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REVIEW

Asymptomatic Lesions of the Pancreas: An Overview

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ABSTRACT

The issue of pancreatic incidentaloma is relevant in clinical practice, and the correct management of these asymptomatic lesions found incidentally at imaging techniques requires prospective studies with adequate follow-ups. The current literature on this issue was reviewed and incidentalomas, both solid and cystic, are frequently diagnosed at an advanced age and the percentage of males ranged from 14.3 to 80.7%. The percentage of incidentalomas varies from 6% to 23% of the pancreatic resections performed for any cause. The prevalence of cystic incidentalomas diagnosed with imaging techniques varies from 1.2 to 2.6%. Further injury can be identified on the basis of biochemical or endoscopic examinations. Incidentalomas are found more frequently in examinations carried out for genito-urinary symptoms, chest pain or screening tests for cancer surveillance. Up to 50% of these lesions are solid and the vast majority are malignant or precancerous. Biopsy and analysis of the CEA and amylase in the cystic fluid obtained especially with an endoscopic ultrasonography is of particular importance. Given the imperfect diagnostic information available, it is necessary to evaluate the risk and benefit of a pancreatic resection when deemed appropriate because pancreatic resection involves high morbidity, and a surgical approach should be avoided for a benign condition. Solid incidentalomas generally seem to have a better prognosis than symptomatic lesions.

Key words: Cystic lesions; Solid lesions; Pancreatic neoplasms; Magnetic resonance imaging; Computer tomography; Endoscopic ultrasonography

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INTRODUCTION

The definition of incidentaloma is "a chance discovery in a patient which may warrant further investigation"[1]; the definition of pancreatic incidentaloma was introduced in 2010 and defines the asymptomatic lesions of the pancreas as "a solid or cystic lesion detected incidentally by computed tomography, magnetic resonance imaging or other imaging techniques carried out for other purposes and which never gave signs by which they could be predicted"[2]. The term previously used for incidentaloma was "anticipated lesion", but these lesions discovered by chance cannot be anticipated clinically or radiologically[3]; thus, the correct term is incidentaloma. From the point of view of forensics, also arises the problem of why it had not been not suspected on the basis of the information at hand also arises[4]. From the point of view of health economics, there is the need to develop medical strategies to optimize results, minimize costs and ensure the proper application of clinical decision-making[5].

LITERATURE REVIEW

The current literature on this issue was reviewed and very few papers dealing this topic were found. In tables 1 and 2. are summarized the characteristics of the studies selected as related to solid and cystic lesions diagnosed incidentally, and the type of study (all retrospective), the number of patients enrolled, age at diagnosis, the reasons for which they had undergone the radiological investigation as a result of which the incidentaloma was diagnosed, the final diagnosis of incidentaloma, the type of surgery performed and, finally, the percentage of non-operated on patients have been reported.

Table 1 Animal studies investigating the effect of tocotrienols on liver function.

Paper	Sachs *et al*[6]	Winter *et al*[7]	Lahat *et al*[8]	Fitzgerald *et al*[10]	Bruzoni *et al*[11]	Goodman *et al*[12]
Type the study	Retrospective	Retrospective	Retrospective	Retrospective	Retrospective	Retrospective (only solid lesions)
Number of patients enrolled	110	118	64	7	57	24
Age at diagnosis [mean and (range)]	NR	66 (26-85)	64 (19-84)	50 (32-68)	66 (16-89)	-
Male gender (%)	NR	55.9	39.3	14.3	80.7	32.4
Reason for imaging evaluation	-	-	-	-	-	-
Symptoms of genito-urinary tract/pelvis (%)	16.0	-	-	71.4	33.3	33.3
Abnormalities of blood examination (%)	13.0	14.4	-	-	8,.8	-
Screening/surveillance tumors or chronic diseases (%)	7.0	24.6	-	28.6	14.0	41.7
Chest pain (%)	6.0	-	-	-	15.8	8.3
Cholangitis/cholecystitis/colic (%)	6.0	4.2	-	-	-	-
Preoperative work-up for surgery (%)	-	50.8	-	-	-	-
Postoperative follow-up (%)	6.0	-	-	-	-	-
Trauma (%)	5.0	-	-	-	-	-
Abdominal discomfort (%)	5.0	-	-	-	7.0	4.2
Diverticulitis/ pain localized in the lower abdominal quadrants (%)	4.0	-	-	-	14.0	-
GERD (%)	3.0	-	-	-	-	-
Anemia (%)	3.0	-	-	-	-	-
Intergumentary (%)	3.0	-	-	-	-	-
Others (%)	25.0	5.9	-	-	7.0	12.5
Diagnosis	-	-	-	-	-	-
IPMN (%)	17.0	35.6	23.4	14.3	9.0	-
Mucinous cystic neoplasm (MCN) (%)	-	17.0	15.6	-	7.0	-
Serous cystadenoma (%)	14.0	Evaluated together with MCN	-	28.6	12.0	-
Ductal adenocarcinoma (%)	-	18.6	17.2	-	30.0	58.3
Pancreatic neuroendocrine tumor (%)	13.0	9.3	15.6	42.9	19.0	41.7
Solid-cystic-papillary tumor (%)	-	-	9.4	14.3	-	-
Other cancers (%)	-	19.8	18.8	-	14.0	-
No diagnosis (%)	-	-	-	-	9.0	-
> 1 diagnosis (%)	6.4	-	-	-	-	-
Surgery	-	-	-	-	-	-
Pancreatic head resection (%)	29.1	100	43.8	71.4	26.4	NR
Distal pancreatectomy (%)	38.2	-	53.1	28.6	22.8	NR
Central pancreatectomy (%)	6.4	-	-	-	5.3	NR
Total pancreatectomy (%)	2.7	-	-	-	3.5	NR
Enucleation (%)	4.5	-	-	-	-	NR
Explorative laparotomy/other (%)	19.1	-	-	-	-	NR
No surgery (%)	-	-	3.1	-	42.0	33.3

