Diagnostic value of a pancreatic mass on computed tomography in patients undergoing pancreatoduodenectomy for presumed pancreatic cancer

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Introduction. *Previous studies have shown that 5–14% of patients undergoing pancreatoduodenectomy for suspected malignancy ultimately are diagnosed with benign disease. A "pancreatic mass" on computed tomography (CT) is considered to be the strongest predictor of malignancy, but studies describing its diagnostic value are lacking. The aim of this study was to determine the diagnostic value of a pancreatic mass on CT in patients with presumed pancreatic cancer, as well as the interobserver agreement among radiologists and the additional value of reassessment by expert-radiologists.*

Methods. *Reassessment of preoperative CT scans was performed within a previously described multicenter retrospective cohort study in 344 patients undergoing pancreatoduodenectomy for suspected malignancy (2003–2010). Preoperative CT scans were reassessed by 2 experienced abdominal radiologists separately and subsequently in a consensus meeting, after defining a pancreatic mass as "a measurable space occupying soft tissue density, except for an enlarged papilla or focal steatosis".*

Results. *CT scans of 86 patients with benign and 258 patients with (pre)malignant disease were reassessed. In 66% of patients a pancreatic mass was reported in the original CT report, versus 48% and 50% on reassessment by the 2 expert radiologists separately and 44% in consensus (*$P < .001$ *vs original report). Interobserver agreement between the original CT report and expert consensus was fair (kappa = 0.32, 95% confidence interval 0.23–0.42). Among both expert-radiologists agreement was moderate (kappa = 0.47, 95% confidence interval 0.38–0.56), with disagreement on the presence of a pancreatic mass in 29% of cases. The specificity for malignancy of pancreatic masses identified in expert consensus was twice as high compared with the original CT report (87% vs 42%, respectively). Positive predictive value increased to 98% after expert consensus, but negative predictive value was low (12%).*

Conclusion. *Clinicians need to be aware of potential considerable disagreement among radiologists about the presence of a pancreatic mass. The specificity for malignancy doubled by expert radiologist reassessment when a uniform definition of "pancreatic mass" was used. (Surgery 2015;158:173-82.)*

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In patients with suspected pancreatic or periampullary cancer, differentiation between malignant and benign disease can be difficult. Clinically, benign diseases, such as various types of pancreatitis, can mimic pancreatic malignancy because both may present with symptoms as jaundice and weight loss. Also, on imaging, groove pancreatitis and other types of (chronic) pancreatitis can be mistaken for pancreatic carcinoma as the result of pseudotumor formation.[1-5] Similarly, autoimmune pancreatitis can mimic distal cholangiocarcinoma when the bile ducts are involved (sclerosing cholangitis), and discrimination between the different types of cystic pancreatic lesions remains challenging, despite improvements in imaging techniques.[2,6,7] Tumor markers or immunoglobulin levels are currently not specific enough to differentiate between malignant and benign disease. Consequently, approximately 5–14% of patients undergoing pancreatoduodenectomy for suspected malignancy will ultimately have benign disease.[8,9]

In symptomatic patients (eg, with jaundice and weight loss), a resectable pancreatic mass on computed tomography (CT) and/or endoscopic ultrasonography (EUS) frequently is sufficient to proceed to surgery, because pancreatoduodenectomy is the only curative option for patients with pancreatic or periampullary cancer and malignancy cannot be excluded otherwise. This commonly accepted policy is endorsed by the recent International Study Group of Pancreatic Surgery consensus statement on pancreatoduodenectomy in the absence of histology.[9] The International Study Group of Pancreatic Surgery recommends that in the presence of a solid mass in the head of the pancreas, which is suspicious for malignancy, histo- or cytopathologic proof is not required before proceeding with pancreatoduodenectomy.

