# Pancreatic solid incidentalomas

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## INTRODUCTION

In the changing landscape of modern medicine, the use of advanced imaging studies is constantly increasing. This trend has led to an increase in incidental findings on imaging examinations performed for unrelated causes, colloquially termed "incidentalomas." The reported prevalence of pancreatic incidentalomas (PIs) varies greatly in different series and differs between cystic and solid lesions. In two large series, Laffan *et al.*[1] and de Jong *et al.*[2] reported that the prevalence of unsuspected pancreatic cysts discovered by multidetector computerized tomography or magnetic resonance imaging (MRI) is 2.4%–2.6%, and the prevalence increased with age. This figure is even higher (9.3%) when using high-resolution MRI.[3] As cystic lesions are common, a number of guidelines addressing their management have been issued.[4,5]

The prevalence of solid PIs is less clear. Strang *et al.* reported a 0.6% prevalence of pancreatic masses in healthy potential kidney donors;[6] a similar prevalence of 0.49% was reported among 2941 patients undergoing $^{18}$F-fluorodeoxyglucose-positron emission tomography (FDG-PET) for unrelated causes.[7] Of 39,785 FDG-PET scans performed for cancer screening in Japan, the prevalence of pancreatic malignancy was lower than 0.001%;[8] a figure more closely related to SEER (The Surveillance, Epidemiology, and End Results Program) reported a new pancreatic cancer incidence of 12.5/100,000.[9]

The differential diagnosis of pancreatic solid lesions is broad and includes malignancy (exocrine, endocrine, lymphoproliferative, or metastatic tumors), premalignant lesions (solid pseudopapillary tumors and low-grade neuroendocrine tumor [NET]), and focal inflammatory or infectious causes. Rarer diagnoses have also been described.[10]

## SOLID PANCREATIC INCIDENTALOMA

The characteristics of these incidentalomas are derived mostly from data provided from retrospective pancreatic resection series published in recent years [Table 1]. In these series, the proportion of incidental findings varied from 6% to 61%.

The percentage of solid lesions was 31%–65% of all lesions incidentally identified. The four most common diagnoses of these solid lesions were pancreatic carcinoma (34%–31%), pancreatic NET (pNET, 23%–42%), solid pseudopapillary tumor (3%–15%), and focal chronic pancreatitis (0%–11%).

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| Quick Response Code: | Website: www.eusjournal.com |
| | DOI: 10.4103/eus.eus_72_17 |



**How to cite this article:** Santo E, Bar-Yishay I. Pancreatic solid incidentalomas. Endosc Ultrasound 2017;6:S99-103.

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**Received:** 2017-07-12; **Accepted:** 2017-08-31

**Table 1. Characteristics of pancreatic incidentalomas**

| Type of study | Winter *et al.*[11] Retrospective (pancreaticoduodenectomy) | Bruzoni *et al.*[12] Retrospective | Sachs *et al.*[13] Retrospective | Lahat *et al.*[14] Retrospective | Goodman *et al.*[15] Retrospective (solid lesions) | Takeda *et al.*[16] Retrospective (PDAC) | Birnbaum *et al.*[17] Retrospective (pNET) | Crippa *et al.*[18] Retrospective (pNET) | Chiarelli *et al.*[19] Retrospective (distal pancreatectomy) |
|---|---|---|---|---|---|---|---|---|---|
| Overall cases | 1826 | 356 | 381 | 475 | 321 | 569 | 108 | 355 | 34 |
| Incidental finding (%) | 118 (6) | 57 (16) | 110 (29) | 64 (13) | 24 (7) | 163 (29) | 65 (61) | 124 (35) | 20 (59) |
| Method of detection (%) | | | | | | | | | |
| Imaging | 86 (73) | 52 (91) | 80 (73) | 52 (81) | 24 (100) | 99 (61) | | | 18 (90) |
| Biochemistry | 21 (18) | 5 (9) | 16 (16) | 9 (14) | | 68 (42) | | | 2 (10) |
| Endoscopic | 11 (9) | | 14 (12) | 3 (5) | | | | | |
| Solid lesion (percentage of total PI) (%) | 36 (31) | 35 (61) | 53 (48) | 36 (56) | 24 (100) | 163 (100) | NR | 111 (89) | 13 (65) |
| Carcinoma* (percentage of solid PI) (%) | 19 (53) | 17 (49) | 18 (34) | 17 (47) | 14 (58) | 163 (100) | | | 8 (61) |
| pNET (%) | 11 (30) | 11 (31) | 14 (26) | 13 (36) | 10 (42) | | 65 (100) | 111 (100) | 3 (23) |
| Metastatic disease (%) | 2 (5.5) | ‡ | 1 (2) | | | | | | |
| Chronic pancreatitis (%) | 4 (11) | 4 (11) | 2 (3) | 0 | | | | | |
| Pseudopapillary tumor (%) | | ‡ | 2 (3) | 6 (17) | | | | | 2 (15) |
| Other | | ‡ | † | | | | | | |
| Location (%) | | | | | | | | | |
| Head | 100 | 54 | 37 | 44 | 29 | 45 | 40 | 48 | |
| Body/tail | | 48 | 63 | 53 | 71 | 55 | 60 | 50 | 100 |

