 50-80% will reoccur in the first 2 years after resection

- **CT scans + EUS**



Pancreatic Cancer – Treatment

- Surgery:
  - Whipple
  - Subtotal pancreactomy
  - Distal pancreatectomy

- Chemotherapy:
  - Gemcitabine + Paclitaxel
  - Folfirinox

- Radiation:
  - IMRT
  - Cyberknife (SBRT)

Pancreatic Cancer:
Locally advanced / Borderline Resectable

- **Borderline Resectable:**
  - Although there is no consensus regarding the definition, BR-PDAC is often defined as a tumor confined to the pancreatic bed with limited involvement of the adjacent vascular structures where vascular reconstruction options are feasible.

- **Locally advanced:**
  - Often defined as the involvement of the CA or the encasement of >180° of the SMA (T4) and/or involvement of SMV/PV with no reconstruction options, irrespective of nodal involvement, provided that no distant metastasis exists outside the pancreatic bed.

Pancreatic Cancer:
A systemic disease

- Goal being to get patients to R0 surgery

- Recognizing pancreatic Adenocarcinoma is likely a “systemic disease”

EUS ablation options in Borderline resectable/Locally advanced cancer

PDAC (Adenocarcinoma) – EUS- RFA data

Table 1. Summary of studies reporting on EUS-RFA for PDAC.

Authors and Year	Study Type	No. of Patients	PDAC Staging	Tumor Location	Mean Tumor Size	Type of RFA Electrode	RF Generator	Power Settings	No. of RFA Sessions	Technical Success Rate	Survival	Adverse Events
Arcidiacono et al., 2012 [26]	P	22	Stage III LA-PDAC	Head and neck (16), uncinate process (2), body and tail (4)	35.7 mm (range 23–54 mm)	1.8 mm diameter 20 mm long cryotherm probe	VIO 300D RF-Surgery System ERBEKRYO CA system (Erbe Elektromedizin GmbH, Tübingen, Germany)	18 W	1 session	72.72%	Median 6 months in 13/16 pts	Abdominal pain—3 (18%) Minor duodenal bleeding—1 (6%) Rise in amylase level—3 (18%)
Song et al., 2015 [20]	P	6	LA-PDAC and mPDAC	Head (4), body (2)	3.8 cm (range 3 cm–9 cm)	18-gauge endoscopic RFA electrode	VIVA RF generator (STARmed, Koyang, Republic of Korea)	20 to 50 W	1–2 sessions	100%	Not evaluated	Mild abdominal pain in 2 patients, no major adverse events
Crinò et al., 2018 [29]	P	7	LA-PDAC	Head (2), uncinate process (2), body (3)	36 mm (range 22–67 mm)	18-gauge internally cooled electrode (EUSRA)	VIVA RF generator (STARmed, Seoul, Republic of Korea)	30 W	1–3 sessions	100%	Not reported	Mild abdominal pain in 3 patients, no major adverse events
Scopelliti et al., 2018 [30]	P	10	uPDAC non-metastatic	Head (4), body (6)	49.2 mm (range 35–75 mm)	18-gauge electrode (EUSRA)	VIVA RF generator (STARmed, Seoul, Republic of Korea)	20–30 W	1–2 passages	100%	Not evaluated	No major adverse events
Wang et al., 2021 [31]	R	11	uPDAC (7 LA-PDAC and 4 mPDAC)	Head (4), neck (3), body (3), tail (1)	27.9 mm (range 16.4–38 mm)	Habib EUS RFA catheter through 22G FNA needle	RITA System Generator 1500X (RITA Medical Systems, California, USA)	5–10 W	1–8 sessions	100%	1/11 pts survived at 12 months follow-up	Abdominal pain in 2 patients, no major adverse events
Oh D et al., 2022 [32]	P	22	uPDAC (14 LA-PDAC and 8 mPDAC)	Head (14), body (4), tail (3), resection margin (1)	38 mm (32.75–45 mm)	19-gauge RFA needle	VIVA RF generator (STARmed, Koyang, Republic of Korea)	50 W	5 sessions (median)	100%	Median OS 24.03 months	Early procedure-related adverse events—3.74% Abdominal pain—3 Peritonitis—1
Thosani et al., 2022 [33]	P	10	7 LA-PDAC, 3 mPDAC	Head (4), neck (2), body (2), tail (2)	39.2 mm (range 14—68 mm)	19- or 22-G through FNA probe, Habib 6500 ablation catheter (Boston Scientific, Marlborough, MA, USA)	Not specified	10–15 W	1–4 sessions	100%	Median survival 13.4 months	Mild abdominal pain in 12/22 treatments (55%), no major adverse events

