REVIEW AND CASE SERIES

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Pancreatic neuroendocrine tumors – going beyond surgery. Literature review and experience of a tertiary center

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Abstract

Background: Surgery is the standard therapy for pancreatic neuroendocrine tumors (pNETs), but since post-resection fistulae and other surgery related complications are common, new minimal invasive approaches are emerging. Endoscopic ultrasound-guided radiofrequency ablation (EUS-RFA) is a promising tool for pNETs, with a good safety profile and favorable results. *Patients, Materials and Methods*: This is a single-center, retrospective case series including all patients with functional (F) and non-functional (NF) pNETs treated with EUS-RFA in the Department of Gastroenterology, Emergency Clinical Hospital of Bucharest, Romania, between March 2023 and March 2024 and followed for a mean period of 11.6 months. Technical success, clinical, sonographic and radiological response, adverse events (AEs) rate and severity were assessed. *Case series*: A total of five out of nine EUS-RFA were performed for pNETs, with a majority of NF-pNETs. In this pNET group, the mean size of the lesions was 13 mm. Technical success was achieved in 100% of patients and persistent clinical remission of hypoglycemia in the insulinoma case was attained. In the NF-pNET subgroup, two patients were successfully radiologically treated with complete disappearance of the lesions, one lesion showed cystic transformation, and one had modest size reduction at follow-up imagery. One procedure-related early AE occurred: mild abdominal pain with quick resolution. No major complications, nor death were reported. *Conclusions*: Reports from this literature review and small case series suggest that EUS-RFA can be effective in both F- and NF-pNETs, offering the best combination of real-time imaging guidance and minimal invasiveness with no severe AEs and short hospital stay.

Keywords: neuroendocrine tumors, pancreas, EUS-RFA, insulinoma, NF-pNETs.

Introduction

Neuroendocrine neoplasms (NENs) are a group of tumors that originate from neuroendocrine (NE) cells distributed across all organs but generally exhibit three main locations – pulmonary, digestive tract and pancreas [1]. Lesions localized in the pancreas are classified into two subgroups: functional (F) or non-functional (NF) neoplasms. In Netherlands, in a population-based study focused on overall survival (OS) and relative survival (RS), pancreatic neuroendocrine neoplasms (pNENs) represented nearly one fifth (18%) of all gastrointestinal tract NENs [2]. According to the *Surveillance, Epidemiology, and End Results* (SEER) *Program*, pancreatic neuroendocrine tumors (pNETs) had an incidence of 0.48 per 100 000 new cases per year, with a predominance of NF-pNETs and a worse OS [1, 3–5]. Median survival of patients with G1 and G2 pNETs was 42 months and reached 136 months in lesions confined to the pancreas [6, 7].

The difference between a F- and a NF-pNET is related to the presence of a clinical manifest secretion syndrome and not on the immunohistochemical (IHC) staining, as many tumors can have stored hormones or secrete inert substances but produce no clinical syndrome [6].

Insulinomas are a rare type of F-pNET that secrete insulin, which can cause hypoglycemic episodes during fasting; additionally, subsequent sympathetic activation may lead to tachycardia, generalized weakness and diaphoresis [8–10]. Nevertheless, it is the most common type of F-pNET [11]. Most insulinomas are predominantly located in the head and body of pancreas, having a benign evolution. The malignant character should always be questioned until the contrary is proved, since malignant insulinomas are estimated to be around 6% [12].

Surgery is the standard treatment recognized by most of the Guidelines [*European Society for Medical Oncology* (ESMO), *European Neuroendocrine Tumor Society* (ENETS), *North American Neuroendocrine Tumor Society* (NANETS)], trending more and more towards parenchymal-sparing techniques [tumor enucleation, duodenum-preserving

pancreatic head resection (DPPHR), and pancreatic middle segment resection]. However, surgical associated morbidity (fistula, postoperative long-term metabolic disorders – diabetes and exocrine insufficiency, steatohepatitis) and mortality rates resulted in the quest for approaches safer but still effective especially in the case of young patients.

In a recent study, which included 587 patients, it was discovered in histopathology (HP) that half of pancreatic resections represented low-grade (G1) tumors [13]. Even if parenchyma-sparing, local resections are associated with low-grade metabolic dysfunctions [14] and the frequency of biliary fistula remains important, Beger *et al.* concluding on a 4.5% frequency of biliary fistula following partial and total DPPHR [9].

