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Clinical implications of multidisciplinary team pancreatic cyst evaluation

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ABSTRACT

INTRODUCTION. The detection of incidental pancreatic cysts (PCs) is increasing due to frequent use of imaging. The aim of the present study was to evaluate the clinical consequences of regular multidisciplinary team (MDT) conferences for patients with PCs.

METHODS. All patient data were obtained by review of patient medical records. PCs were assessed at the weekly MDT in accordance with the revised Fukuoka guidelines.

RESULTS. A total of 455 patients were evaluated within 12 months. A large proportion of the cysts could not be characterised and was handled as branch duct (BD)-intraductal papillary mucinous neoplasia (IPMN). A total of 245 patients were included in a follow-up programme, whereas 175 patients were excluded. Further diagnostic work-up was recommended for 31 patients. A total of 66 patients were reviewed on MDT a second time during the study period, eight of whom received a diagnosis different from that given at the first MDT. A total of 35 patients with mucinous PC or cysts treated as BD-IPMN had either worrisome features (WF) or high-risk stigmata (HRS), four of these patients had a PC ≤ 10 mm. Indication for surgery was WF or HRS and, in the course of 12 months, six patients were recommended surgery taking their PS into account. Two patients had a malignant and two had a premalignant lesion.

CONCLUSION. In all, 455 patients were evaluated to find 35 patients with suspected premalignant PCs. This means that almost 8% of the referred patients had suspicious lesions, which indicates a need for a regular MDT conference.

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The detection of incidental pancreatic cysts (PCs) is increasing owing to more frequent use of imaging. In a large American study, the prevalence of PC was approx. 2.5% among 40-84-year-olds [1]. In other studies, PCs have been found to range from 3% to 20% of abdominal scans, the vast majority of which are random findings [2-5]. Most PCs are benign and only a very small proportion are premalignant lesions. PCs are categorised as either neoplastic or non-neoplastic. Neoplastic cysts include serous cyst neoplasia (SCN), mucinous cyst neoplasia (MCN) and intraductal papillary mucinous neoplasia (IPMN). Pseudocysts are the most common non-neoplastic cysts. A division of the neoplastic cysts into mucinous and serous is clinically relevant as, unlike the serous cysts, mucinous cysts have a malignant potential. IPMN cysts communicate with the pancreatic duct system and involve a branch duct (BD-IPMN) or the main duct (MD-IPMN), or both (mixed-type IPMN). This classification is of great clinical importance as the risk of malignancy is significantly higher for both mixed-type IPMN and MD-

IPMN than for BD-IPMN. BD-IPMN is associated with a very low risk of malignancy [6].

CT and MRI are the preferred radiological (cross-sectional) imaging methods for the surveillance of patients with PC. For characterisation of PCs, it has been reported that MRI and CT have a similar accuracy [7-9]. But MRI is more sensitive to identified mural nodules or internal septations and communication between a PC and the pancreatic duct. MRI is also more sensitive for assessing whether one or more cysts exist, where multiple cysts speak for side branch IPMN [7, 10, 11]. CT should be considered in case of suspicion of pseudocyst/chronic pancreatitis or tumour as it is superior in identifying calcification and in assessing vascular tumour involvement. Due to ionising radiation from CT, MRI is frequently the preferred modality in lifelong imaging follow-up.

