Long-term outcome after EUS-guided radiofrequency ablation: Prospective results in pancreatic neuroendocrine tumors and pancreatic cystic neoplasms



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ABSTRACT

Background and study aims Endoscopic ultrasoundguided radiofrequency ablation (EUS-RFA) for pancreatic neuroendocrine tumors (NETs) and intraductal pancreatic mucinous neoplasia (IPMN) with worrisome features or high-risk stigmata (WF/HRS) has been evaluated in few series with short-term outcomes. This study's primary endpoint was to assess the long-term efficacy of EUS-RFA in patients with NETs or pancreatic cystic neoplasms (PCNs) over at least 3 years.

Patients and methods Twelve patients had 14 NETs with a mean 13.4-mm size (10–20) and 17 patients had a cystic tumor (16 IPMN, 1 MCA) with a 29.1-mm mean size (9–60 were included. They were treated with EUS-guided RFA, evaluated prospectively at 1 year, and followed annually for at least 3 years.

Results The mean duration of follow-up was 42.9 months (36–53). Four patients died during follow-up (17–42 months) from unrelated diseases.

At 1-year follow-up, and 85.7% complete disappearance was seen in 12 patients with 14 NETs. At the end of follow-up (45.6 months), complete disappearance of tumors was seen in 85.7% of cases. One case of late liver metastasis occurred in a patient with initial failure of EUS-RFA. At 1-year follow-up, a significant response was seen in 70.5% of 15 patients with PCNs. At the end of the follow-up, there was a significant response in 66.6% with no mural nodules. Two cases of distant pancreatic adenocarcinoma unrelated to IPMN occurred.

Conclusions EUS-RFA results for pancreatic NETs or PCNs appear to be stable during 42 months of follow-up.

Introduction

Endoscopic ultrasound-guided radiofrequency ablation (EUS-RFA) has recently emerged as a new technique for pancreatic tumor ablation, mainly for neuroendocrine tumors (NETs), pancreatic cystic neoplasms (PCNs), or pancreatic adenocarcinoma. NETs are probably the indication of choice for EUS-guided RFA. NETs are mostly non-functional and do not induce a secretory disorder [1]. Once their nature is determined with diagnostic tests like EUS-FNA, incidental nonfunctional NETs currently lead to difficult management when their largest diameter is < 2 cm [2–4]. In patients with tumors ranging from 1 to 2 cm, EUS-guided treatment may be an alternative to surgery [5–7]. PCNs are common pancreatic lesions that are mainly discovered fortuitously [8–11]. Most PCNs, including intraductal papillary mucinous neoplasms (IPMNs) and mucinous cystadenoma (MCAs), have a benign pattern, and few of them transform to become malignant. Branch duct IPMNs develop malignancy in about 5% to 10% of cases, requiring imaging follow-up [2]. PCNs presenting at imaging with worrisome features or highrisk stigmata (WF/HRS) (presence of mural nodules >5mm and cyst size >3 cm) are considered high-risk factors for malignancy [9–11]. An interesting alternative to surgery could be the destruction using EUS-RFA [12–15].

About five series have been published, including NETs or PCNs, most of them being retrospective or including only a few patients [16–20]. In addition, the follow-up of the patients in these series is <13 months [16–20]. The short-term efficacy in these series ranges between 71.4% and 100% for NETs and around 60% for PCN but the long-term outcome and risk of recurrence have been unknown until now [16–20]. Although these results regarding short-term efficacy are interesting, surgery remains the treatment of choice in the absence of long-term follow-up and randomized series. However, regarding the results of surgical resection of benign tumors like NETs, the mortality rates range from 3% to 14% and morbidity rates from 15% to 30% compared to no mortality and morbidity ranging from 3% to 10% with EUS-RFA [21, 22].

Studies assessing the results of EUS- RFA were conducted between 2015 and 2019 [16–20]. Of them, three were prospective studies with follow-up ranging from 6 months to 1 year [16, 18, 19]. Our team conducted a multicenter prospective study between February 2015 and February 2017 for which 1-year follow-up was published [18], including patients with NETs or PCNs. Because the last patient included has now had at least 3 years of follow-up, we decided to assess the long-term outcome of these patients with follow-up ranging from 3 to 5 years prospectively.