Endoscopic ultrasound (EUS)'s vast utility ranges from detection of tumors *via* EUS-guided fine-needle biopsy (EUS-FNB) tissue sampling to providing additional information for treatment selection (tumor site, relationship with pancreatic main duct and vessels). Studies suggest that the rate of tumor seeding after FNB in pancreatic cancer typically ranges from 0.06% to 1.6%, depending on the study, technique, and other factors [15]. Furthermore, EUS-guided fine-needle tattooing (EUS-FNT) and EUS-guided fiducial implantation (EUS-FI) of small "deep" lesions may help facilitate surgical localization, but these are rarely performed in clinical practice. Since recently, EUS offered a new feasible alternative therapeutic approach to surgery in high-risk patients with F- and NF-pNETs: alcohol injection or radiofrequency ablation (RFA) [16].

RFA uses high frequency alternative current (400–500 kHz) that generates high temperatures to induce cell apoptosis and coagulative necrosis [17, 18] and it is also believed to have durable oncological response through immunomodulatory effects by release of tumor-related antigens [17, 19–22].

The *ENETS* Guidelines for F-pNETs recommend considering EUS-RFA for localized insulinomas smaller than 2 cm as treatment option if the patients are unfit for surgery. Clinical success rate from recent retrospective studies ranges between 86–96% with only minor treatment-related adverse events (AEs) [23–25]. As for small NF-pNET, *ENETS* Guideline's preliminary experience has shown that RFA can be an alternative and effective treatment to surgery. Therefore, in 2023 *ENETS* recommend a personalized therapeutic management of patients with NF-pNET >1 cm and ≤2 cm, without dilation of the main pancreatic duct [5].

Rimbaş *et al.* concluded in a more recent publication that EUS-RFA may be regarded as a standard treatment option in the case of pancreatic insulinomas owing to its strong safety record and effectiveness, but for the rest of the NF-pNENs the application of selection criteria is needed [26].

Patients, Materials and Methods

We performed a retrospective analysis of all patients (nine) who underwent EUS-RFA for different indications in one of the few specialized centers in Romania who performs EUS-RFA – Department of Gastroenterology, Emergency Clinical Hospital of Bucharest, Romania, between March 2023 and March 2024, and selected only the pNETs ablation candidates. The mean follow-up time was 11.6 months. Based on multidisciplinary team decision (MTD), small (<2 cm) pNETs, either insulinomas or NF-pNETs with previous confirmed histopathological diagnosis (<12 months) and with no signs of lymph node involvement or distant metastasis were eligible for EUS-RFA.

Out of nine patients who had EUS-RFA performed for different indications, five cases were NE indications: one sporadic insulinoma and four NF-pNETs. Indications in the non-NE groups were locally advanced adenocarcinoma and hepatic metastasis from colorectal cancer.

All patients agreed with the intervention and signed the informed consent.

Immediate technical success was represented by complete mass ablation on contrast-enhanced harmonic EUS (CH-EUS) after procedure (absence of contrast enhancement). Other follow-up parameters were clinical outcomes (symptom remission with a normal concentration of blood glucose for insulinomas) and the complete (complete mass ablation, signs of necrosis or cystic transformation) or partial (>50% decrease in size) radiological response minimum three months after ablation, AE rate and severity.

Procedures were performed by one interventional endoscopist with an expertise of around 600 EUS procedures per year. The same linear echoendoscope was used for all procedures (GF-UCT180 Curvilinear Array Ultrasound Gastrovideoscope, Olympus, Tokyo, Japan). A 19-gauge (5 mm or 10 mm in length) RFA needle was used with a dedicated radiofrequency (RF) current generator, which allows control of power and impedance and has an inner cooling system. After the procedure, CH-EUS was performed to evaluate residual enhancing neoplastic tissue to assess the need for further ablation. RFA energy was applied at a slightly similar power setting ranging from 30 to 35 W, in one or two cycles, each pass with a maximum duration of 20 seconds (Table 1). CH-EUS with intravenous injection of SonoVue® was performed at the beginning of the procedure to better define the location, margins, enhancement type, pattern of distribution and dynamics of vascularity of the lesions and immediately after RFA procedure in order to delineate real-time vascular perfusion and detect residual neoplastic tissue to ablate.

