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Review Article

Role of Interventional Radiology in Endocrine Diseases- Review Article

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Abstract

Recently, a number of procedures for interventional radiology diagnosis and treatment have been developed by the radiologists. The 'Interventional Radiology' refers to the therapeutic procedures performed under imaging guidance. The emergence of this specialty has been made possible by a lot of advances in the technology, imaging systems, and radiologists experience. Interventional radiologists are physicians who are experienced in minimally invasive procedures and targeted treatments which have less risk, less pain and less recovery time in comparison with the surgery. Minimizing the patient discomfort, avoid of general anesthesia, lower incidence of morbidity and mortality, and decreases the length and cost of hospitalization are some advantages of interventional radiology procedures. Similar to all medical fields, interventional procedures have been introduced and developed for the diagnosis and treatment of endocrinology procedures. In this article we aim to review and report our experience about the role of interventional radiology in venous sampling for endocrine diseases (such as parathyroid venous sampling, inferior petrosal sinus sampling, adrenal venous sampling, and venous sampling for islet cell tumors). In addition, interventional treatments of neuroendocrine cancer metastases to the liver, percutaneous ethanol injection therapy for secondary hyperparathyroidism, treatment of hyperfunctioning thyroid nodules by percutaneous ethanol injection, radiofrequency ablation of the adrenal gland neoplasms, and also establishing a cGMP pancreatic islet processing facility have been discussed in this article.

Keywords: Interventional radiology, Endocrine diseases, Endovascular, Treatment

Introduction

Nowadays, interventional procedures have been opened new horizons in the medicine. They constitute wide spectrum procedures from diagnosis to treatment in different medical disciplines. Various tissue samplings, specific intravascular samplings, different intravascular interventions in central and peripheral vascular systems for congenital and acquired vascular pathologies and complications [including neurointerventions], musculoskeletal interventional procedures and vast field of oncointerventions are examples of the long list of interventional radiology field. Similar to all medical fields, interventional radiology has been introduced and developed in the field of endocrinology. In this regard, interventional techniques have been used for intravascular blood samplings in specific vascular beds [for determination of hormonal level assessments] and different ablation methods in endocrine neoplasms [including metastatic malignancies and adenomas]. In this review paper, we are going to describe a brief on the application of

the interventional radiology procedures in the field of endocrinology.

Venous sampling for Endocrine Diseases

Interventional radiology applies imaging procedures for the placement of catheters and biopsy needles either for diagnosis or minimally invasive therapies. Its application in the field of endocrinology can be either diagnostic or therapeutic.

Parathyroid venous sampling

Primary hyperparathyroidism may be caused by adenoma, hyperplasia or carcinoma, and causes symptoms associated with hypercalcemia.

Surgery in more than 95% of patients is curative with low complication rates. Although, bilateral surgical exploration had been considered as the 'gold-standard', highly specific localization techniques with high frequency ultrasound, CT, MRI and most importantly, Technetium (99mTc) have increased the trend towards minimally invasive parathyroid surgery (1). Venous sampling is indicated in localization of the site of excess parathyroid hormone secretion by selective sampling before re-operation for parat-hyroidectomy, differentiation of diffuse hyperpla-sia from a single parathyroid adenoma (2). This procedure should only be applied in patients who are planned for surgical procedures and not be used as a triage to decide who should be referred for surgery. In outpatient setting under local anesthesia, a 5–7 French catheter via the common femoral vein must be introduced into the various veins of the neck and mediastinum that potentially drain the abnormal hormone production; and subsequently 4–5 ml of blood should be withdrawn from each location for PTH assay. Although, the parathyroid glands normally drain through the superior, middle and inferior thyroidal veins, there are various anatomical variations particularly in patients who have undergone previous surgical exploration of the neck. The catheter should be withdrawn from the groin after the procedure and hemostasis achieved by compression of the puncture site for 5 minutes. The patient must be monitored and lie supine for two hours in the recovery room; and if there is no problem, discharged to home. This procedure has the highest sensitivity of any localization procedure for overlooked or ectopic parathyroid adenoma (3). In a systematic meta-analysis study for comparison between selective venous sampling with other non-invasive preoperative localizations, Seehofer et al. (4) reported that the sensitivity of selective venous sampling was at least90%, with no false-positive results. They also concluded that Tc99m scintigraphy is the procedure of choice, with selective venous sampling as the gold standard in those with negative results from non-invasive localization procedures. Complications of this procedure are very rare and include groin hematoma, thrombosis, contrast reaction, arrhythmia and renal failure.