The primary objective of this series was to assess in patients with at least 3 years follow-up the efficacy of EUS-RFA and the secondary objective was to assess the risk of recurrence and outcomes in patients with complications.

Patients and methods

Patients and criteria for inclusion

This prospective, multicenter, non-randomized study started in 2015 and included 30 patients with NETs or PCNs. It received the approval of an independent ethics committee (Comité de protection des personnes Sud Méditerranée I; November 17th 2014; reference number 2014-AO1474-43) and received ClinicalTrials.gov ID registration: NCT02330497

The included patients presented with either pancreatic NETs <2 cm on computed tomography (CT) scan with histological proof (EUS-FNA result yielded endocrine tumor belonging to the G1 WHO classification) or branch duct IPMN (connecting duct identified on magnetic resonance imaging [MRI] and/or EUS) with WF/HRS including mural nodules >5 mm (HRS) or MCA. The patients were non-operable due to severe comorbidity or they refused surgery that was offered as first-line treatment. The patients were 16 males and 14 females with a mean age of 54.4 years (49–84 years), 12 with NETs and 17 with PCNs (**► Table 1**). One patient who had a final diagnosis of late pancreatic metastasis of renal carcinoma was excluded.

The patients were included over 2 years from February 2015 and were followed up during the 3 years after inclusion. At 1 year, recorded data were analyzed and published [18]. Followup included repeated EUS and CT/MRI every year.

Objectives and endpoints

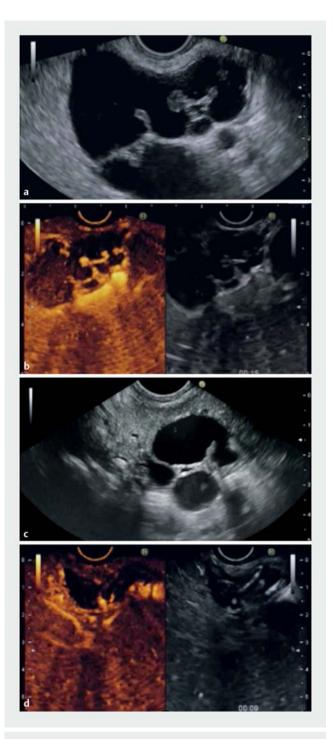
The primary objective was the antitumor efficacy after at least 3 years of follow-up. The criteria for efficacy in PCNs were complete necrosis, diameter decrease >50%, diameter decrease < 50%, and the disappearance of mural nodules assessed by EUS/MRI (▶ Fig. 1). The diagnosis of disappearance or necrosis in NETs was made at the CT scan according to the lesion's disappearance or the absence of contrast enhancement at the arterial time in a low-density lesion (▶ Fig. 2). Contrast-enhanced harmonic (CEH) EUS was not used in all the centers included in the study. Results were classified as complete resolution (disappearance or necrosis), significant response (decrease >50% or complete resolution), failure (decrease <50% or no effect).

The secondary objectives were to assess the recurrence on the treated site or other sites and the outcome of patients with complications. In the case of recurrence, a second session was proposed to the patient in the absence of malignancy.

► Table 1 Characteristics of lesions treated with EUS-RFA							
Type of lesion	Location	Diameter (mean, range)	Special findings				
NET 12 patients	Head 3 Body 6 Tail 5	13.4mm (10-20mm)	2 cystic NETs 2 double NETs (1 MEN 1)				
PCN 17 patients (16 IPMN, 1 MCA)	Head 10 Body 4 Tail 3	29.1 mm (19–60 mm)	12 mural nodules > 5 mm 4 increased thickness wall 5 multiloculated cysts				

NET, neuroendocrine tumor; PCN, pancreatic cystic neoplasm; IPMN, intraductal pancreatic mucinous neoplasm; MCA, mucinous cystadenoma.