Table 1 – ***Summary of patient and tumor characteristics, and EUS-RFA procedure data***

Case No.	Age [years]	F/NF	Size [mm]	Grading	Distance from Wirsung duct [mm]	RFA power [W]	No. of passes per treatment	Procedure AEs
1.	53	F	15/8	G1	>2	30	2	Mild abdominal pain
2.	71	NF	12/10	G1	>2	30	1	None
3.	57	NF	20/15	G1	>2	30	2	None
4.	48	NF	9/8	G1	<1	35	2	None
5.	62	NF	9/9	G1	>2	30	1	None

AEs: Adverse events; EUS: Endoscopic ultrasound; F: Functional; G1: Grade 1; NF: Non-functional; RFA: Radiofrequency ablation.

Previous antiplatelet or anticoagulant therapy was tapered or discontinued in accordance with current guidelines. All patients received prophylactic antibiotics (Ceftriaxone 2 g, single dose) and intrarectal nonsteroidal anti-inflammatory drugs (NSAIDs). Mild analgesic treatment was needed in one case and one patient received prophylactic stenting of the Wirsung duct prior to the intervention during the same hospital visit as a preventive measure to reduce the risk of complications. Most patients were discharged the following day (median hospital stay of three days).

Case series

Case No. 1

A 52-year-old female with a history of recurrent symptomatic episodes of hypoglycemia (30–40 mg/dL) was referred to our Unit after a computed tomography (CT) scan that identified a 15/8 mm solid lesion in the pancreatic body. EUS-FNB (Figure 1) was performed and confirmed the diagnosis, G1 NET insulinoma. After declining surgery, EUS-RFA was performed, with favorable outcome. No post-intervention signs of pancreatitis, perforation or infection were noticed, only mild post-ablative upper abdominal pain, ameliorated by non-opioid analgetic treatment.

The patient became euglycemic one-month post-ablative treatment, and the three months re-evaluation confirmed persistence of normal blood glucose. Abdominal magnetic resonance imaging (MRI) three months later still describes a nodular lesion but with a moderate decrease in dimensions, measuring this time 11/10 mm with minimal peripheric gadolinium uptake after injection of contrast.

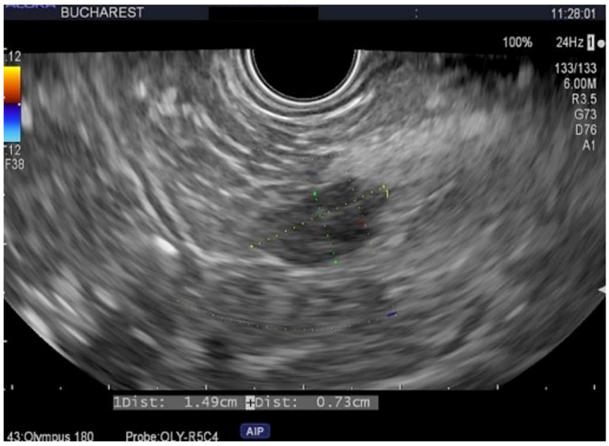

Figure 1 – ***EUS image of a hypoechogenic lesion (insulinoma before EUS-FNB). EUS: Endoscopic ultrasound; FNB: Fine-needle biopsy.***

Case No. 2

Male of 71 years old, with serious cardiovascular and pulmonary associated pathology, *American Society of Anesthesiologists* (ASA) *Physical Status Classification* III, under antiplatelet therapy, unfit for surgery at the time of diagnosis of a G1 NF-pNET (Figure 2, A–D). The lesion situated in the body tail region of the pancreas measured 12/10 mm and an EUS-RFA approach (Figure 2, E and F) was decided in an MDT meeting. Early arterial phase SonoVue® contrast enhancement was noticed before ablation and after one passage, absence of post-procedural contrast uptake confirmed technical success.