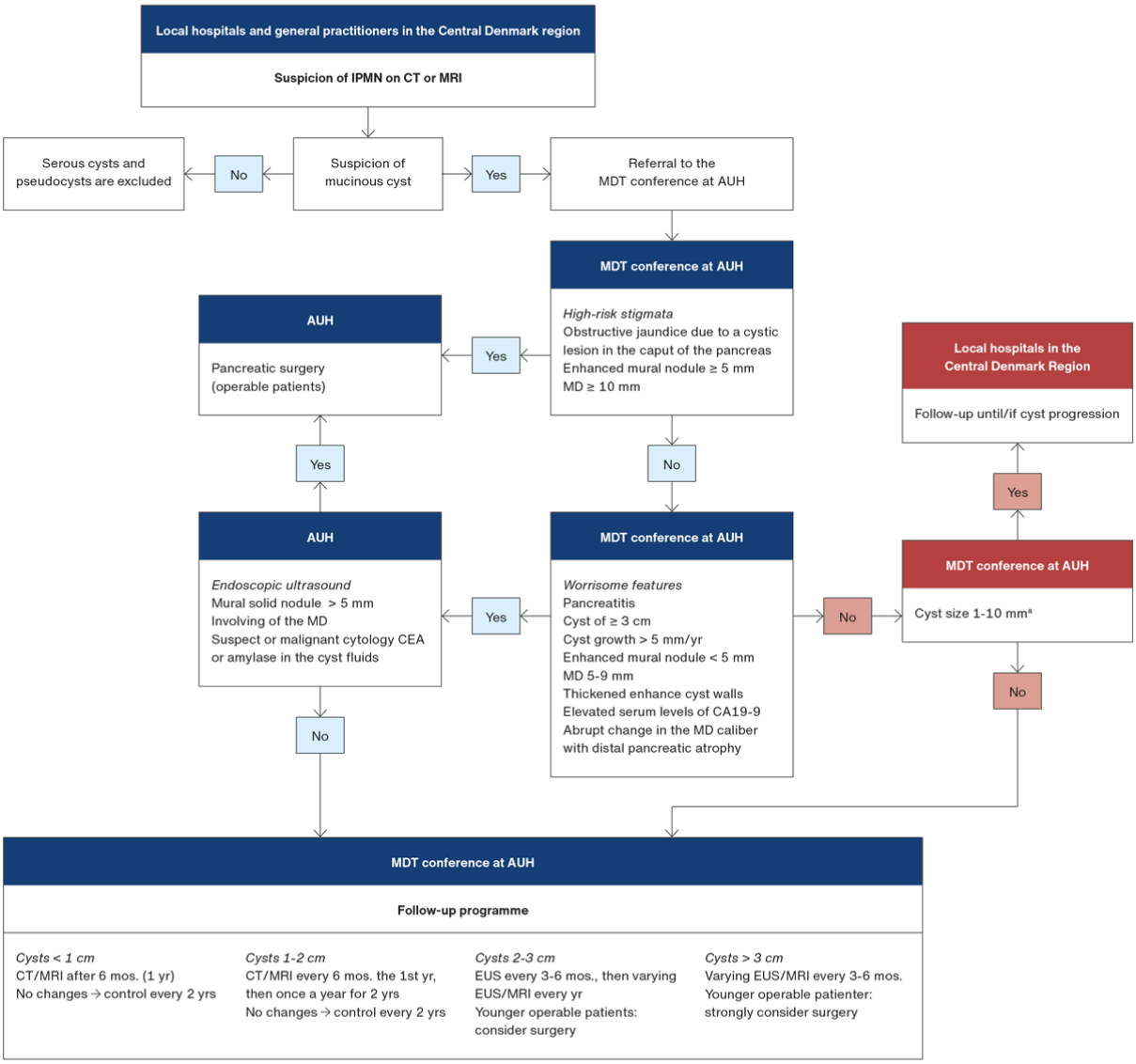
Transabdominal ultrasound (TAUS) is an unfavourabl screening modality for PC. Due to the deep location of the pancreas, interfering bowel gas and obesity reduce and disrupt US transmission. Moreover, body conditions such as obesity result in poor visualisation of the pancreas. However, some studies have indicated that TAUS may be considered in surveillance of PC > 1 cm and not located in the tail of the pancreas [12, 13].

Endoscopic ultrasound (EUS) may be used as a further diagnostic tool in PCs larger than 15-20 mm. By the EUS approach, PCs may be punctured for fluid collection and cytology. Furthermore, a histological biopsy may be performed.