*PDAC, ampullary adenocarcinoma, adenosquamous carcinoma, distal bile duct cancer, acinar cell carcinoma, ‡Lipomatosis, pseudopapillary tumor, metastasis (colon, kidney), †Ampullary adenoma (*n*=6), PanIN (*n*=1), fat necrosis, splenule, normal, ectopic, and inflammatory tissue. NR: Not reported, PI: Pancreatic incidentalomas, PDAC: Pancreatic ductal adenocarcinoma, pNET: Pancreatic neuroendocrine tumor, PanIN: Pancreatic intraepithelial neoplasia

The low prevalence of focal chronic pancreatitis is similar to that of 4.8%–6.3% in large pancreatoduodenectomy cohorts described in two historical series from the United States[20] and from Holland.[21]

In a recent multicenter Italian trial[22] on endoscopic ultrasound-guided fine-needle biopsy (EUS-FNB), pancreatic inflammation was diagnosed in 13% of 333 biopsies taken. Pancreatic carcinoma (70%) and pNET (11%) were the other common diagnoses in that trial.

## PANCREATIC CARCINOMA

The most common cause of an incidentally identified solid lesion is pancreatic ductal adenocarcinoma (PDAC). In a review of 475 pancreatic resections, Lahat *et al.*[14] showed that the tumor was smaller in incidental compared to symptomatic lesions (2.5 cm *vs.* 3.5 cm) and was more likely to be well differentiated (37.5% *vs.* 14.8%). Interestingly, the rate of lymph node (LN) involvement was similar between the two groups, and median survival was not significantly different (22 months *vs.* 19 months).

Takeda *et al.*[16] reviewed 569 PDAC patients; 250 were resectable. Overall tumor resectability (64% *vs.* 36%) and median survival (16 months *vs.* 10 months) were higher in patients with incidental compared with symptomatic lesions. In patients who underwent surgery, LN involvement was similar between the groups (68% *vs.* 77%) and a trend of increased median survival was observed (31 months *vs.* 20 months).

In a review of 1826 pancreatoduodenectomies, Winter *et al.*[11] found that the likelihood of diagnosis in Stage I was higher (34% *vs.* 10%) in incidentally identified PDAC, and 5-year survival rates were 50% *vs.* 14%.

Agarwal *et al.*[23] showed that patients with a smaller tumor size had a higher proportion of resectable tumors and a better median survival. Tumors smaller than 2 cm had a median survival time of 17.2 months compared to 7.6 months in tumors over 3 cm. Takeda *et al.*[16] showed that in the rare cases of tumors smaller than 1.5 cm, LN involvement was only 14%, compared to 76% when the tumor was over 2 cm. R0 resection was achieved in all cases when the tumor was smaller than 2 cm, compared to 80% for larger tumors.

## PANCREATIC NEUROENDOCRINE TUMORS

The second most common cause of a solid PI is a pNET. Birnbaum *et al.*[17] presented the prognostic significance of incidental discovery of pNET in a series of 108 patients. Tumors discovered incidentally were more likely to be smaller than 2 cm (65% *vs.* 42%) and with G1 differentiation (66% *vs.* 33%). Patients undergoing surgery had a higher rate of pancreatic-sparing resections (62% *vs.* 30%), but there was no change in the rate of perioperative morbidity and mortality. Five-year disease-free survival was higher for incidental pNET (92% *vs.* 82%).