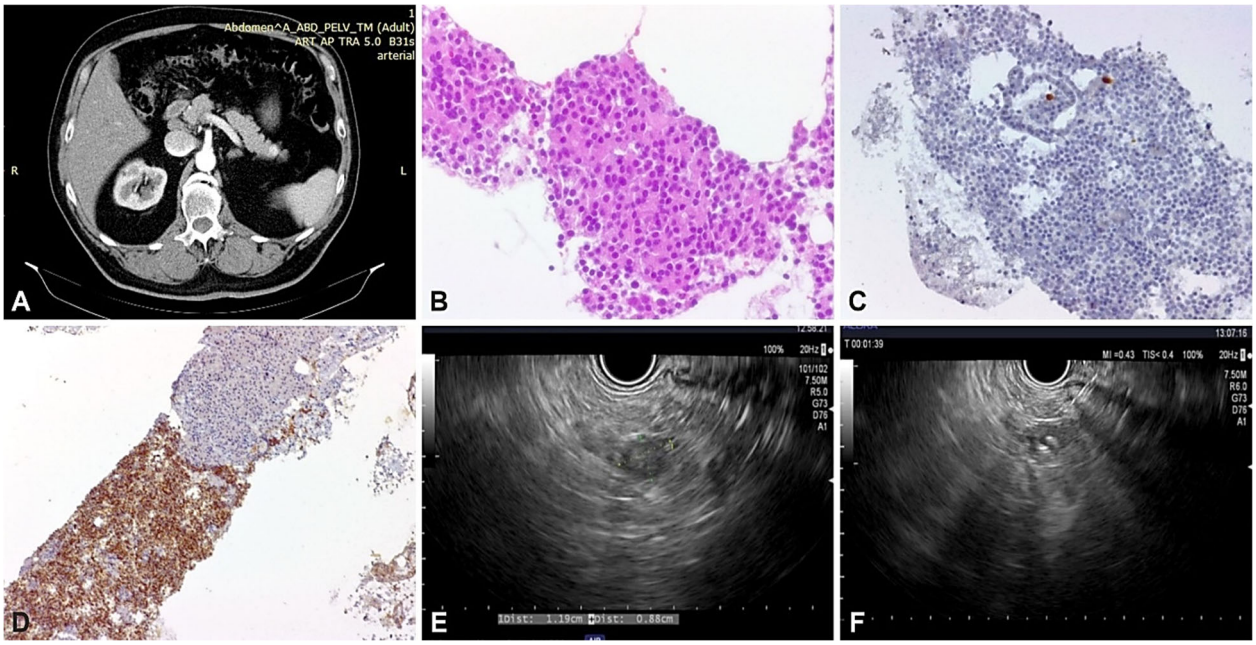

Figure 2 – ***(A) CT in arterial phase showing a body tail-enhanced lesion; (B) Proliferation of small to medium monotonous cells with coarse nuclear chromatin and minimal atypia, pink cytoplasm – the tumoral cells are arranged in solid nests (HE staining, ×400); (C) Chromogranin A IHC staining (×400) reveals positive tumoral cells (brown colored) in contrast to acinar pancreatic tissue; (D) IHC staining for Ki67 (×100) reveals rare positive nuclei (brown colored), a Ki67 index less than 2%; (E) EUS evaluation of a pancreatic body hypoechogenic lesion; (F) EUS-RFA ablation in a patient with NF-pNET. Histopathology and immunohistochemistry microscopy images: Leica DM750 microscope; LEICA IC50W camera for image capture; Leica Application Suite image acquisition and processing system. CT: Computed tomography; EUS: Endoscopic ultrasound; HE: Hematoxylin–Eosin; IHC: Immunohistochemical; NF: Non-functional; pNET: Pancreatic neuroendocrine tumor; RFA: Radiofrequency ablation.***

CT was performed three months later showing no sign of the anterior contrast-enhanced lesion, sign of effective treatment. Patient confirmed no clinical symptoms, with normal biological markers and good quality of life and it was proposed for imagistic reassessment in three months.

Case No. 3

A 57-year-old female was diagnosed with a nearly 20 mm grade G1 NF-pNET localized in the pancreatic head (Figure 3A), typically representative for a NE lesion on EUS examination – a hypoechogenic well differentiated lesion exhibiting positive Doppler signal, however invading the superior mesenteric vein which may have complicated the surgical approach. We performed two passages with the RFA needle, each with good technical success and no periprocedural complications. Abdominal MRI performed six months post-ablation (Figure 3B) showed dimensional regression down to 12.5/11.5 mm, so a new ablation session was suggested for future therapeutic management.