Different international guidelines recommend how to diagnose and treat mucinous cysts [14-16]. In Denmark, numerous local and regional guidelines are available. However, no national (Danish) guidelines exist.

A weekly PC multidisciplinary team (MDT) conference is held at Aarhus University Hospital (AUH) to ensure the systematic and uniform handling of PCs. The MDT starting point is a radiological evaluation. If a radiological diagnosis other than IPMN can be established, the recommendation is given as follows: non-neoplastic cyst and SCN - no further follow-up. MCN is evaluated and treated according to size and symptoms [17, 18]. Suspected cystic neuroendocrine tumour (NET) are referred to the local NET MDT. Patients with suspected solid tumours are referred to the malignant pancreas MDT conference. If IPMN cannot be excluded, the revised international Fukuoka guidelines from 2017 [14] with few local changes are followed (**Figure 1**). Patients are assessed with respect to their need for additional diagnostic workup, treatment or future controls. The aim of this study was to investigate the clinical significance of regular PC MDT for the referred patients and to revise the current local guideline in relation to local conditions.

FIGURE 1 Assessment algorithm used for the pancreatic cyst MDT conference at AUH (blue boxes) with a draft for new/revised regional guidelines based on this study. Changes in relation to the starting point in the figure are described in the orange boxes or with orange coloured text. The changes involve: Patients with SCN are not included in the study, the first study scan is performed only after one year for cysts up to 10 mm[a], and patients with cysts 1-10 mm and BD-IPMN are followed up at local hospitals in The Central Denmark Region until possible cyste progression.



AUH = Aarhus University Hospital; BD = branch duct; CA = cancer antigen; CEA = carcinoembryonalt antigen; EUS = endoscopic ultrasound; IPMN = intraductal papillary mucinous neoplasia; MD = main duct; MDT = multidisciplinary team; SCN = serous cyst neoplasia.
a) Does not apply to patients with MD-IPMN or mixed-type IPMN.

METHODS

This was a retrospective follow-up study, approved as a quality control project at AUH and assessed by the Science Ethics Committee (1-10-72-1-22). All patients assessed at the conference from 1 December 2019 to 31 November 2020 were included. The patients were primarily referred for MDT conference from hospitals and general practice in the Central Denmark Region. Prior to this study, all gastro-medical and surgical departments and radiological departments in the Central Denmark Region were encouraged to refer all patients with PCs to the MDT conference. Exceptions were patients in a performance status (PS) excluding them from pancreatic surgery and patients with recognised pancreatitis as a cause of cyst formation.

All patient data were obtained by systematic review of patient records and collected in a REDcap database [19, 20].

Entry to the PC MDT was a CT or MRI with finding of a suspected cystic pancreatic lesion. We obtained clinical data such as abdominal pain, pancreatitis, newly developed diabetes, steatorrhoea, serum levels of bilirubin, CA-19-9, amylase and information on imaging type, total number of PCs, PC localisation and cyst size. Information on the presence of worrisome features (WF) or high-risk stigmata (HRS) (elaborated in Figure 1) was added to the REDcap database. Information on comorbidities and PS was also included.

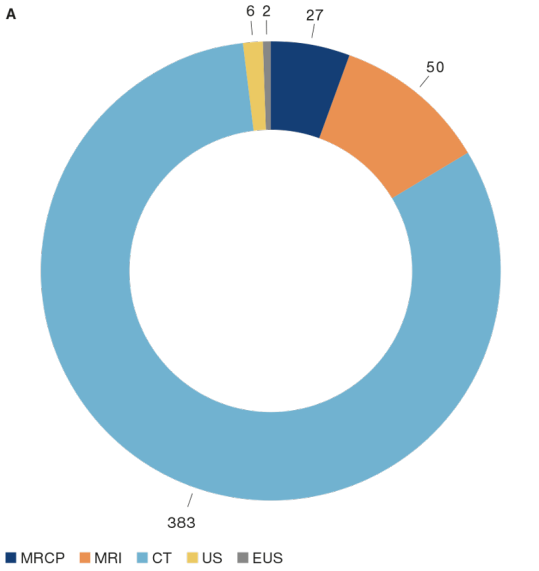
Based on the information above, the MDT conference made the following recommendations: no further follow-up (SCN, pseudocyst or PS > 2), follow-up imaging within 6-24 months (MCN and IPMN, etc.), additional diagnostic workup (large cysts and cysts with WF) or surgery (large cyst and HRS, etc.). The collected patient data were used to establish a descriptive statistical overview.