Incidentalomas, both solid and cystic, are frequently diagnosed at an advanced age[6,14] and the percentage of males ranged from 14.3 to 80.7%[6-12,14]. The percentage of incidentalomas varies from 6% to 23% of the pancreatic resections performed for any cause[6,7,11]. This is due in large part to a growing number of radiologic studies performed for other reasons; the prevalence of cystic incidentalomas diagnosed with imaging techniques varies from 1.2 to 2.6%[8,15]. Further injury can be identified on the basis of biochemical (alterations of serum liver and/or pancreatic enzymes) or endoscopic examinations (abnormalities of the duodenum or papilla of Vater) [6,7,16]. Incidentalomas are found more frequently in examinations carried out for genito-urinary symptoms, chest pain or screening tests for cancer surveillance[7,8,10,11]. Up to 50% of these lesions are solid[6] and the vast majority are malignant or precancerous. Evaluation of the best management strategy for incidental cystic lesions is complex because not all lesions have a malignant potential; thus, they require a careful preoperative evaluation. In this regard it should be noted that the biopsy and analysis of the CEA and amylase in the cystic fluid obtained, especially with an endoscopic ultrasonography is of particular importance[9,14]. Given the imperfect diagnostic information available, it is necessary to evaluate the risk and benefit of a pancreatic resection when deemed appropriate because pancreatic resection involves high morbidity, and a surgical approach should be avoided for a benign condition. Solid incidentalomas generally seem to have a better prognosis than symptomatic lesions[7,8].

INCIDENTALOMAS IN FAMILIAL PANCREATIC CANCER

Similarly to other cancers, such as colon cancer, pancreatic adenocarcinoma may be present in the same family[17]. It should be pointed out that subjects from families with a history of pancreatic cancer have an inherited predisposition of developing the disease, and subjects having familial pancreatic cancer may have at least two first-degree relatives with this disease, probably demonstrating autosomal dominant transmission[18]. A computer-based risk assessment tool has been developed and it has been shown to provide an accurate risk assessment for relatives with familial pancreatic cancer[19]. In addition, several studies have been carried out on patients with familial pancreatic cancer[20-26] and the most frequent pre-neoplastic lesions incidentally found are intraductal papillary mucinous neoplasms.

COST-EFFECTIVENESS OF FOLLOW-UP

Information on cost-effectiveness in the case of lesions found incidentally is largely lacking and the information comes mainly from studies enrolling patients with cystic lesions. It has been reported that, even in patients operated on for lesions greater than 3 cm, the survival rate is good; the only contraindication in patients having

Table 2 Epidemiological and clinical characteristics of cystic incidentalomas. NR: not reported; SD: standard deviation.