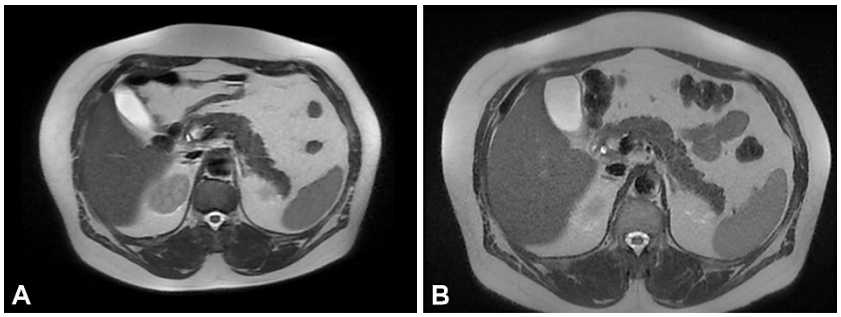

Figure 3 – ***(A) Before procedure T1-weighted MRI imaging showing pancreatic head lesion; (B) Post EUS-RFA T1-weighted MRI imaging showing pancreatic lesion decreasing in size. EUS: Endoscopic ultrasound; MRI: Magnetic resonance imaging; RFA: Radiofrequency ablation.***

Case No. 4

A young male patient of 48 years old, with chronic hepatitis B infection and a recent less than 10 mm incidentaloma finding in the head of the pancreas (Figure 4, A–C and E) situated less than 1 mm distance away from the Wirsung duct decided on an active approach instead of watchful-wait. The MDT decided on a loco-regional ablation with prior prophylactic stenting of the main pancreatic duct. Therefore, a 5 Fr/10 cm plastic stent was placed under fluoroscopic vision during the same hospitalization. Three days later, EUS-RFA (Figure 4D) was performed from the duodenal station with two cycles of RFA needed for complete ablation of the lesion and with no periprocedural complications. Three-month follow-up imagery proved complete ablation (Figure 4F), with no sign of precedent nodular lesion in the pancreas, so removal of the pancreatic stent was performed.

After pancreatic stent extraction, patient suffered a mild post-endoscopic retrograde cholangiopancreatography (ERCP) pancreatitis based on *American Gastroenterology Association* (AGA), with prompt resolution following appropriate treatment.