PDAC (Adenocarcinoma) – EUS- RFA data

Table 1. *Cont.*

Authors and Year	Study Type	No. of Patients	PDAC Staging	Tumor Location	Mean Tumor Size	Type of RFA Electrode	RF Generator	Power Settings	No. of RFA Sessions	Technical Success Rate	Survival	Adverse Events
Kongkam et al., 2023 [34]	P	14	stage III—1, IIIb—3, IV—10	Target lesions (30 sessions in 14 pts): head (5), body (11), neck (12), uncinate process (2)	59.7 ± 18.6 mm (IQR 39.8–66.1)	19-gauge RFA needle (EUSRA)	VIVA RF generator (STARmed, Koyang, Republic of Korea)	50 W	2.5 times per patient (1–4 times)	100%	6-month mortality rate 70%	Mild pancreatitis 1 (7.1%)
Napoléon et al., 2023 [35]	R	6 PDAC cases among 104 solid and cystic lesions	Not specified	Not reported specifically for the subgroup of PDAC pts	27 mm (13–60)	19-gauge RFA needle (EUSRA)	VIVA RF generator (STARmed, Koyang, Republic of Korea)	50 W	Not reported specifically for the subgroup of PDAC pts	97.1% for all lesions	Not reported specifically for the subgroup of PDAC pts	Overall AE 21.2% for all 100 lesions (NEN, metastasis, IPMN, SPEN)
Robles-Medranda et al., 2024 [36]	R	26	15 LA-PDAC, 11 mPDAC	Head (22), isthmus (2) body (1), tail (1)	39.5 mm (35.0–43.3)	19-gauge RFA needle	VIVA combo RF Generator System (TaeWoong Medical, Seoul, Republic of Korea)	50 W	1–3 sessions	100%	Median OS 7 (4–12) months	No major adverse events, mild pain in 3 patients
Wray et al., 2024 [37]	P	3	resectable PDAC	Head (3)	2.97 cm (2.7–3.2)	19-gauge RFA catheter	Not specified	Measured electrical impedance of 200 Ohm	2–3 sessions	100%	22.4 months	No adverse events observed related to the ablation

PDAC (Adenocarcinoma) – EUS- RFA data

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Original article

Clinical endoscopy

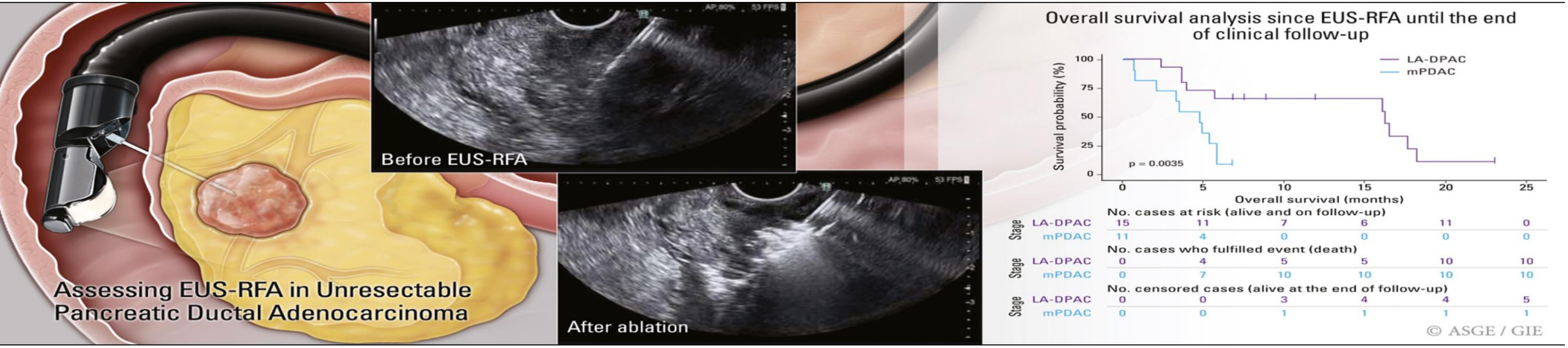
Assessing EUS-guided radiofrequency ablation in unresectable pancreatic ductal adenocarcinoma: a single-center historic cohort study