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▶ Fig. 1 EUS-guided RFA for IPMN with mural nodules. a EUS view showing a large IPMN with mural nodules located in the body of the pancreas. b CEH EUS showing enhancement of the mural nodules. c Follow-up at 42 months after EUS-RFA showing no disappearance of the cystic lesion but complete disappearance of mural nodules. d Follow-up at 42 months with CEH EUS showing no enhancement of mural nodule.

Technique

All endoscopic examinations were performed with an EUS therapeutic scope (EG-3870UTK, HOYA corporation Pentax life care division, Tokyo, Japan, or GF-UCT180 Olympus, Tokyo, Japan). In the case of NET, the operative needle was used directly. In the case of PCN, fine-needle aspiration (FNA) with a 22 G regular needle was performed first to suck the fluid content until a thin layer of fluid content remains to target the remaining cystic lesion, then the operative needle was used. If the fluid content was too viscous, the 22 G fine needle was exchanged with a 19 G FNA needle. In the case of multiloculated cysts, septations were torn with fanning movement of the needle tip to suck the main part of the fluid content.

EUS-RFA was performed with an 18 G RFA needle (STARmed, Taewoong, Korea) applying a 50W current with Continuance Mode setting until reaching 100 Ohms impedance (white bubble appearance) and not exceeding 500 Ohms. RFA was stopped either when the operator saw white bubbles on the EUS screen alongside the needle and outside the targeted lesions or when the impedance exceeded 100 Ohms. With the STARmed needle, the mean duration of radiofrequency exposure was related to both impedance surveillance and white bubble diffusion, usually ranging between 20 and 45 seconds.

Prophylaxis for complications

Prophylaxis was administered for acute pancreatitis, infection, and perforation following complications in the first two patients [18]. Rectal diclofenac was given as recommended before endoscopic retrograde cholangiopancreatography to prevent post-endoscopic pancreatitis. Antibiotic prophylaxis (2 g of amoxicillin and clavulanic acid intravenously) was given to avoid infection. Sucking the main part of the fluid content in the PCN procedure was performed previously before RFA to avoid excessive radiofrequency current into the liquid component.

Results

Patients and follow-up

At inclusion, there were 12 patients with 14 NETs and 17 patients with PCNs (16 IPMN and 1 MCA).

NET patients were seven males (58%) and five females with a mean age of 59.9 years (45–77). All were well-differentiated and non-functional NETs belonging to OMS grade 1 classification and associated, in one case, with multiple endocrine neoplasia (MEN) type 1. The mean size of the NETs was 13.1 mm (10–20 mm). Their location was three in the head, six in the body, and five in the tail. PCN patients had branch duct IPMNs in 16 cases and one MCA. They were seven males and 10 females (44%/56%) with a mean age of 65.7 years (65–83). The mean diameter size was 28 mm (9–60 mm). They were located on the head in 10 cases, the body in four cases, and the tail in three cases. Among 16 cases with branch duct IPMNs, 12 patients had mural nodules (mean size 5.7 mm [5–10 mm]) and with increased thickness of the cyst wall in 4 cases (mean size 3.3 mm [2–7 mm]).

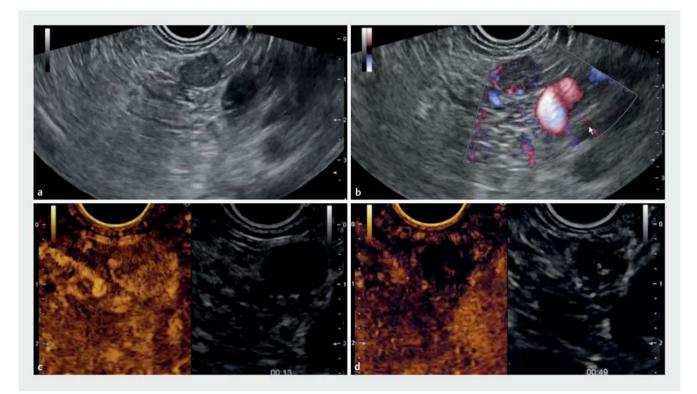


Fig.2 EUS-guided RFA with CEH control for NET located to the body of the pancreas. a EUS view of NET located to the body of the pancreas, 11 mm size, homogenous. b EUS view of NET with fine doppler showing peripheral arterial vascularization. c CEH EUS view of NET showing early hyperenhancement. d immediate CEH EUS view of NET after EUS-RFA showing no more enhancement of the treated NET.