Inferior petrosal sinus sampling

Approximately, 80–90% of ACTH-dependent causes of Cushing's syndrome are Pituitary corticotroph adenoma (Cushing's disease), and contrast-enhanced MRI is the first imaging modality for its diagnosis with low sensitivity and specificity (50–75%) (5-8).

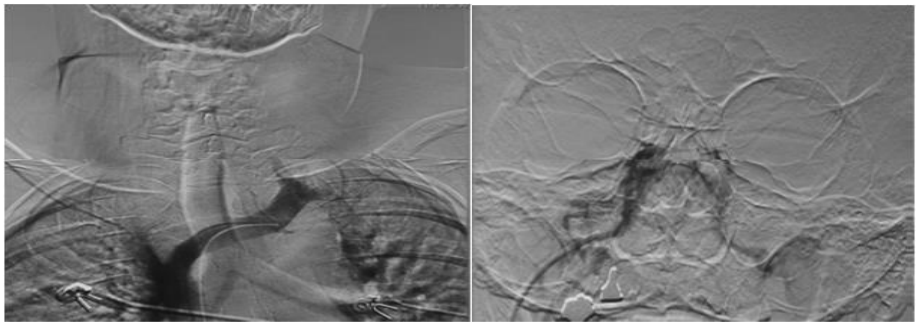

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Fig. 1: Inferior petrosal sinus sampling

Venous sampling should be taken from the inferiorpetrosal sinuses for the differentiation of adrenocorticotropic hormone (ACTH) dependent (pituitary) Cushing syndrome from ectopic ACTH secretion (Fig. 1) (2).
A) Catheter in the left brachiocephalic vein. B) Catheter in the right inferior.
Bilateral inferior petrosal sinus sampling uses the central measurement of ACTH produced by pituitary tumor cells in comparison with peripheral ACTH levels and expressed as a ratio. This technique is indicated in patients whose clinical, biochemical, or radiological studies are contradictory (9, 10).
The best catheter placement should be confirmed by showing crossover flow into the contralateral petrosal sinus after contrast administration, and this is vital to ensure the diagnostic results and avoiding false negative results.
The sensitivity and specificity of bilateral inferior petrosal sinus sampling in the localization of corticotroph secreting pituitary tumors are 88–100 and 67–100%, respectively and has significant value in children whom conventional MRI performs poorly (6, 11-14).
A side-to-side gradient of at least 1.4 before or after CRH stimulation points to a lateralizing tumor and a gradient less than 1.4 shows a midline lesion, with an accuracy of 70% (15).
In centers which expertise in bilateral inferior petrosal sinus sampling is not available, jugular venous sampling may be a useful and less selective technique (sensitivity of 82% versus 94% for bilateral inferior petrosal sinus sampling in comparative studies) in the confirmation of Cushing's disease (16, 17).

Adrenal venous sampling

Hypertension secondary to hyperaldosteronism may be caused by adrenal adenoma (Conn,s syndrome) or hyperplasia. Unilateral disease is amenable to surgical resection.
Although, CT scan and MRI are highly used in the detection of adrenal adenomas with the sensitivities of 90, recent studies have highlighted the pitfalls of such noninvasive modalities in the diagnosis and lateralization of such tumors (18).
Adrenal venous sampling is indicated in the detection of excessive aldosterone secretion (conn,s syndrome), differentiation of bilateral hyperplasia, aldosterone secreting adenoma, and primary adrenal hyperplasia, confirmation of unilateral hyperaldosteronism before adrenalectomy, and also in the diagnosis of pheochromocytoma. However, diagnosis of pheochromocytoma is typically based on the combination of clinical presentations and increased plasma or urinary catecholamine levels, plus CT/MRI and/or nuclear medicine scan results (19).
The gold standard method in the preoperative localization of aldosterone secreting adenomas in patients with primary hyperaldosteronism is Adrenal vein sampling, with the accuracy ranging from 92–100% (Fig. 2) (20-23).

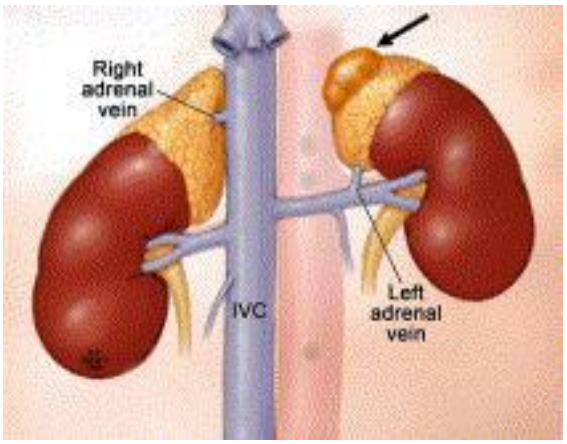


Fig. 2: Adrenal Sampling

Successful catheterization can be achieved in 90% of cases and in 10% the right adrenal vein drains into the posterior aspect of a hepatic vein near the IVC.
For episodic variation in hormone secretion, a number of samples should be taken at 5 minute intervals; and ACTH stimulation may helpful in the differentiation between aldosteronoma and bilateral adrenal hyperplasia.
Complications of this technique are rare especially when perform by expertise physician. Rough catheterization of the veins may cause spasm and failure in the sampling. Rupture of the veins that