Carlos Robles-Medranda MD, FASGE, AGAF [1], Raquel Del Valle MD [1], Miguel Puga-Tejada MD, MSc, PhD [1], Martha Arevalo-Mora MD [1], Domenica Cunto MD [1], Maria Egas-Izquierdo MD [1], Lorena Estrada-Guevara MD [1], Orlando Bunces-Orellana MD [1], Daniel Moreno-Zambrano MD [1], Juan Alcivar-Vasquez MD, MSc [1], Haydee Alvarado-Escobar MD [1], Ruxandra C. Merfea MD [1], Jonathan Barreto-Perez MD [2], Jorge Rodriguez MD [1], Daniel Calle-Loffredo MD, MSc [1], Hannah Pitanga-Lukashok MD [1], Jorge Baquerizo-Burgos MD [1], Daniela Tabacelia MD [3 4]

26 total patients:

- 15 locally advanced
- 11 metastatic

- Retrospective



Pancreatic Neuroendocrine Tumors – PNETs

PNETs account for 5-10% of pancreatic cancer.

- Actually, they probably represent up to 10% of pancreatic tumors [1]. Moreover, their prevalence at autopsy ranges from 0.8% to 10% [2].

- **7% (5-10%) of all Neuroendocrine tumors are PNET**

- **A considerable part of PNET (up to 60%) have a metastatic disease at diagnosis, while 21% present a locally advanced disease [3, 4]**

What to do with alL these SMALL NF-NETS?

Organization	PNET Observation Recommendations
European Neuroendocrine tumor society.	Non Functioning PNET Less than 2 cms Low Tumor Grade (G1/G2) Pancreatic head tumor location. No signs of malignancy on imaging. MRI or EUS Every 6 months Extend to every 12 months if no changes observed.
National Comprehensive cancer Network	Non Functioning PNET Less than 1cm Incidentally Discovered tumors.
Canadian National Expert Group	Non Functioning PNET Less than 2 cms Low Mitotic Index (Ki67) Without signs of local tumor invasion or distant spread Biochemical and Imaging every 6 months.
North American Neuroendocrine tumor Society	Tumors less than 1cm - Observation Tumors 1 to 2 cms – Individualized based on patient factors like Age, Co morbid conditions, preference and access to long term follow up.

Guidelines on observation in small NF-PNET.

Small <2cm PNETs

- **Most Data supports observation in <2cm NF-PNET**
- **Of all guidelines – ENETs has the most robust data**
  - >200 cohort controlled trials
  - Less economic & medical-legal influences
  - More collaborative data across long term studies

PNET – Pancreatic Neuroendocrine

Techniques and Innovations in Gastrointestinal Endoscopy
Available online 26 March 2026, 250971
In Press, Uncorrected Proof What's this?

Original Research

Endoscopic Ultrasound–Guided Radiofrequency Ablation for Nonfunctioning Pancreatic Neuroendocrine Tumors

Prahan Chetlur [1], Daniel Marino [2], John M. DeWitt [3], Patrick Joseph Magahis [4], SriHari Mahadev [5], Reem Sharaiha [5], John Lee [6], Jason Samarasena [6], Amirali Tavangar [6], Frances Dang [6], Stefano Francesco Crinò [7], Kavel Visrodia [8], Amrita Sethi [8], John Doyle [8], Nirav Thosani [9], Gregory Haber [2], Lauren Khanna [2], Tamas Gonda [2]

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ABSTRACT

BACKGROUNDS AND AIMS

Endoscopic ultrasound–guided radiofrequency ablation (EUS-RFA) is a minimally invasive treatment option for nonfunctional pancreatic neuroendocrine tumors (NF-PanNETs). This study aimed to evaluate the efficacy, safety, and predictors of response to EUS-RFA.

METHODS

We conducted a retrospective, multicenter case series across 7 tertiary care centers, including 46 patients with biopsy-proven NF-PanNETs. Demographic, tumor, and procedural data were collected. Technical success was defined as completion of at least 1 radiofrequency ablation (RFA) application. Radiographic response was assessed at ≥10 weeks and ≥3 months using modified Response Evaluation Criteria in Solid Tumors: complete response (CR, 100% reduction), partial response (PR, 30–99%), and no response (NR, <30%). Predictive factors were evaluated using logistic regression. Adverse events were classified per AGREE criteria. This study was exempt from institutional review board review after assessment.