In the series presented by Crippa *et al.*,[18] the pNET incidence in 355 patients was 30%. The proportion of incidentally discovered tumors increased from 9% to 40% over the two decades of data collection, most likely reflecting the increasing use of imaging modalities in medical practice over that period.

Incidentally discovered tumors were smaller than 35 mm (65% *vs.* 45%) and more likely to have G1 differentiation (73% *vs.* 42%). Surgical intervention with curative intent was more frequent (85% *vs.* 49%), and higher R0 margins were achieved (82% *vs.* 46%). Five-year disease-free survival was higher (95% *vs.* 65%).

## DISCUSSION

The majority of incidentally discovered solid lesions of the pancreas are malignant or premalignant. Incidentally

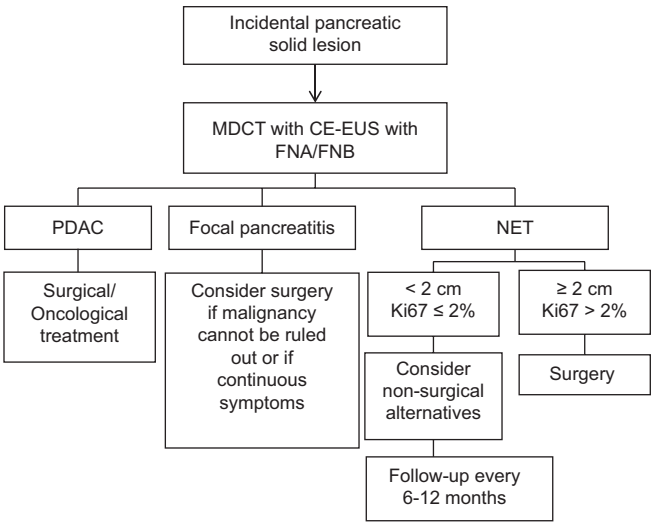


**Figure 1.** Management of solid pancreatic incidentalomas. MDCT: Multi-dimensional computed tomography, CE-EUS: Contrast-enhanced endoscopic ultrasound, PDAC: Pancreatic ductal adenocarcinoma, NET: Neuroendocrine tumor

discovered PDAC are smaller, are discovered at an earlier stage, and have a higher resectability rate. Survival data are conflicting, but it seems that incidental discovery has better survival. This is specifically true for tumors smaller than 2 cm.[16]

The rate of incidental pNET discovery is increasing.[18,24] Smaller incidentally discovered pNETs are at lower stages, are more likely to be resected using pancreatic-sparing resection such as enucleation, and generally have much more favorable survival.

The role of EUS in the assessment of pNET has taken center stage as treatment options are guided by the tumor grade and the Ki67 index, which can be assessed only by histology.[25,26] Recently, EUS-guided radiofrequency ablation for pNET[27-29] has become an option, increasing the role of the endosonographer in the multidisciplinary management team.

Focal inflammatory lesions such as focal chronic pancreatitis constitute approximately 5%–13% of solid pancreatic lesions. Although these lesions are benign and normally do not require surgical treatment, they are notoriously difficult to differentiate from pancreatic cancer by imaging alone. Even when biopsies are negative for malignancy, many still advocate resection of suspected lesions due to fear of sampling errors.

In recently published data, the utility of contrast-enhanced EUS to differentiate a hypervascular chronic pancreatitis from a relatively hypovascular pancreatic cancer has been demonstrated, with a sensitivity and specificity of over 90%.[30]

## SUMMARY

Pancreatic solid incidentalomas present a unique opportunity to the clinician as early diagnosis may increase treatment options and lead to higher cure rates. The role of EUS in the evaluation of pancreatic lesions is pivotal, with a higher diagnostic yield than that of other imaging modalities. This is especially true for smaller lesions, which may be more amenable to early treatment. The role of tissue acquisition in diagnosis and guiding therapy is also of paramount importance. Moreover, as new technological advances evolve, EUS will undoubtedly play an important role in the treatment of these lesions. An algorithm for the investigation of pancreatic solid incidentalomas is presented in Figure 1.

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