may result to adrenal infarction and loss of function is a possible complication (19).
Where adrenal venules join the central adrenal vein, the vessel is fragile and susceptible to rupture which may cause to adrenal hemorrhage and infarction after injection of contrast too forcibly. Thus only limited (0.2–0.5 ml) contrast should be injected to confirm catheter position.

Venous sampling for islet cell tumors

Pancreatic neuroendocrine tumors are rare tumors arising from the islet of Langerhans, and account for 1–2% of all pancreatic neoplasms (24). These neoplasms divided into two groups of functioning and nonfunctioning tumors (25).
Insulinomas are the most common functioning tumors accounting for 50% of patients, and Gastrinomas are the second most common group of them which are more likely to be malignant, multiple, smaller and extrapancreatic (26, 27).
As these tumors are often small and difficult to distinguish in their early stages, early localization with imaging is important for their management.
CT, MRI, endoscopic ultrasound and somatostatin receptor (octreotide) are among diagnostic methods for these tumors (2).
If the tumor remains occult, or in patients that further information is required; venous sampling techniques with or without arterial stimulation may be indicated. The most common indication for venous sampling in this group is for the localization of Insulinomas or gastrinomas (2).
In non-functional tumors there is no role for venous sampling, because they have a tendency for being larger at presentation and cause mass effect symptoms such as jaundice in pancreas head tumors.
It is very important that we have comprehensive information about the vascular anatomy of hepatic and pancreatic region, and also various congenital variations before venous sampling.
One highly sensitive and specific approach for localization and treatment planning of Pancreatic neuroendocrine tumors is selective arterial stimulation by calcium and concurrent venous sampling which specifically used for insulinomas and gastrinomas.
Indications of arterial stimulation and venous sampling in the diagnosis and management of Pancreatic neuroendocrine tumors are including: failure to localization of tumors by using other imaging methods; localization of tumors in the presence of multiple dormant pancreatic lesions; lateralization of tumor within the pancreas, in relation to the superior mesenteric artery for surgical approach planning (28).
Relative contraindications include uncontrolled hypertension, uncorrectable coagulopathy, severe allergy to iodinated contrast, severe renal failure, and congestive heart failure.
For calcium stimulation venous sampling; cardiac glycosides are a relative contraindication, because glycosides and calcium are synergistic in their inotropic and toxic effects. Administration of calcium may cause arrhythmias in those patients who are taking glycosides.
Complications of this procedure are uncommon and related to the angiography procedure. For calcium arterial stimulation venous sampling; symptomatic hypoglycemia, and Pancreatitis are potential complications (20).

Interventional Treatments of Neuroendocrine Cancer Metastases to the Liver

Neuroendocrine tumors are a heterogeneous group of tumors which are defined by their ability to secrete hormones resulting in a variety of hormonal syndromes such as carcinoid syndrome. Population based studies demonstrate a significant increase in the incidence of these tumors over time with the annual incidence of 5.25 cases per 100,000 population in the United Stated (29). Neuroendocrine tumor metastases typically have a long course which often causing bulk- related symptoms due to significant tumor burden within the liver, and rarely cause rapid hepatic dysfunction (30).
Many patients with slow, low-volume, asymptomatic metastases can be followed without treatment until there is evidence of progression or symptoms develop, and the treatment options of patients with progressive disease, or disease-related symptoms varies base on the tumor subtype (31).

Hepatic resection is feasible in less than 10% of patients at the time of diagnosis, and systemic chemotherapy has limited efficacy especially in those with carcinoid tumors (32).

In contrast to many metastatic gastrointestinal and pancreatic carcinomas, the clinical progression of metastatic Neuroendocrine malignancies can be remarkably slow, and patient survival may be prolonged (33).