Currently, CT is the imaging modality of choice in patients with suspected pancreatic cancer, because it can identify and localize the primary tumor, determine resectability, and detect distant metastases.[10] Although several studies have focused on the diagnostic accuracy of CT in the detection, staging, and resectability of pancreatic cancer,[11] there is a lack of data on the diagnostic value of a pancreatic mass on CT in the differentiation between malignant and benign disease, even though clinical decision making strongly depends on this finding. The proportion of patients with benign disease undergoing pancreatoduodenectomy for suspected malignancy on the basis of the presence of a pancreatic mass on CT is therefore unknown. In addition, there is a discrepancy in the reporting of a pancreatic mass. Sometimes, not only a visible lesion but also indirect signs of tumor invasion (eg, duct obstruction) are considered as a "pancreatic mass," since up to 20% of pancreatic adenocarcinoma present as an isoattenuating lesion on CT.[12-14] Recent guidelines on standardized radiology reporting in cases of pancreatic adenocarcinoma also lack a clear definition of a pancreatic mass.[15] Hence, the interobserver agreement may be lower than generally assumed, but studies on interobserver variability among radiologists are lacking. Furthermore, it is unknown which additional value can be obtained by expert reassessment of CT scans for the presence of a pancreatic mass.

The aim of this study was to determine the diagnostic value of a pancreatic mass on CT in patients with presumed pancreatic cancer. In addition, we aimed to determine the interobserver agreement among radiologists and the additional value of CT reassessment by experienced abdominal radiologists for the presence of a pancreatic mass.

METHODS

Patients. We performed a retrospective analysis within the dataset of a previously published multicenter cohort study in patients undergoing pancreatoduodenectomy between January 2003 and July 2010 in 11 medium- to high-volume centers in the Netherlands.[8] In this study, all adult patients who underwent either a pyloric-preserving pancreatoduodenectomy or a classic Whipple for suspected malignancy were included. This suspicion was either based on a pancreatic mass identified

on CT or EUS, duct dilation with symptoms, and/or highly suspicious or conclusive histo- or cytopathology. Patients with a history of chronic pancreatitis, preoperative suspected duodenal carcinoma, or of whom no preoperative digital CT scan was available were excluded from this study. For pragmatic reasons, given the expected ratio of benign/malignant diagnoses after pancreatoduodenectomy of 1:10, patients with malignant disease were randomly selected in a 1:3 ratio (ie, for each patient with benign disease, 3 cases of malignant disease were randomly selected) by a previously described method.[8]

CT scan. All patients underwent preoperative CT examination. The CT scan generally was performed in the referring hospital and reassessed in the referral center or repeated when the scan was of inadequate quality or outdated. Scans were made according to a pancreas-specific protocol by the use of a thin-section, multiphase technique with pancreatic phase and portal venous phase images in the vast majority of patients.

Data collection. Data were retrospectively collected from (digital) patient charts. Baseline characteristics collected included patient demographics (age, sex) and symptoms. The final diagnosis was based on the postoperative pathology report. The following diagnoses were classified as (pre)malignant: carcinoma, duodenal/ampullary adenoma, mucinous cystadenoma, intraductal papillary mucinous neoplasm or neuroendocrine tumor. All other diagnoses were classified as benign. Original or reassessment reports of the most recent preoperative CT scan were collected and data on the presence of a pancreatic mass were extracted from these reports.

Radiologic reassessment. The most recent preoperative CT scan of all included patients was reassessed by 2 experienced abdominal radiologists (T.L.B., C.Y.N.) with special interest in pancreatic disease. Both reviewers were blinded to any clinical data, results from previous investigations, and the final diagnosis. At first, each scan was evaluated by the 2 radiologists independently for the presence of a pancreatic mass, according to their expert opinion. Subsequently all scans were reassessed by the 2 radiologists together in a consensus meeting, after defining a pancreatic mass as "a measurable space occupying soft tissue density, except for an enlarged papilla or focal steatosis."

Statistical analysis. Data were analyzed using SPSS for Windows version 21 (SPSS Inc, Chicago, Illinois). Interobserver agreement was analyzed using Cohen's kappa. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) for the identification of malignancy were calculated. Taking into account the 1:3 sampling fraction and original 107:1,522 (1:14.22) benign/malignant ratio, the malignant cases were multiplied by factor 4.74 (ie, 14.22 divided by 3) for the calculation of the PPV, and NPV, under the assumption that the proportions of patients not fulfilling the inclusion criteria were similar in the benign and malignant group. Sensitivity analysis was performed after we excluded patients with cystic or ampullary lesions and patients with a biliary stent in situ as it impedes CT evaluation. In addition, a subgroup analysis was performed in patients with and without a double duct sign on CT and in patients with no, 1 or 2 symptoms. Additional subgroup analysis was performed based on the type of original CT report from which the data for this study were extracted.