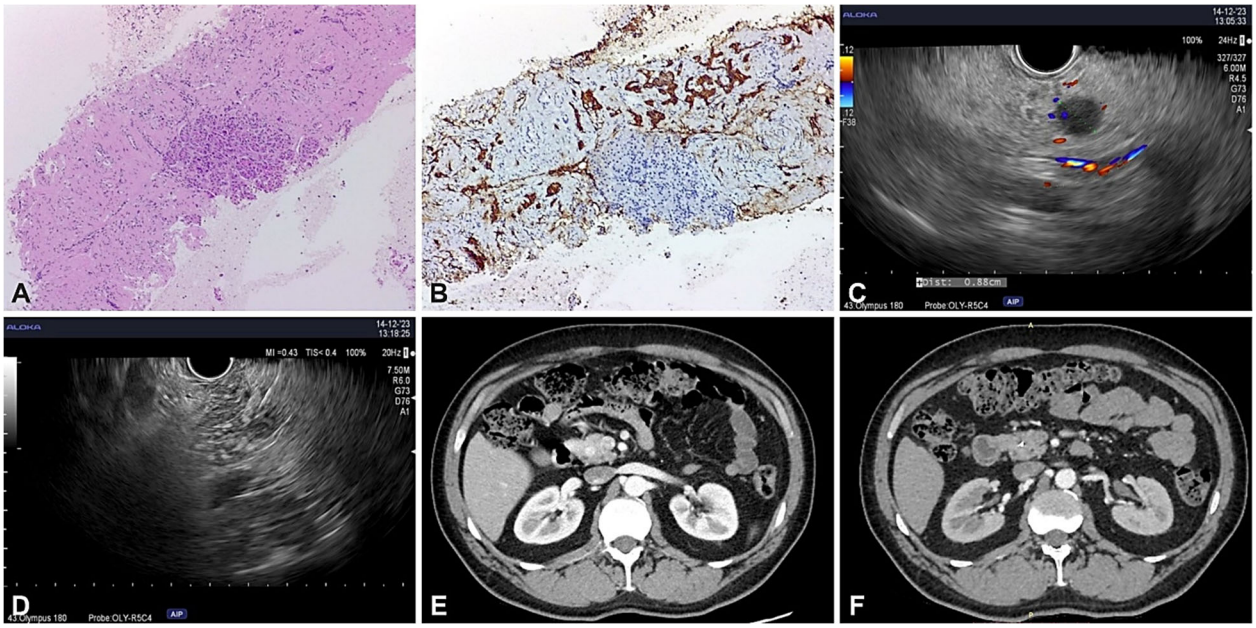

Figure 4 – ***(A) Pancreatic tissue biopsy fragment with fibrotic area in which are observed small cellular aggregates with variable shape – no mitotic activity, no necrosis (HE staining, ×100); (B) Chromogranin A IHC staining (×100) reveals positive tumoral cellular aggregates (brown colored) in contrast to acinar pancreatic and fibrotic tissues; (C) EUS images of a pancreatic head hypoechogenic lesion; (D) EUS-RFA procedure of the lesion; (E) Abdominal CT scan before EUS-RFA; (F) Abdominal CT scan after EUS-RFA – absence of head pancreatic lesion. Histopathology and immunohistochemistry microscopy images: Leica DM750 microscope; LEICA IC50W camera for image capture; Leica Application Suite image acquisition and processing system. CT: Computed tomography; EUS: Endoscopic ultrasound; HE: Hematoxylin–Eosin; IHC: Immunohistochemical; RFA: Radiofrequency ablation.***

Case No. 5

Sixty-two-year-old female patient performed an abdominal-pelvic CT scan (Figure 5A) in the context of unclear etiology recurrent abdominal pain. A 9/9 mm pancreatic body lesion with iodine enhancement similar to the spleen was discovered. Most probable differential diagnoses at that point were: insulinoma or intrapancreatic accessory spleen. Blood test showed normal levels of insulin and C-peptide, and pathology report concluded a G1 NF-pNET. EUS-RFA was performed with no peri-procedural AEs. Post-ablation MRI showed a cystic post-interventional lesion (Figure 5, B and C) and EUS also proved a transonic lesion of 6 mm with negative Doppler signal, a sign of efficient ablation.

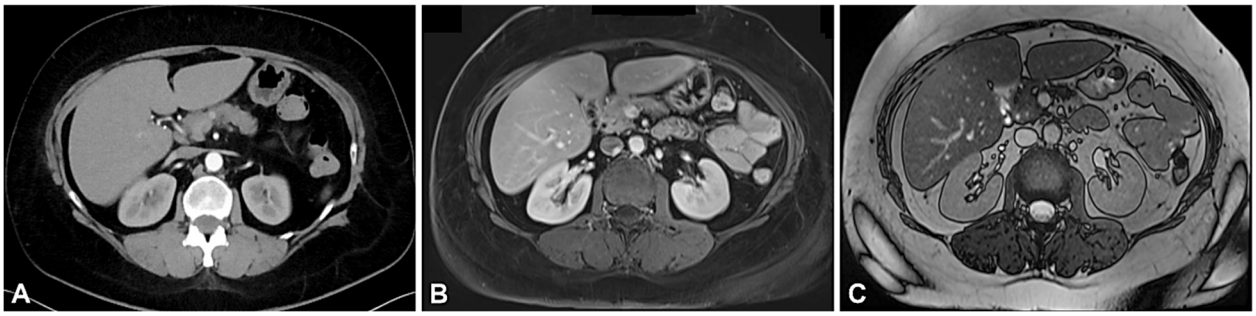

Figure 5 – ***(A) CT in arterial phase showing a round, well-defined, moderately enhanced pancreatic isthmo-corporeal lesion with iodine concentrations similar to that of the spleen; (B and C) Four months follow-up MRI after EUS-RFA ablation showing findings consistent with cystic changes secondary to treatment – hypointense on T1-weighted imaging (B) and hyperintense on T2-weighted imaging (C). CT: Computed tomography; EUS: Endoscopic ultrasound; MRI: Magnetic resonance imaging; RFA: Radiofrequency ablation.***