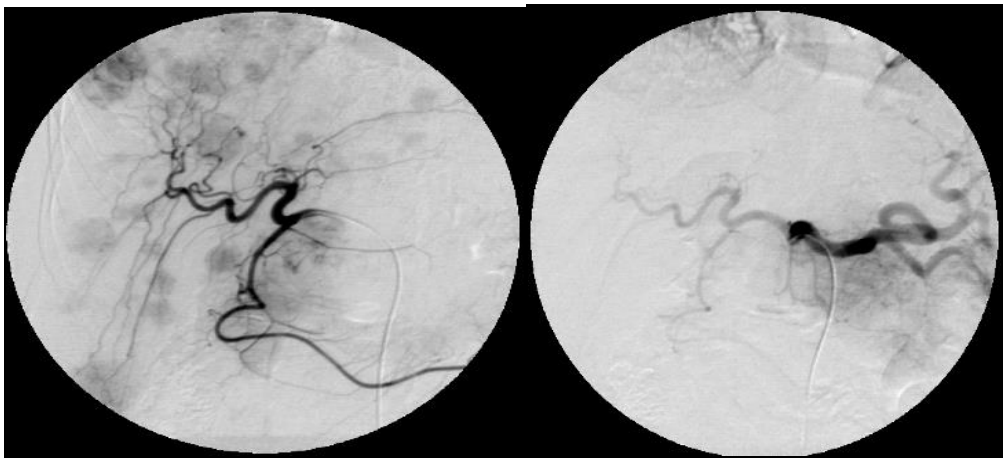
The small number of patients who are suitable for curative surgery, the limited value of chemotherapy, the long course, and the importance of palliation in such patients have led to the emergence of alternative therapeutic methods (34).

In Neuroendocrine hepatic metastases, when possible, surgical resection is the gold standard for care of patients. Indications for Image-Guided Ablation include: (1) adjunct intraoperative ablation performed with surgical resection; (2) treatment of hepatic metastases in patients who are not suitable for surgery; (3) palliation of symptoms; and (4) treatment of recurrent disease.

Catheter-based therapies can be further sub-divided into transarterial embolization (TAE) and transarterial chemoembolization (TACE) and both of these techniques have been effectively used in the palliative management of neuroendocrine hepatic metastases.

Hepatic Artery Embolization (TAE) &Transarterial chemoembolization (TACE)

Hepatic artery embolization is an alternative effective palliative therapy in patients with unresectable neuroendocrine tumors. This is mainly effective due to healthy hepatocytes derive most of their blood supply from the portal vein in contrast to the tumors in this site which derive most of their blood supply from the hepatic artery (Fig. 3).



A) B)

Fig. 3: Neuroendocrine tumor with multiple metastases. Superficial catheterization of right pro pre hepatic artery. A) Before embolization B) After embolization

Hepatic artery embolization with or without chemotherapy not only can improve patient's symptoms but also can reduce tumor size. Response rates of 50–96% have been are measured either by a decrease in hormonal secretion or by radiographic regression, with median duration of response ranging from 4 to 51 months in uncontrolled patient series (35-38).

In one study Gupta et al. performed embolization or chemoembolization for 81 patients with carcinoid tumors, and finally the median duration of response was 17 months, and the probability of progression-free survival at 1, 2, and 3 years was 75%, 35%, and 11%, respectively (36).

There are various reports about the beneficial therapeutic effects of TACE and TAE for patients

with Neuroendocrine tumors liver metastases, but it is still unclear whether TACE
has a significant advantage in comparison with TAE.
In another study, Gupta and his colleagues reported better survival (31.5 versus 18.2 months) and a better imaging response rate (50% versus 25%) in patients with islet cell tumors which treated by TACE in comparison with those patients treated with TAE, but their results was not statistically significant. However, there was not statistically or otherwise differences in overall survival or response rate for carcinoid tumors after either TACE or TAE.
This may be due to that islet cell tumors tend to respond better to systemic chemotherapy compare with carcinoid tumor (39).