► Table 2 NET follow-up							
Inclusion	1-year follow-up	>3-year follow-up	Final results				
14 NETS 12 patients	12 disappearance	11 successes 1 late recurrence	Success 85.7%				
	2 failures	1 late success 1 metastatic evolution	Failure 14.3%				

NET, neuroendocrine tumor.

Patients were followed up at least 3 years after inclusion, the last one being included in February 2017. The mean age at the end of the follow-up was 62.5 years (52–87 years). Mean duration of follow-up was 42.9 months (36–53). Four patients died during the follow-up. There were two males and two females with ages ranging between 52 years to 77 years. They died respectively at 42, 42, 17, and 26 months from different causes than from the NETs or IPMNs: one suicide in a patient with MEN1 and NET; one of a hemorrhagic stroke, one of hepatocellular carcinoma; and one developed a distant pancreatic cancer in the tail of the pancreas after being treated with EUS- RFA for IPMN located in the head of the pancreas (without cystic lesions in the tail of the pancreas).

Long-term efficacy

Results in NETs

All of the patients were followed up for at least 3 years with a mean of 45.6 months, despite one patient who died at 42 months follow-up from suicide, with complete disappearance of the two NETs treated (**> Table 2**).

At 1-year follow-up, 12 NETs had completely disappeared or appeared necrotic (85.7%) (► Fig. 2). Two were considered a failure.

At the end of the follow-up (45.6 months), 12 NETs had completely disappeared (85.7%). One of them had a small hyperechoic scar after 6 months of follow-up without contrast enhancement on CT scan and EUS with negative FNA. The scar remained stable from 6 to 41 months follow-up. One of them was initially considered as a failure at 1 year because the cystic lesion, which was located at the tail of the pancreas, still measured 20 mm. No contrast enhancement was seen on EUS. At the end of follow-up (53 months), the lesion disappeared entirely on CT scan and EUS.

Failure and second EUS RFA session

There were two failures, of which one was a recurrence after disappearance at 1 year; another one was a failure at 1-year follow-up. One was a NET occurring in a 73-year-old male patient. The lesion was located in the body of the pancreas, and measured 18 mm at inclusion. At 6 months, the lesion was 13 mm, and at 1 year, the lesion could not be found anymore, considered as a success. At the end of the follow-up (42 months), the lesion was again measured at 16 mm on EUS with no contrast enhancement at contrast-enhance harmonic EUS. The FNA showed well-differentiated neuroendocrine cells, G1 of the WHO classification. A second session was scheduled for the patient, but he refused.

The second one occurred in a 65-year-old female patient. The lesion was located in the body of the pancreas and measured 19 mm at inclusion with a G1 WHO classification. Treatment was considered a failure at 1 year with the lesion measuring 12 mm at 6 months and 16 mm at 1 year. The patient received a second session of EUS-RFA at 23 months. A CT scan at 2years follow-up showed no liver metastasis and the persisting lesion measured 13 mm in the body of the pancreas. On the CT scan, at 3-year follow-up, asymptomatic liver metastases were shown on a positron emission tomography scan that identified intense uptake on liver metastases and pancreatic tail. The patient is doing well and receives somatostatin therapy. The second report of the pathological examination of the first FNA was corrected from G1 to G2 of the WHO classification.