RESULTS

Among 46 patients (mean age, 60.9 years; 53% men), most tumors (93.6%) were well-differentiated grade 1, with a mean size of 12.7 mm. Technical success was 100%, with a mean of 2.9 RFA applications. At initial follow-up, CR was achieved in 32.6%, PR in 47.8%, and NR in 19.6%. Of patients with PR/NR ($n=31$), 58.1% underwent repeat RFA. At final follow-up (mean, 15.7 months), cumulative response rates were as follows: CR, 60.0%; PR, 31.1%; and NR, 8.9%. Longer probe tips (odds ratio, 5.31; 95% CI, 1.10–33.87) and more RFA applications (odds ratio, 2.61; 95% CI, 1.19–3.9) predicted CR. Adverse events occurred in 15.2% ($n=7$), including mild abdominal pain, mild pancreatitis, and 1 grade III bleed.

CONCLUSION

EUS-RFA for NF-PanNETs demonstrates high technical success, durable tumor response, and an acceptable safety profile. Probe length and application number may influence outcomes.

PNET – Pancreatic Neuroendocrine

EUS RFA Limitations:

- **Typically limited to 3cm or less**
- **Grade 1 tumors**
- **>1mm away from main pancreatic duct**

- **All Data has been retrospective:**
- A multicenter, international RCT is ongoing—EUS-RFA Versus Surgery for Pancreatic Insulinoma (ERASIN-RCT), with completion expected by 2026

Value of Ablation in PNETs

- Useful in functional Small PNETs: up to 2-3cm

- Decreased mortality and morbidity
- Less overall cost to patient
- Minimally invasive
- Future Potential

- NEEDS:
  - Long term follow up
  - Better understanding of Dosimetry

  - Is it better than just surveillance for non functional PNET ?????
    - Studies needed

Key Points

- The Guidelines for small <2cm PNET are varied with low-quality, limited data
  - *Strongest Data comes from ENET guidelines*
- Small PNETs are ↑ incidence due to better imaging & EUS
- Nonfunctional PNETs <2cm, G1-G2 likely are best treated by observation
  - *Age, location, Ki-67, patient concerns all must be taken into account*
- Expect tumor ablation to play a role in the future

Future Applications

ERCP RFA for Unresectable Disease

Stent Patency VS Immune Stimulation .. Or Both????

- Endoscopists look at LFTs and are concerned with “patency”
- Medical Oncologist are concerned with tolerance and response to systemic therapy

- One can effect the other: low level obstructions can be “smoldering cholangitis”
  - Chills / night fevers often reported to medical oncologists rather than interventional endoscopists
  - Under treating? Awaiting too long for LFT increase?

EUS Ablation for Unresectable Disease

- We can destroy small Tumors:
  - PNET <2cm, grade 1
  - Need to ensure long term durability and complete destruction
- **We can shrink locally advanced tumors as a bridge to resection**
- **But… Pancreatic Cancer is a systemic disease**

Immune Stimulation?

- **It has been postulated that the use of RFA on tumor tissue can incite an immune response:**

- In situ tumor ablation creates an antigen source for the generation of antitumor immunity. den Brok MH, Sutmuller RP, van der Voort R, Bennink EJ, Figdor CG, Ruers TJ, Adema GJ. Cancer Res. 2004 Jun 1;64(11):4024-9. PubMed PMID: 15173017.

- Immuno-thermal ablations – boosting the anticancer immune response. Journal for Immunotherapy of Cancer. Slovak R, Ludwig JM, Gettinger SN, Herbst RS, Kim HS. 2017;5:78. doi:10.1186/s40425-017-0284-8.

Immune Stimulation?

- In the articles, it has been proposed that exposing tumor antigen with modalities such as RFA, antigen presenting cells can direct the immune system against targets that were previously unexposed.

- There have been numerous examples of immunotherapy having strong efficacy in cancer care.

Immune supercharging?

- Can ERCP with RFA lead to exposure of circulating antigens and incite an immune response that can either be targeted by new agents or augmented through existing immunotherapies?

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Thank you!



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