Discussions and literature review

In our pNETs group, the mean age at intervention was 58.2 years with 3:2 female/male ratio. Most (4/9) of the lesions were NF-pNETs, with a mean size of 13 mm (Table 1). Regarding outcomes, the patient with EUS-RFA for insulinoma had persistent remission of clinical-biological hypoglycemic syndrome and all but one patient with NF-pNET had complete radiological response (Table 2). Moreover, our good outcomes were achieved with only a limited number (1–2) of ablation passages per EUS-RFA session as opposed to Marx *et al.* (1–5 passages) [27], Oleinikov *et al.* (3–10 passages) [28] or Lesmana's short series (11–19 passages) [29]. Excellent technical success of EUS-RFA for pNENs – 99.2% was published in the 2024 meta-analysis of Khoury *et al.* This updated version of the 2023 Armellini *et al.* publication included three large cohort studies by Crino *et al.*, Napoleon *et al.*, and Ritazzi *et al.* and excluded case reports and small case series. Eleven studies (292 patients) up until April 2023 also focused on radiological response as primary outcome and other few secondary outcomes also proved high complete radiological response (87.1%), high clinical success rate in patients with F-pNENs (94.9%) and the overall AE rate of 20%, but very low rate of severe AEs 0.9% [30], which is similar to our series results.

Table 2 – ***Imaging response post EUS-RFA***

Case No.	Size [mm]	Imaging method – time from procedure	Imaging results	Recurrence
1.	15/8	MRI – 3 months	Regression to 11/10 mm	/
2.	12/10	CT – 3 months	Absence of lesion	None
3.	20/15	MRI – 6 months	12.5/11.5 mm	/
4.	9/8	CT – 3 months	Absence of lesion	None
5.	9/9	MRI – 4 months	Cystic transformation	/

CT: Computed tomography; EUS: Endoscopic ultrasound; MRI: Magnetic resonance imaging; RFA: Radiofrequency ablation.

Regarding AEs, only one case of acute pancreatitis (APT) was noted. It was not related to the RFA procedure, since it occurred after pancreatic stent removal, which was quite a surprising event. We can conclude that in our NE series in terms of safety, all procedures were well tolerated by the patients with only mild abdominal pain as early AEs. Published data regarding AEs frequency and severity in EUS-RFA are heterogenous. The most common complication in the 2022 meta-analysis and systematic review of Fahmawi *et al.* was APT (3.3%), followed by pancreatic duct stenosis, peripancreatic fluid collection, and ascites with a frequency of 2.8% each and one perforation (2.1%), balanced by a great pooled overall clinical response rate of almost 90% at an acceptably low AE rate of 6.7% [31]. On the opposite side, in a large French retrospective study of 104 heterogenous pancreatic lesions [predominantly NET (61.4%)], the expected AEs frequency exceeded the expectations: 22 AEs were reported with two severe ones (9.5% APT and 1.7% severe cases of pancreatitis). The main independent risk factor for pancreatitis after EUS-RFA seemed to be correlated to the distance from the main pancreatic duct of less than 1 mm [32].

In the prospective, non-randomized *American Society of Parenteral and Enteral Nutrition* (ASPEN) trial study (NCT03084770), which included 500 pNETs treated with either active surveillance or surgery, even though there were no deaths related to pancreatic surgery, the rate of severe complications (13%) was not neglected. Moreover, in the active surveillance arm, in the context of a small number of patients with tumor growth and in the absence of distant metastases during follow-up, it was considered as a safe management strategy [33]. Active surveillance was also an option in the MDT meetings in most of our cases, but since patients declared anxiety and concerns about potential future risks regarding a non-interventional approach even though our team explained the negligible risk of progression, we opted for a loco-regional intervention.

Prophylaxis for our patients with antibiotics and NSAIDs

prior to the procedure might have contributed to the absence of infections and post-EUS pancreatitis, but due to the small number of patients included in the study and lack of control group, this conclusion might not be accurate. No EUS-RFA severe AEs, nor deaths were noted with short hospital stay period (mean hospitalization three days). In a heterogenous pancreatic lesions, yet multicenter prospective study (NETs and some pancreatic cystic neoplasms) with a one year follow-up period the 10% AEs rate was improved to 3.5% by prophylaxis introduction against APT (rectal NSAIDs), infection (antibiotic), and perforation [34].

In Armellini's meta-analysis and systematic review, pooled estimates for the overall AE rates were lower in F-pNETs (17.8%) than NF-pNETs (24.6%), with mild AEs being the most frequent [35]. Bleeding can be an important periprocedural event and a French small study of insulinoma cases, with high clinical success (six out of seven patients), reported one older patient death one month after development of a retrogastric bleeding 15 days post-intervention [36, 37].