Results in pancreatic cystic neoplasms (PCNs)

Patients treated for PCNs were followed for a mean of 42.6 months and two were excluded because they died at 17 and 26 months, respectively. One died from hepatocellular carcinoma related to liver cirrhosis associated with alcoholism. He had a 76-mm branch duct IPMN with mural nodule and high-grade dysplasia at inclusion. At the end of follow-up, the IPMN measured 60 mm with no mural nodule. The second patient died at 26 months from a distant pancreatic adenocarcinoma not related to the side branch IPMN that was treated.

At 1 year with 17 patients, 11 had complete disappearance (64.7%), and one diameter decreased by more than 50%. The response rate was 70.5%. Four cases presented with a diameter decrease < 50% and one with no changes. Mural nodes all disappeared at EUS follow-up in 12 of 12 cases (100%).

At the end of 42.6-month follow-up on 15 patients, six (40%) had complete disappearance of the lesion with an initial median size of 18 mm (range 11–37 mm). Four patients (26.6%) had a decrease >50% with an initial median size of 12 mm (range 9–32 mm) changing to 4-mm median size (4–16 mm). Three of them were small recurrences with size ranging between 4 and 6 mm.

In five patients, treatment was a failure or lesions decreased <50% with an initial median size of 35mm (25–76mm) changing to 30-mm median size (25–60mm). Three had no growth increase, two a slight size decrease. In all cases, the 10 patients with mural nodules at inclusion had no more mural nodules (3, 4, 3 had complete disappearance, >50% decrease, and <50% decrease, resspectively) (**Fig.1**).

Second EUS-RFA session

Two patients underwent a second EUS-RFA session. One had a decrease in tumor size >50% (32 mm to 12 mm) and complete disappearance of the mural nodule. One had no change in size (25 mm) of a PCN located in the head and she underwent a second session at 19 months. A severe complication occurred (biliary leakage endoscopically managed) after seven RFA shots had been given with no effect on the tumor size.

Distant pancreatic adenocarcinoma

One patient died from a hemorrhagic stroke during follow-up at 42 months (>3 years) and, therefore, was not excluded. That person had an IPMN located in the head of the pancreas that measured 40 mm. At 1 year, the IPMN remained stable in but without a mural nodule. At the end of 42-months follow-up, there was no cystic lesion located in the head of the pancreas and complete disappearance of the previous one. Nevertheless, a pancreatic adenocarcinoma appeared in the tail of the pancreas without a previous cystic lesion. The patient was scheduled to have a left pancreatectomy, but he died from a hemorrhagic stroke.

The second patient died at 26 months from distant pancreatic carcinoma located in the tail of the pancreas with liver metastases. He was included for management of branch duct IPMN located in the head of the pancreas that measured 46 mm with a 6-mm mural nodule. At that time, there was no cystic lesion located in the tail of the pancreas. At 1 year and 26 months, the cystic lesion located in the head of the pancreas measured 10 mm with no mural nodule.

Overall complications

Three patients had immediate complications following EUS-RFA: one had pancreatitis, which was conservatively managed; one had a perforation that was surgically managed with suturing and a favorable outcome with complete disappearance of the IPMN; one had pancreatic duct stenosis that was endoscopically managed no late symptoms. All had full recovery without sequelae and total disappearance of the initial lesions (2 NETs in the first case, IPMN with high-grade dysplasia in the second case, NET in the third case).

One patient had a biliary leakage after a second RFA session at 19 months. She had biliary leakage treated with EUS-guided cyst-gastrostomy and biliary stenting. One year later, all the stents were removed with no sequelae but with no change in the size of the IPMN.

The overall complication rate was four of 29 patients (13.79%). When the protocol changes after the two first complicated patients (nonsteroidal anti-inflammatory drug, antibiotic prophylaxis, sucking the fluid content) were considered, the rate was reduced to 7.4%.

No delayed adverse events related to the initial RFA session occurred during the follow-up.