Trial registration: not relevant.

RESULTS

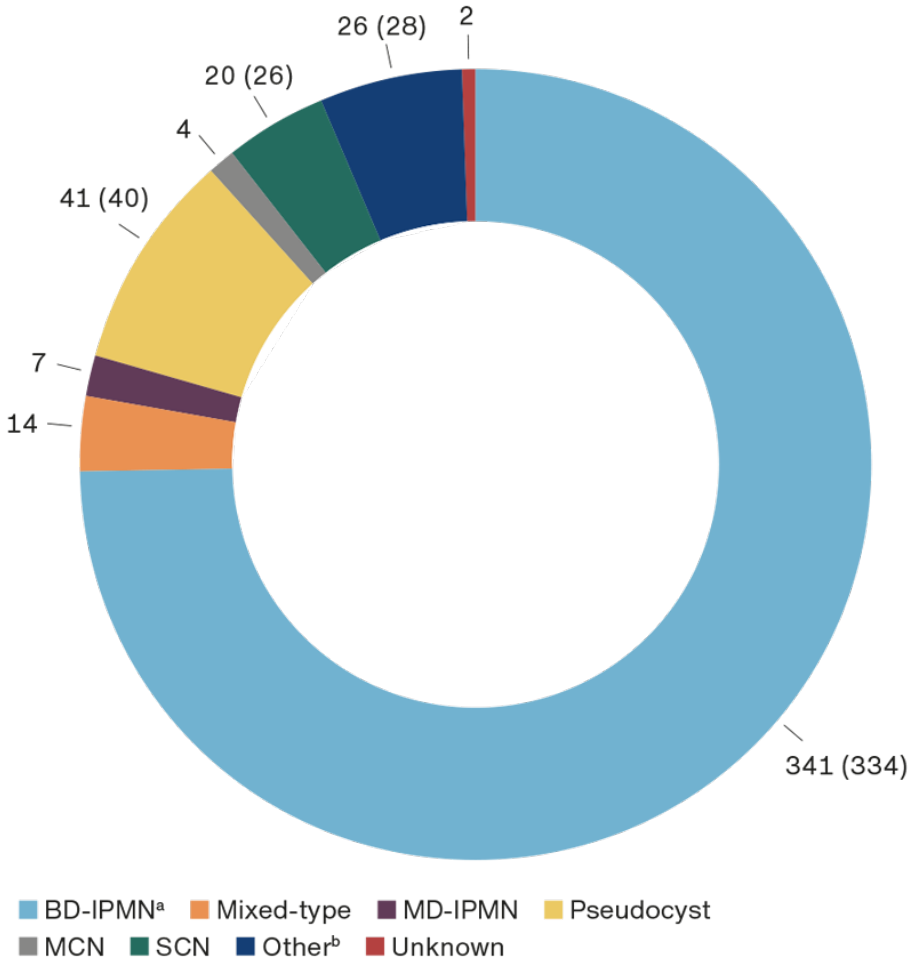
A total of 455 patients were assessed at pancreatic cyst MDT conferences within 12 months (**Figure 2**A). **Figure 3** illustrates the tentative diagnoses in the cohort after the first PC MDT. A large proportion of the cysts could not be characterised due to their small size. These cysts were handled as BD-IPMN (Figure 3). **Figure 4**A and B show the diagnoses and recommendations from the first MDT conference for each patient presented by cyst size (Figure 4A) and age (Figure 4B). A total of 245 patients were included in a follow-up programme, and 175 patients were excluded after the initial assessment. No suspicion of malignancy or premalignant lesions was raised in 57% of the 175 patients. A further 42% were assessed to have > PS 2. The final 1% had no interest in future controls.