Radioembolization Therapy

The high rate of somatostatin receptor expression in neuroendocrine tumors causes the rationale for radionuclide therapy in the treatment of patients with metastatic disease.
In contrast to external beam radiation, Yttrium90-microspheres cause point-source of radiation with limited radiation range of a few millimeters.
Radioembolization has two different therapeutic effects including embolization by microparticles which cause micro-vascular occlusion and brachytherapy by implantation of radiating microparticles. The radio-particles selectively will deliver a high dose of radiation to the tumor tissue with reduced radiation exposure to the surrounding normal tissues as a result of increased intra-tumor vascu-larization.
Various radiolabeled somatostatin analogs have been used in the treatment of patients with neuroendocrine metastatic tumors and differ in their affinity for the different somatostatin receptor subtypes and conjugated radionuclides (40).
The most frequently used radionuclides for radiotherapy are yttrium (90Y) and lutetium, which differ in the emitted particles, particle energy, and tissue penetration (41,42).
We should exclude patients with significant impaired liver function due to toxicity of radionuclides for the liver using liver function tests; such as prothrombin time, serum albumin levels, and total bilirubin. Extrahepatic tumor spread is another contraindication for radionuclide therapy.
The major complications of this procedure are less than 5% and including: liver abscess, transient hepatorenal failure, pleural effusion, sepsis, bowel ischemia, septicemia, hepatic infarction, ischemia of the biliary tree due to excessive embolization ,radiation-induced liver disease, biliary complications, accidentally administered nontarget radiation, radiationinduced pneumonitis due to shunts resulting in an increased radiation dose to the lungs (43-48).
Post-embolization syndrome contains fever, leukocytosis, abdominal pain, transient increase in liver enzymes, and increased bilirubin levels, may be seen in 80%–90% of the patients (44).
In Bushnell et al. study, 90 patients with symptomatic metastatic carcinoid tumor refractory to octreotide were treated with 90Y. Finally, more than 50% of their patients had reported improvement in their symptoms and 70% of them had stable disease following the treatment (49).

Cryotherapy

Cryosurgical ablation may be used as an alternative therapeutic modality for hepatic malignancies and has generally involved treatment of colorectal metastases.
Cryotherapy is effective in the treatment of patient symptoms and reducing tumor markers in more than 90% of patients (50-52).
In one study was conducted by Seifert et al (50) the authors treated 13 patients with 52 neuroendocrine liver metastases (7 carcinoids, 3 apudomas, 2 gastrinomas, 1 paraganglioma) using cryosurgery. After cryotherapy, among seven who had symptoms; Complete and partial responses were seen in five and two patients, respectively.
There was 85% decrease in tumor markers and only one death occurred due to pneumonia unrelated to disease.
Recurrent liver disease was reported in two cases, and one had new metastatic lesions in the liver.
The complications were coagulopathy associated with bleeding, acute renal failure, and pulmonary embolism which occurred in 31% of cases.

Percutaneous Alcohol Injection

Percutaneous alcohol injection (PEI) under ultrasound guidance is an effective treatment for small hepatocellular carcinoma (53), and also can be incorporated into the treatment of metastases from neuroendocrine malignancies (54-56)(Fig. 4).

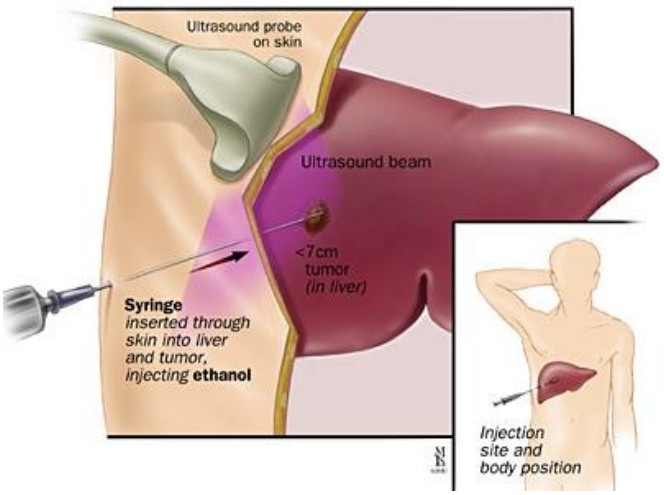


Fig. 4: Percutaneous alcohol injection for HCC

Very small size metastases can be successfully treated with alcohol, with limited injury to adjacent liver parenchyma.

In one study Livraghi et al, a complete response was achieved in all four neuroendocrine hepatic metastases treated with alcohol (55).