RESULTS

Patients. During the study period, 1,629 consecutive patients underwent pancreatoduodenectomy for suspected malignancy. A total of 107 patients ultimately were diagnosed with benign disease, of whom 21 patients were excluded because of a history of chronic pancreatitis ($n = 11$) or unavailability of a digital CT scan ($n = 10$). The remaining 86 patients with benign disease were included along with 258 randomly selected patients with malignant disease (1:3 ratio). Baseline characteristics and specifications of histopathologic diagnoses are shown in Table I.

CT findings. The most recent preoperative CT scan was performed in a referring center in 123 of 344 (36%) patients and in the pancreatic center in the remaining 221 (64%) patients. Median interval between CT examination and surgery was 44 days (interquartile range, 28–64). In 118 of 344 (34%) patients, a biliary stent was in situ. In 212 of 323 (66%) available original CT reports, a pancreatic mass was reported. Most pancreatic masses were located in the head of the pancreas and the median tumor size was 22 mm (15–30) (see Table II). On expert reassessment, a pancreatic mass was reported in 166 of 344 (48%) patients by expert 1 and 172 of 344 (50%) patients by expert 2. During the consensus meeting a pancreatic mass was reported in 150 of 344 (44%) patients with the use of the predefined definition ($P < .001$ vs original CT report). Tumor location and median tumor size were similar to the pancreatic masses reported in the original CT reports (see Table II).

Table I. Baseline characteristics and histopathologic diagnoses of 344 patients undergoing pancreatoduodenectomy for suspected malignancy

	N = *344*
Male	209 (61%)
Age (±SD), yr	63 (±11)
Symptoms	
Weight loss	196/261 (75%)
Jaundice	241/321 (75%)
Diagnoses	
Unexpected benign	86 (25%)
Chronic fibrosing pancreatitis	52
Chronic fibrosing cholangitis	17
Autoimmune pancreatitis	9
Serous cystadenoma	2
No abnormalities	2
Other*	4
(Pre)malignant	258 (75%)
Pancreatic adenocarcinoma	135
Ampullary adenocarcinoma	60
Cholangiocarcinoma	30
Duodenal/ampullary adenoma	11
NET	6
Carcinoma derived from IPMN	5
Duodenal adenocarcinoma	4
IPMN	3
Mucinous cystadenoma	3
Other†	1

*Ectopic gastric tissue, Brunner gland adenoma, and purulent inflammation.
†Metastasis of colorectal carcinoma.
IPMN, Intraductal papillary mucinous neoplasm; *NET*, neuroendocrine tumor.

Interobserver agreement. Interobserver agreement regarding the presence of a pancreatic mass between the original report and expert consensus was fair (kappa = 0.32, 95% confidence interval 0.23–0.42). Interobserver agreement between both expert-radiologists was moderate (kappa = 0.47, 95% confidence interval 0.38–0.56). The expert radiologists disagreed on the presence of a pancreatic mass in 90 (29%) cases. Most of these disagreements could be attributed to differences in considering ampullary lesions ($n = 35$), cystic lesions ($n = 8$) or focal steatosis ($n = 2$) as a pancreatic mass and were resolved in consensus with the use of the predefined definition. In 24 patients, the presence of a biliary stent led to disagreement. In the remaining 21 (6%) patients there was true disagreement between the 2 expert radiologists about the presence of a measurable pancreatic mass.

Correlation to histopathologic diagnosis. A total of 167 of 212 (79%) pancreatic masses identified in the original CT report proved to be malignant after pancreatoduodenectomy. Of 150 pancreatic masses identified in expert consensus, 139 (93%) were malignant ($P < .001$ vs original CT report). A total of 36 of 45 (80%) false-positive pancreatic masses identified in the original CT report were not identified in expert-consensus. In 21 of these patients, features of autoimmune or groove pancreatitis, pseudocysts or focal steatosis were identified by the expert radiologists but not recognized as such by the original radiologist and reported as a pancreatic mass suspicious for malignancy (see Figs 1–4). In the remaining 9 of 45 (20%) patients, a pancreatic mass was identified in both the original CT report and expert-consensus, whereas postoperative histopathology showed chronic pancreatitis ($n = 7$) and serous cystadenoma ($n = 2$). In 4 of these patients, the expert radiologists excluded malignancy with a high level of certainty based on findings indicating serous cystadenoma ($n = 2$), autoimmune ($n = 1$), or groove pancreatitis ($n = 1$). In 2 patients with chronic fibrosing pancreatitis on postoperative histopathology, the experts in consensus identified a false positive pancreatic mass, whereas the original radiologist did not.