FIGURE 2 A. Imaging diagnostic modalities evaluated at the first pancreatic cyst multidisciplinary team conference: 17 of the 455 patients had > 1 imaging modality done including the patients with pancreatic cysts detected by ultrasound (N_1 = 468). **B.** Imaging diagnostic modalities evaluated at the second pancreatic cyst multidisciplinary team conference: one of the 66 patients had > 1 imaging modality done (N_2 = 67).



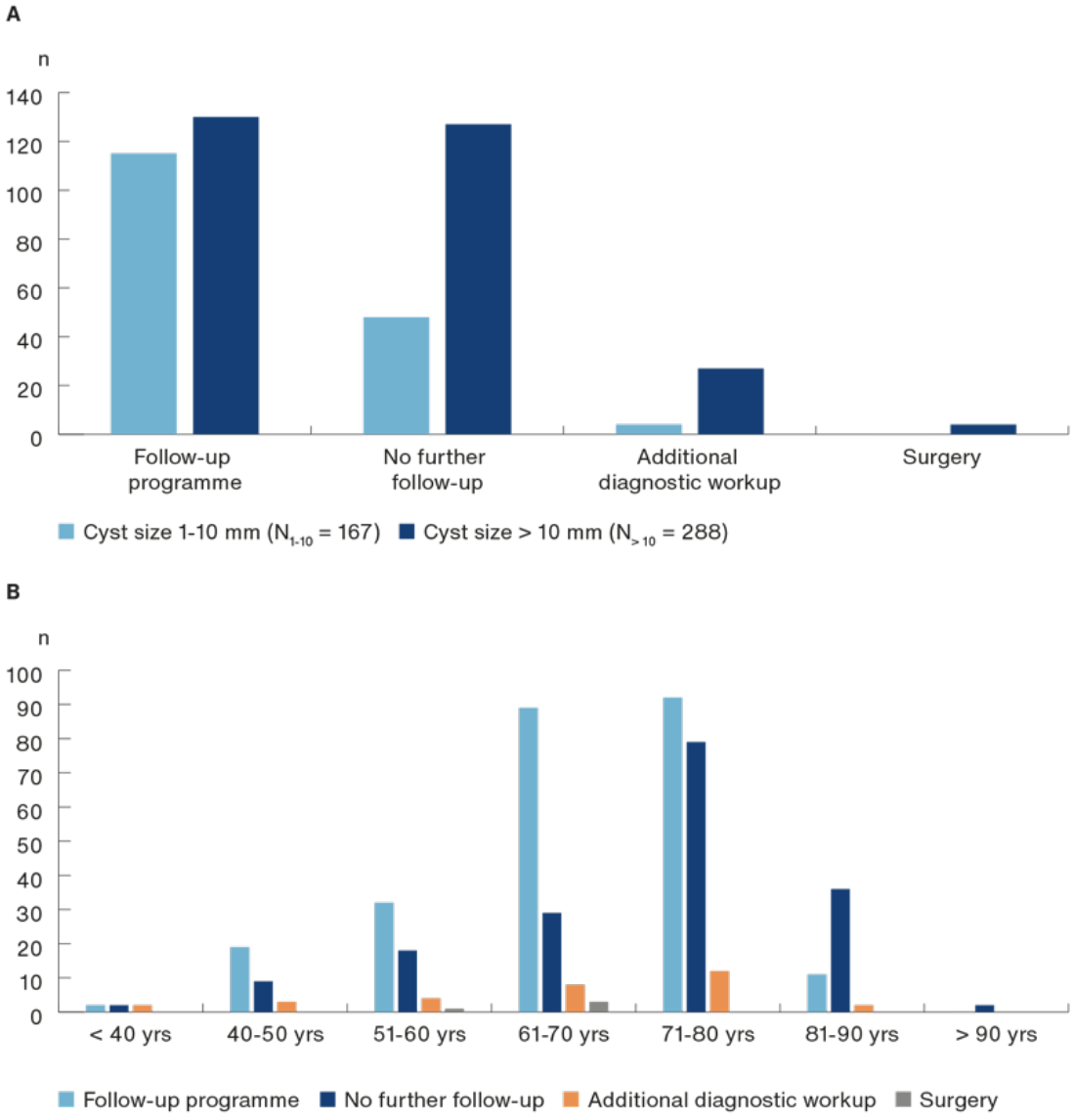
CP = cholangiopancreatography; US = ultrasound; EUS = endoscopic ultrasound.