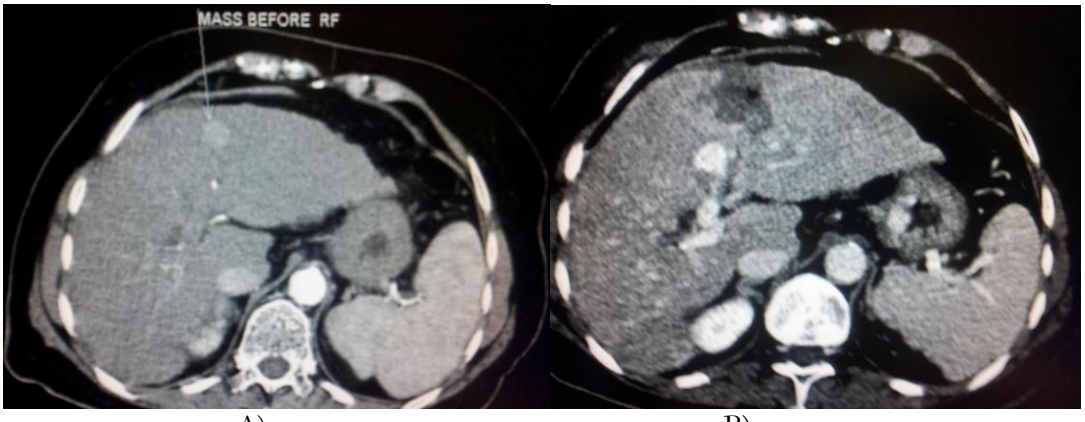
In one study by Giovanni and Seitz, (54) the authors performed PEI in five patients with liver metastasis from carcinoids under ultrasound guidance and found a complete response in one patient.

Ability to treat multiple tumors on repeated sessions, simplicity, outpatient treatment capability, and sparing of the liver parenchyma are some advantages of PEI. Difficulty of controlling ethanol diffusion in normal liver and the difficulty of treating metastatic lesions and lesions more than 3 cm in size are some disadvantages of PEI.

Radiofrequency Thermal Ablation (RFA)

Radiofrequency ablation (RFA) is an alternative therapeutic modality for primary and secondary hepatic malignancies. The basic principle of this procedure includes generation of high-frequency alternating current (approximately 400 MHz), which causes ionic agitation that is converted to heat. The heat induces cellular death due to coagulation necrosis (57).

This procedure involved percutaneous placing the thermoablation catheter into the tumors under ultrasound guidance (Fig. 5).



A) B)

Fig. 5: A) Dynamic CT scan, arterial phase shows hyperdense high vascular mass in the 4th segment of the liver. B) Dynamic CT scan, arterial phase, 5 min after RFA, shows a hypovascular area and complete vanishing of the enhancement

The efficacy of RFA in the treatment of hepatic metastases is well established (58-60).

There is greater success rate typically in lesions smaller than 3 cm in diameter (61,62). The maxi-

mum numbers of lesions which can be treated by RFA in metastatic and primary hepatic disease is four lesions (62,63).
The largest study of RFA for the treatment of Neuroendocrine hepatic metastases includes the ablation of 234 hepatic metastases in 34 patients in which 95% of patients reported improvement in their symptoms and 65% of them had decreased levels of at least one hormone marker. After a mean follow-up of 1.6 years, new hepatic metastases were developed in 28% of the patients (64).
In another study, 21 patients with 43 liver metastases (mean size 2 cm, range 2-7 cm), were treated by percutaneous or intra-operative RFA and finally 95% of the lesions were successfully treated with no evidence of local recurrence at 2-year follow-up (65).
In one study by Henn and colleagues on 7 patients with symptomatic Neuroendocrine liver metastases which treated by RFA, symptom relief was occurred in 5 patients. Mean duration of symptom relief in this study was prolonged and after a mean follow-up of 23 months, only two patients had recurrence of symptoms (66).

Percutaneous ethanol injection therapy (PEIT) for secondary hyperparathyroidism

Secondary hyperparathyroidism commonly occurs in those patients who are on long term dialysis and may be cause mineral bone disorder. Vitamin D supplements are commonly used as standard medical therapy for this condition which may be have some difficulties to maintain serum calcium and phosphate levels within the normal range (67,68). In the advanced stages the patient may be have resistant to medical therapy and surgical resection of parathyroid is indicated for them (69). Ultrasound guided percutaneous ethanol injection therapy (PEIT) can be used as an alternative effective therapeutic procedure for resistant cases. The stage of secondary hyperparathyroidism and the number of enlarged parathyroid glands are factors which influence the efficacy of PEIT. As the parathyroid glands become larger than 0.5 cm^3, or 1 cm in size, they became resistant to medical therapy, so the presence of enlarged glands is a strong indication for PEIT (70).
PEIT combined with active vitamin D supplements strongly influence long-term post-procedure prognosis and when PEIT is successful, serum Ca and P, and PTH levels decrease immediately after therapy; which causes inhibition of the PTH level with vitamin D administration (71).
Finally, the efficacy of PEIT is largely influenced by the skill of the interventionalist and superior prognosis including high efficacy, low recurrence, and long-term remission period could be obtained after PEIT when there is only one enlarged gland more than 0.5 cm^3 in diameter.