Discussion

An increasing number of studies evaluating EUS-RFA for treating premalignant pancreatic tumors such as NETs and PCNs are available. Most of them have included a small number of patients and some are retrospective [16–20]. Five series about EUS-RFA of NETs have been published [16–20], three of them prospective, including one to 12 patients [16–20, 23, 24]. Three studies about EUS-RFA of PCNs have been published, two prospective, including 6 to 17 patients [16, 18, 25]. In addition, the follow-up was limited to 1 year (10–13 months). If the efficacy for NETs ranged between 71.4% and 100% and for PCNs was between 48.4% and 65%, the long-term results are still unknown and the clinicians cannot rule out the risk of recurrence or unfavorable outcomes such as early malignancy [18, 23–25].

We decided to extend the follow-up of the prospective multicenter study that started in February 2015 and ended in February 2017, with 1-year follow-up. All the patients were checked annually at least 3 years after inclusion, with a mean follow-up of 42.9 months (36–53). Four patients died during follow-up due to unrelated diseases (1 suicide, 1 hepatocellular carcinoma, 1 hemorrhagic stroke, and 1 distant pancreatic cancer). The latter was a distinct pancreatic adenocarcinoma located in the tail, whereas the IPMN was in the head of the pancreas, and probably developed on ductal PanIN 3 lesions. In all of the patients, controlled was achieved with EUS at the end of follow-up, as shown in MRI in the case of PCN or CT scan/MRI in the case of NET.

Regarding the RFA results for NETs, the long-term results of EUS- RFA in 14 lesions occurring in 12 patients appeared to be stable, with 85.7% at 1 year and the end of follow-up (>Ta**ble 2**). These apparently stable results included one late response and one late recurrence. The late response was a case considered as a failure at 1 year despite negative CEH EUS; the tumor disappeared completely at 53-month follow-up. We postulate that it could be a delayed success related to the activated immune response associated with RFA [18-26]. Conversely, an 18-mm NET located in the body of the pancreas seemed to disappear at 1 year after the size decreased to 13 mm at 6 months. It reoccurred at 42-month follow-up at a size of 16 mm. No contrast enhancement could be seen on CEH EUS, but EUS-FNA showed well-differentiated endocrine cells belonging to the G1 WHO classification. We have no clear explanation for this late and benign recurrence.

Although the protocol of this study included only one RFA shot with 50 W not exceeding 100 Ohms, we now apply one to three shots, depending on the results of immediate CEH EUS (**> Fig. 2**). After considering the complete diffusion of the white bubbles into the volume of the tumor, the tumor was assessed by CEH EUS. In the case of persisting contrast enhancement, we added a targeted RFA shot. The same protocol also has been supported by other authors [23, 24, 27]. A recent series demonstrated in 19 patients with solid abdominal tumor the usefulness of targeting EUS- RFA with CEH-EUS findings [27]. Nevertheless, in the protocol for the study we began in 2015, CEH EUS was not required in all the centers included because it was not available in all the institutions.

The risk for developing metastatic lymph nodes or liver metastasis during follow-up of NETs is probably the main uncertainty of EUS-RFA management. Unfortunately, in our series, one case showed an unfavorable outcome with metastasis in a 65-year-old female. The lesion was classified as G1 of the WHO classification, located in the body of the pancreas, and measured 19 mm. Her treatment was considered a failure at 1 year. She received a second session of EUS-RFA at 23 months and the size of the lesion decreased to 13 mm. She developed asymptomatic liver metastases at 36 months with a PET scan identifying an intense uptake on liver metastases and in the pancreatic tail. Because we did not understand the metastatic outcome, we asked for a second opinion on the pathological examination of the first FNA. It was corrected from G1 to G2 of the WHO classification. It has been shown in the literature that the accuracy of FNA for adequate WHO classification ranges from 74% to 87.5% [28]. This could explain the discrepancy between the two pathological reports, which underscores the need for long-term follow-up. In case of failure at 1 year, surgery should be recommended despite the fact that delayed healing can occur after a 1-year follow-up. The risk of developing further malignancy during the follow-up of NETs < 2 cm is estimated to be up to 27.3% for lymph nodes and 9% for metastases [29]. The European NET guidelines and the revised National Comprehensive Cancer Network guidelines suggest surveillance for lesions <2 cm (and no more surgery) [30-32]. Pancreatic surgery for NETs is associated with a mortality rate ranging between 3 % to 6% and morbidity rate ranging from 14% to 58%, mainly due to pancreatic fistula [21]. The 5-year overall survival and diseasespecific survival rates are 85% and 93%, respectively [21]. A randomized series comparing surgical resection and EUS-RFA should be conducted. Looking at the metastatic outcome in this patient, we recommend referring the patient to surgery in case of failure of EUS-RFA at 1 year.