FIGURE 3 The tentative diagnoses in the cohort after the first pancreatic cyst multidisciplinary team conference. The figures in parentheses show the diagnostic changes made at the second pancreatic cyst multidisciplinary team conference (N = 455).



BD = branch duct; IPMN = intraductal papillary mucinous neoplasia; MCN = mucinous cyst neoplasia; MD = main duct; SCN = serous cyst neoplasia.
a) Also contains non-characterizable pancreatic cysts.
b) Includes neuroendocrine tumour, lipoma, duodenal diverticulum, pseudoaneurysm, duplication cyst and accessory spleen, these patients were registered as having 0 cysts.

FIGURE 4 The diagnoses and recommendations from the first multidisciplinary team conference for each patient. **A.** Assessments/recommendations for each patient by cyst size, the average cyst size was 14.4 mm. **B.** Assessments/recommendations for each patient by age, the average age of patients who completed their first multidisciplinary team conference was 72 years. Patients excluded due to comorbidity had an average age of 76 years. The average age of patients who were recommended surgery was 64 years.



A total of 35 patients had either WF or HRS; four of whom had a PC ≤ 10 mm. Four patients were referred directly for surgery. Additional diagnostic workup was recommended for 31 patients at the first MDT conference. Further diagnosis involved EUS in 11 patients. For six of these patients, the tentative diagnosis was altered, two of whom were referred for surgery. The remaining 20 patients were re-evaluated by another CT or MRI.

A total of 66 patients were reviewed at a second MDT conference during the study period (Figure 2B).

The numbers in parenthesis in Figure 3 show the diagnostic changes made after the second MDT. Eight patients

received a diagnosis different from that given at the first MDT conference. Five of the 66 patients assessed a second time were excluded from further follow-up. For patients evaluated by MDT a second time, an average cyst growth of 0.5 mm/6 months was found.

In the course of 12 months, six patients were recommended surgery at the MDT conference. In addition, five patients who had undergone pancreatic cyst surgery prior to the introduction of PC MDT were included in the study. Five of the six patients who were recommended surgery at the MDT conference had a WF and one had a HRS. A premalignant diagnosis was found in six of the 11 surgical patients: four patients had IPMN with low-grade dysplasia, one had IPMN with high-grade dysplasia and one patient had MCN with low-grade dysplasia. A malignant diagnosis was found in three of the surgical patients: one patient with an undifferentiated carcinoma, one with a pleomorphic tumour consisting of IPMN and focal pancreatic NET and one patient with pancreatic NET. Two of the surgical patients had SCN.

DISCUSSION

During the study period, 455 patients were evaluated at PC MDT conferences in AUH. After the initial assessment, 245 patients were included in a follow-up programme and 175 patients were excluded. In total, 11 surgical patients were included in this study, five of whom had pancreatic surgery prior to the introduction of PC MDT at AUH.

In the present study, 68% of the patients had a cyst of 1-10 mm, 94% of which classified as BD-IPMN/uncharacterisable cysts. BD-IPMN is associated with a very low risk of malignancy, but the risk of malignancy increases in the presence of WF or HRS. Only 0.3% of patients with BD-IPMN *and* with a cyst size below 10 mm had WF or HRS. The risk of malignancy for these patients is so low that future controls could be conducted at the referring hospital and only re-evaluated at the MDT in case of cyst progression. This approach does not apply to patients with MD-IPMN or mixed-type IPMNs, all of which should be evaluated regularly at PC MDT conferences.