Treatment of hyperfunctioning thyroid nodules by percutaneous ethanol injection

Hyperfunctioning thyroid nodules are common and there is controversy about their management (72-74). The different modalities used in their management including surgery, radioiodine, and percutaneous ethanol injection (72,75). Ethanol injection is a relatively inexpensive alternative to surgery or radioactive iodine in the treatment of autonomous thyroid nodules which has not require hospitalization.
This procedure is more practical in younger patients due to it leaves no residual surgical scar, involves no exposure to radiation, and is not associated with a long-term risk of hypothyroidism, and leads to a reduction in nodule volume without recourse to surgery (76-78).
Studies have shown that ethanol causes coagulative necrosis of nodular tissue through hemorrhagic infarction and vascular thrombosis (79, 80). Hypothyroidism is not observed even after prolonged follow-up, and recurrence of hyperthyroidism has not been reported in patients who have had a complete response to PEI (81,82).
The most important factors in predicting response to PEI are initial nodule volume and the skill of the physician performing the procedure.
There exists a direct linear relationship between reduction in nodule volume and initial nodule volume ($r = 0.94$, $P = 0.007$), that is to say the greater the initial size of the nodule, the larger the reduction in size.

For this procedure, under ultrasound guidance, 0.5–10 ml of sterile 95% ethanol should inject inside each nodule (0.1 ml per ml nodule volume, using a disposable plastic syringe and 22- gauge needle). The injection needle should keep in place for 1–2 minutes in order to avoid any ethanol leakage, and patient must advise to take oral analgesia before injection. It is better to repeat this once every 1–2 weeks.

In one study for the evaluation of the efficacy of percutaneous ethanol injection in treating autonomous thyroid nodules we injected sterile ethanol under ultrasound guidance for 35 patients with hyperfunctioning nodules and suppressed sensitive TSH who was diagnosed by technetium-99 scanning (78).

Among our patients, 29 had clinical and biochemical hyperthyroidism and the other 6 cases had sub-clinical hyperthyroidism with suppressed sTSH levels (<0.24 μIU/ml) and normal thyroid hormone levels.

Ethanol injections were performed once every 1–4 weeks and were stopped when serum T3, T4 and sTSH levels had returned to normal, or else injections could no longer be performed because significant side effects. The mean pre-treatment nodule volume was 18.2 ± 12.7 ml and decreased by 5.7 ± 4.6 ml at 6 months [$P < 0.001$]. The success rate for this study (91.3%) is consistent with that reported elsewhere (54–100%) (76-78).

All patients had normal thyroid hormone levels at 3 and 6 months follow-up [$P < 0.001$]. sTSH levels increased from 0.09 ± 0.02 μIU/ml to 0.65 ± 0.8 μIU/ml at the end of therapy [$P < 0.05$]. T4 and sTSH did not change significantly between 6 months and 2 years [$P > 0.05$]. Ethanol injections were well tolerated by the patients, and we had only 2 cases of transient dysphonia, one patient completely recovered after one week, the other one recovered after six months (78).

Transient dysphonia has been reported in 2–5% of cases in the literature (83,84). The pathology is either direct chemical injury to the recurrent laryngeal nerves as a result of alcohol leakage, or nerve injury due to a sudden elevation in pressure inside the nodule. Real-time ultrasound may be used to monitor the PEI procedure and can identify ethanol leakage that shows a hyperechogenic area.

Two large studies from Italy, one on 132 patients followed up over 8.5 years (77) and the other on 117 patients followed up over 5 years, (85) suggest that PEI be recommended as treatment for hyperfunctioning thyroid adenoma with sub-clinical hyperthyroidism.

Radiofrequency ablation of the adrenal gland neoplasms

The first therapeutic modality in for the adrenal gland malignancies is surgical resection (86-88).

The reported 5-year survival rate in those patients who perform complete resection is 47%, and recurrence rate is 35% to 85% that shows poor prognosis (89, 90). In those patients who are not good candidates for surgical resection, image guided radiofrequency ablation (RFA) should be observed as an alternative minimally invasive treatment option. Benign functional adrenal lesions like aldosteronoma which cause primary hyperaldosteronism may also yield benefit from RFA (91).

RFA indicated in the treatment of primary and metastatic adrenal malignancies such as adernocortical carcinoma, adenomas, metastases and pheochromocytomas in the selected cases (92, 93). RFA can be performed in the treatment of lesions with 5cm or less in diameter, and larger lesions must be treated using overlapping ablations with lower success rate. Patients who have bilateral metastases may be survived by RFA and in some patients who have bilateral disease could be treated in a single setting (94). RFA is contraindicated in uncorrectable coagulopathies, and bleeding diatheses are relative contraindications for this procedure. Prior hypertensive crisis, elevated levels of catecholamines, comorbid conditions such as chronic obstructive pulmonary disease and congestive heart failure may increase the risks of RFA (19). RFA can perform under conscious sedation or general anesthesia in the CT scans suit or ultrasound guidance.