Regarding the PCN results, the disappearance and size of the tumor showed relative stability, whereas all the mural nodules disappeared (> Table 3). A significant response (disappearance or size decreasing >50%) was shown in 70.5% at 1 year versus 66.6% at the end of the follow-up (**Table 3**). Three patients presented with recurrence of a small cyst ranging between 4 and 6 mm. RFA failures remained stable, occurring in one-third of patients. The initial median size in patients with failure was greater than those with disappearance or size decrease >50% (> Table 3). Even in patients with failure, three had a mural nodule, which disappeared entirely. As for EUS-RFA, the initial protocol called for a one-shot treatment within the cystic lesions. After the end of this study, we applied two to five shots for filling the lumen of the cyst with white bubbles. We never exceeded five shots because we had a biliary leakage in the patient with IPMNs located in the head of the pancreas who had undergone seven shots in a second RFA session at 19-month followup. The biliary leakage was resolved with biliary stenting for 1 year with no stenosis.

Two cases of distant pancreatic adenocarcinoma occurred in the tail of the pancreas, whereas both of the IPMN lesions were located in the head of the pancreas. One patient from liver metastasis and pancreatic adenocarcinoma in the tail of the pan-

► Table 3 PCN follow-up

Inclusion	One year FU		\rightarrow 3 years FU	
	Disappearance 11 cases Significant response	64.7%		Disappearance 6 cases 40 % (Median initial size 18 mm [11–37 mm])
17 patients Efficacy 1 year Significant response 70.5%	1 case	5.8%	15 patients Followed Efficacy 3 years Significant response 66.6%	Significant response 4 cases 26.6 % (Median initial size 12 mm [9–32 mm])
	Failure 5 cases	29.4%		Failure 5 cases 33.3 % (Median initial size 35 mm [25–76mm])
Mural nodules (12 cases)	Disappearance 100%		Mural nodules 100%	Disappearance 100%
	0 mural nodules			0 mural nodules

creas at 26 months, whereas the second one died at 42 months from a stroke before undergoing left pancreatectomy. The association of IPMNs with pancreatic adenocarcinoma arising from PanIN3 lesions distant from the cystic lesion has been described in the literature [33-36]. The 5-year rate of development of distinct adenocarcinoma in patients with IPMNs has been calculated to 6.9%, with an incidence per year of 1.1% [33]. In a surgical series of 40 patients with IPMNs, pancreatic intraepithelial neoplasia was found in 78%, 11% being PanIN-3 lesions [35]. EUS seems to be able to detect 69% of PanIN lesions, 57% with PanIN-3 lesions [35]. In another series assessing the role of EUS, the 3- and 5-year rates of IPMN-concomitant pancreatic ductal adenocarcinoma were 4% and 8.8%, respectively [36]. The EUS strategy should include not only the therapeutic approach with RFA but also sustained surveillance, not only of the treated cystic lesion but also of distinct and distant lesions, such as in these two patients.

Conclusions

In conclusion, EUS-RFA management of pancreatic NETs or PCNs is associated with significant positive long-term outcomes. The complete disappearance of NETs occurred in 85.7% of cases. Treatment was a failure in only one patient, who did not undergo surgery because of metastasis. For PCNs, a significant response occurred in 66.6% of patients, with complete disappearance of all mural nodules. However, two patients developed distinct and distant pancreatic adenocarcinoma, which underscores the need for accurate and sustained EUS follow-up.

Competing interests

Dr. Barthet received a research grant from Boston scientific (endoscopic gastrojejunal anastomosis). Dr. Napoleon is a consultant for Boston Scientific.

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