Paper	Fernández-del Castillo *et al*[13]	Lahav *et al*[9]	Laffan *et al*[16]	Pausawasdi *et al*[14]
Type of study	Retrospective	Retrospective	Retrospective	Retrospective
Number of patients enrolled	78	112	73	93
Age at diagnosis [mean and (range)]	mean±SD 65±12.9	mean±SD 61±15	NR	Females 68, males 75
Male gender (%)	35.9	33.0	NR	-
Reason of imaging evaluation	NR in detail	NR in detail	NR in detail	NR in detail
Type of cyst	-	-	-	-
Macrocystic (%)	-	100	NR	NR
Microcystic (%)	-	-	NR	NR
Presence of a solid component (%)	-	36	NR	6,0
Thickened septa (%)	-	43	NR	NR
Cyst wall thickening (%)	-	43	NR	NR
Cyst localized in the pancreatic head (%)	50.0	53.6	35.8	-
Number of cystic lesions	-	-	-	-
One (%)	-	100	84.9	89.0
Multiple (%)	-	-	15.1	-
Cyst size at diagnosis	Mean±SD 3.3±1.9	<2 mm	8.9 mm (range 2-38 mm)	Mean±SD 1.52±0.71; size of cysts <3 mm in 24% of patients
FNA	-	Data referred to 41 patients	-	-
Cytology	-	-	-	-
Inflammatory (%)	-	7.3	NR	-
Serous (%)	-	12.2	NR	-
Benign mucinous (%)	-	22	NR	6% (2/33)
Malignant mucinous (%)	-	4.9	NR	3% (1/33)
Other (%)	-	2.4	NR	-
No-diagnosis (%)	-	51.2	NR	15% (5/33)
CEA abnormally high (%)	-	12.2	NR	12.1% (4/33)
Pathological diagnosis	-	Data referred to 14 patients		Data referred to 22 patients
IPMN (%)	27.0	35.7	NR	27.3
Mucinous cystic neoplasm (MCN) (%)	28.0	21.4	NR	22.7
Serous cystadenoma (%)	16.6	14.3	NR	18.2
Inflammatory cyst (%)	3.8	7.1	NR	9.1
Ductal adenocarcinoma (%)	2.5	7.1	NR	9.1
Pancreatic neuroendocrine tumor (%)	-	-	NR	4.5
Solid-cystic-papillary tumor (%)	-	7.1	NR	4.5
Other cancers (%)	10.2	7.1	NR	4.5
No diagnosis (%)	11.5	-	NR	-
Surgery	-	-	-	-
Pancreatic head resection (%)	32.0	NR	NR	NR
Distal pancreatectomy (%)	23.0	NR	NR	NR
Central pancreatectomy (%)	11.5	NR	NR	NR
Total pancreatectomy (%)	6.4	NR	NR	NR
Enucleation (%)	2.5	NR	NR	NR
Explorative laparotomy/other (%)	2.5	NR	NR	NR
No surgery (%)	21.8	87.5	NR	76.3

cystic lesions >3 cm is when the patients are >85 years of age and there is the presence of comorbidities[27]. Endoscopic ultrasonography in selected cases adds an additional benefit onto the cost-effectiveness of a follow-up for these patients[28]. At present, in the case of solid pancreatic lesions detected incidentally, only a consensus of experts may assess the cost-effectiveness of the work-up and this suggestion is a reasonable intermediate goal for which additional data is awaited in the near future[2].

In conclusion, in order to initiate chemotherapy, preoperative histologic characterization in the presence of a solid pancreatic incidentaloma is required, especially when distant metastatic lesions are present. Histology is also necessary when clinical and radiologic signs are compatible with benign lesions, such as focal chronic pancreatitis or autoimmune pancreatitis[2]. In the case of a cystic incidentaloma <2 cm in diameter, a radiologic follow-up carried out yearly is recommended; in the presence of cystic lesions between 2 and 3 cm in diameter, a follow-up twice a year is suggested; finally, in the case of the radiographic appearance of worrisome features, such as mural nodules and thickening septa, and a cystic lesion of greater than 3 cm, if the patient does not have a high operative risk, surgery seems to be a good approach[2,29].

Finally, screening relatives from families in which pancreatic cancer is familial has a significant diagnostic yield, even if the major part of the pancreatic lesions found are pre-neoplastic; this is particularly true in relatives >65 years of age, confirming prior studies which show that magnetic resonance cholangiopancreatography as an initial screening modality is safe and effective[26,30].

CONCLUSION

The issue of pancreatic incidentaloma is relevant in clinical practice, and the correct management of these asymptomatic lesions found incidentally at imaging techniques requires prospective studies with adequate follow-ups also regarding the economic evaluation of different diagnostic and treatment strategies.

CONFLICT OF INTERESTS

There are no conflicts of interest with regard to the present study.

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