There is limited data in literature regarding parameters that predict a favorable response to EUS-RFA, however the most recent meta-analysis of Khoury *et al.* presents lesions less than 15 mm to respond better to treatment and the use of power setting of <50 W seems to have better results achieving the primary outcome in 92.4% as opposed to 84.6% in >50 W. Another observation based on the topography of lesions included in the studies was that technical approach for body or tail pNETs seemed easier echoendoscopically (probable better operative window and better scope stability) than cephalo-uncinated small lesions [30]. Moreover, NE differentiation and dimensions less than 20 mm were also related to procedure efficacity [32]. In our cohort, the power used for EUS-RFA was less than 35 W, the mean size of the lesions being 13 mm, with smaller lesions responding better to ablation which could explain better results in the primary outcome in accordance with previously cited literature.

Even though our case series had a short follow-up time and recurrence can emerge years after treatment, some pNETs are indolent, with slow growth, and may not require intensive monitoring if they show no progression or symptoms. It seems reasonable that some patients in our series might benefit from a second or even a third EUS-RFA session at distance from the first one in order to achieve full destruction but factors of prognosis for the need for multiple ablations and timeline for performing a second ablation are yet to be determined. In a French study, a second ablation was performed in 28% of cases after only 60% complete ablation was observed at 12 months [32].

In 2023, a comparative study (89 patients in each research group) for treatment in pancreatic insulinomas proved that EUS-RFA to be as effective as surgery (95.5% *vs* 100%), safer (as primary outcome) with significantly shorter hospital stays (3.4 *vs* 11.1 days). Even though a second procedure was needed in 15 (16.9%) cases after a mean time of 9.5 months, complete relief of symptoms (new session of EUS-RFA in 11 patients and four surgical resection) was achieved during follow-up (23.0 months) [24].

All procedures in our Center were performed by an expert echo-endoscopist with multiple pre-procedural on-site training courses both for doctors and nurses, which could have contributed to technical success. Qualified personnel and good expertise in the field of interventional EUS added positive value to the good procedural results.

It is essential to recognize that treatment goals are different in F- *vs* NF-pNETs. In F-NETs, it is the destruction of NE cells that produce hormones in order to stop the associated clinical hypersecretion syndrome, while the focus in NF-NETs is cessation of further tumor growth and progression free survival [17, 38], therefore homogeneity in indications of EUS-RFA for F- and NF-pNETs might not be plausible. In the case of insulinomas, which are generally benign and do not require lymphadenectomy but only enucleation, if available, EUS-RFA, can be considered as first-line therapy or as part of a step-up approach [24]. Research on EUS-RFA in NF-pNETs is a result of the development of imaging techniques, and the rise in pancreatic NE incidentalomas with a poorly understood natural history but known risks of pancreatic surgery. Similar clinical success in the subgroups was reported in a recent systematic review and meta-analysis that included reports from 20 eligible studies analyzing 196 lesions (101 F-pNETs and 94 insulinomas out of 95 NF-pNETs) where clinical efficacy was 95.1% for F-pNETs and 93.4% for NF-pNETs [35]. Currently, a French multicenter study on pancreatic incidentaloma is ongoing [*Investigating Pompe Prevalence in Neuromuscular Medicine Academic Practices* (IPANEMA) (IPaNeMA), NCT03022188] and a European study (ASPEN for asymptomatic small pNETs, NCT03084770) is also being conducted with results that might change current application of EUS-RFA.

Conclusions

Regarding effectiveness of treatment in pNETs, our patients had good control of tumor growth and symptomatology during a mean follow-up period of 11.6 months with an acceptable rate of low-grade AEs. Taking into consideration that our technical success was 100%, we also obtained favorable results in most cases (complete ablation, tumor reduction or clinical-biological control of symptomatology) with only one EUS-RFA session and few minimum passages. However, this data should be carefully analyzed as it is a small inhomogeneous cohort. What seems to be an important prognostic factor in the complete ablation, as literature also describes, is the dimension of the lesion. As for the effect on normalizing blood glucose, our single case responded perfectly, in accordance with published literature data. Further prospective and comparative studies need to be made to confirm its safety and efficacy in F- and NF-NETs, to fully integrate this therapeutic measure in clinical practice guidelines with precise indication.

Conflict of interests

The authors declare no conflict of interests.

Institutional Review Board Statement

The study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of Emergency Clinical Hospital of Bucharest, Romania (Approval No. 9225/12.11.2024).

Informed Consent Statement

Informed consent was obtained from all subjects

involved in the study. Informed consent to publish images was obtained from relevant participants. The patients have been informed regarding their possible images used for publication in the manuscript.

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