The location of the lesion, surrounding strictures, and safety of the patients should be keep in mind before the procedure; and RFA can be done from

anterior , posterior of lateral approach. International radiologist should avoid injuries to bowel wall, kidney, liver spleen pleura, and stomach. Risk of renal and liver thermal injury is usually inconsequential and transhepatic or transrenal route is often ideal.

Access locations which are very close to edge of moving organs such as liver, kidney, or spleen may increase the risk of organ laceration, and in these lesions it is better to go through the organ and subsequently cauterize on the way out, aggressively.

After positioning the patients, two or four grounding pads should be placed on the patient's thighs, and under CT or ultrasound guidance, the appropriate electrode (single or cluster) must be positioned into the lesion. After confirming the stable homodynamic situation of the patient, the RF generator (200w, 460to480 kHz, alternating curved RF generator) should be turned on for 12 to 16 minutes of overlapping treatments.

Finally, the needle route should be cauterized to prevent tumor seeding and bleeding. Contrast enhanced CT scan may be performed immediately after the procedure for the evaluation of response. Lack of enhancement in the lesion or peripheral usually shows adequate ablation, residual enhancement or post ablation tumor growth shows incomplete treatment or recurrence.

There is lack of sufficient studies for the evaluation of long-term efficacy and survival rates after RFA in adrenal tumors. This modality may be done safely and effectively for small primary as well as metastatic adrenal malignancies. In one study performed by wood and associates (95), the authors were treated 8 patients who had 15 adrenocortical carcinomas, and observed that 57% of the tumors decreased in size, and 27% showed no change in size. They also reported that tumors with less than 5cm size yield better results with 67%completely ablation .

The only complication in their study was abscess formation 11 weeks after third session which was cured after antibiotic therapy (95). RFA for the adrenal glands should be performed by experienced interventional radiologists to decrease complications. Complications are rare and including discomfort, infection, grounding pad burns, tumor seeding, bowel perforation, pneumothorax, pancreatitis, and fistula (96). There are some reports about the hypertensive crisis while right lower liver or adrenal ablation performed (97); and can safely managed by premedication , careful anesthesia and pharmacologic supports. Another possible complication is a flu-like symptom named post ablation syndrome, which may be seen few days after RFA and last for about one week (98).

Establishing a cGMP pancreatic islet processing facility

In addition to the standard treatments for diabetes, there are some promising therapeutic modalities such as beta-cell replacement and stem cell transplantation. Recently, significant progress has been made in beta-cell replacement with a progressive improvement in the short term and long term outcomes, including insulin independence, normalization of HbA1c levels, prevention of severe hypoglycemic episodes and improvements of the quality of life in recipients with type I diabetes and hypoglycemic unawareness (99, 100).

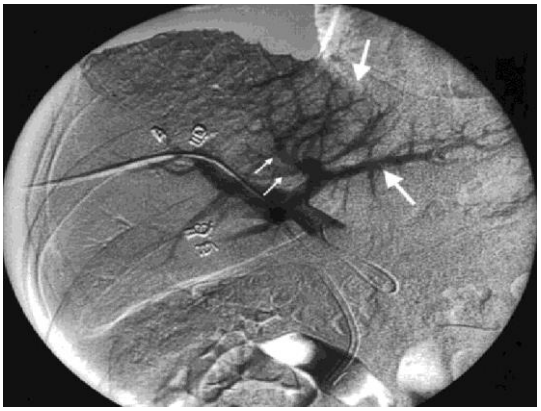


Fig. 6: Percutaneous Simon catheter in the main portal vein. Right portal branches have been embolized with coils

In most countries, the main limitation for starting a transplantation program is organ shortage. On the other hand local donation significantly reduces hypothermic cold storage time which is in favor of islet isolation procedure. We assumed that our access to a local organ donation system is a posi-

tive factor for setting up islet transplantation program. Considering the impact of the disease in Iran and the promising results of the Edmonton protocol (101), we established a cGMP islet processing facility by Endocrinology and Metabolism Research Center (EMRC) (Fig. 6) (100).

Conclusion

The use of interventional radiology procedures seems helpful in the endocrinology diagnosis and treatment. Future developments would improve this application in future. This improvement needs designing and implementation of novel clinical trials for approving the new comers techniques in the field.

Ethical considerations

Ethical issues (Including plagiarism, Informed Consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

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The authors declare that there is no conflict of interest.

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