According to the revised Fukuoka guidelines, the first control scan in the follow-up programme should take place after six months for cysts under 2 cm and after 3-6 months for 2-3-cm cysts. For patients evaluated a second time, an average cyst growth of 0.5 mm was found at six months. This low average cyst growth indicates that the first control scan may be postponed to one year or more after the first assessment on a PC MDT conference. This postponement is suggested for PC up to 10 mm and will reduce the number of scans with no risk to the patients.

The imaging modality in Figure 2B is a direct consequence of the proposed follow-up/additional diagnostic workup proposed at the first MDT. The percentage of MRI increases from 17% to 40% from the first to the second MDT conference. As described above, MRI is highly favourable in younger patients with expected multiple future follow-up scans. CTs remain the major diagnostic follow-up tool as most patients are elderly with a shorter life expectancy and are thereby less vulnerable to ionising radiation. Furthermore, CT is easily accessible, relative low cost and fast. None of the patients in this study had TAUS as follow-up imaging modality. This may, however, be a valid strategy for selected patients with larger cystic lesions. This would be a very fast, low-cost and safe modality. It should be investigated further and compared to CT and MRI.

Twenty-six of the 455 patients assessed by MDT had SCN as a tentative diagnosis. These patients were included in the follow-up programme due to difficulty in distinguishing between SCN and BD-IPMN. Better discrimination will allow us to identify more patients with benign PC.

In the present study, 8% of patients had WF or HRS and were therefore at a higher risk of having or developing malignancy. All the surgical patients belonged to this group. During 12 months, six patients were recommended

surgery and another five patients had undergone pancreatic resection based on cyst pathology immediately before the introduction of PC MDT. These five patients had been offered surgery on the basis of the guidelines also used at the MDT conference.

A premalignant or malignant diagnosis was found in nine of the 11 surgical patients. Only very few patients (three of 455 patients) turned out to have malignant pancreatic disease. This indicates that no need exists to refer PC patients in a fast-track cancer programme. During the study period, none of the referred patients were misclassified by the local radiologists; hence, none of the lesions interpreted as cysts were solid tumours.

A strength of the present study is that 455 consecutive patients evaluated during a one-year period were included for analysis. The study adopted a retrospective design and is therefore, of course, prone to several biases. To overcome these biases, a prospective study investigation of the clinical impact of a weekly PC conference is required.

The introduction of a PC follow-up programme is resource intensive for general practitioners and for radiology and clinical departments. PC-MDT found that 245 were in need of further controls, indicating that PC-MDT has an important impact on the amount of resources used on patients with PCs. It should be emphasised that the initial scan for each patient was performed unrelated to PC MDT as all 455 patients had one or several PC found incidentally during diagnostic imaging. Next, it appears from Figure 4B that the majority of the patients in this study were in the age group 71-80 years, and will therefore exit the follow-up programme relatively quickly due to the life expectancy of this age group.

The aim of this study was to investigate the clinical significance of regular PC MDT for all the referred patients and to revise current local guidelines taking into account local conditions. The present study enabled minor revisions of the Fukuoka guidelines for local use. In all, 455 patients were evaluated to find 35 patients with suspected premalignant PCs. This means that almost 8% of the referred patients had suspicious lesions, which indicates a need for a regular MDT conference.

CONCLUSION

The PC MDT was of crucial clinical significance for the 35 patients with an increased risk of malignancy. This patient group included the surgical patients, patients recommended follow-up due to WF or HRS and patients who had pancreatic surgery prior to the introduction of PC MDT. These patients are pivotal to the introduction of PC MDT. As a result of PC MDT conferences, these patients avoid a potential development of pancreatic cancer or have a cancer diagnosed at a low stage.

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