The sensitivity, specificity, PPV, and NPV of pancreatic masses identified in the original CT report and those identified during the expert consensus meeting are shown in Table III. The specificity for malignancy of pancreatic masses identified in expert consensus was twice as high compared with the original CT report (87% vs 42%, respectively). PPV increased to 98% after expert consensus, but NPV was low for both the original CT report and expert consensus (8% and 12%, respectively).

Sensitivity and subgroup analysis. Sensitivity analysis showed that exclusion of patients with cystic or ampullary lesions ($n = 84$) or patients with a biliary stent in situ ($n = 118$) had no effect on the diagnostic value of pancreatic masses identified in the original CT report or those identified during the expert-consensus meeting. Also, subgroup analysis in patients with and without double duct sign showed no major differences compared with the overall population.

Table IV shows a subgroup analysis according to the number of symptoms present. In the small group of asymptomatic patients ($n = 27$), the specificity for malignancy of pancreatic masses in the original CT report was very low (25%) and significantly better for pancreatic masses identified in expert-consensus (75%). In patients with both jaundice and weight loss, the specificity and PPV

Table II. Identification of a pancreatic mass on CT by radiologists in 344 patients who underwent pancreatoduodenectomy for suspected malignancy

	Original report (n = *323*)	*Expert 1* (n = *344*)	*Expert 2* (n = *344*)	*Expert consensus* (n = *344*)	P *(original report vs expert consensus)*
Pancreatic mass on CT	212 (66%)	166 (48%)	172 (50%)	150 (44%)	<.001
Location					.185
Head	127 (60%)	114 (69%)	97 (56%)	103 (69%)	
Uncinate process	25 (12%)	16 (10%)	16 (9%)	17 (11%)	
Periampullary region	52 (24%)	30 (18%)	44 (26%)	23 (15%)	
Other	8 (4%)	6 (4%)	15 (9%)	7 (4%)	
Size, mm	22 (15–30)	22 (18–28)	24 (19–30)	23 (18–38)	.470
Diagnosis*					<.001
Malignant	167 (79%)	149 (90%)	148 (86%)	139 (93%)	
Benign	45 (21%)	17 (10%)	24 (14%)	11 (7%)	

*Diagnosis based on postoperative pathology report.
CT, Computed tomography.

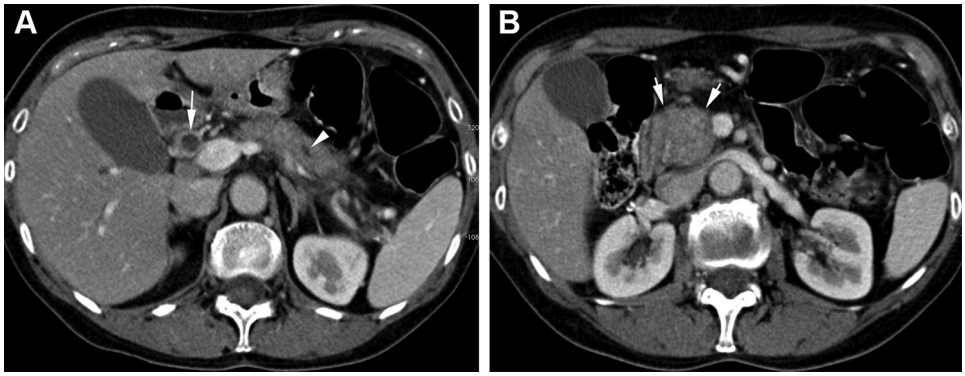

Fig 1. Autoimmune pancreatitis. A 66-year-old woman with focal autoimmune pancreatitis. The fullness of the pancreatic head (*short arrows* in *B*) was interpreted as a "pancreatic mass" suspicious for malignancy by the original radiologist, but identified as autoimmune pancreatitis by both expert radiologists. There is a slightly dilated and irregular pancreatic duct (*arrowhead* in *A*) and dilated common bile duct with wall thickening (*arrow* in *A*), suggestive for accompanying autoimmune cholangitis.

of pancreatic masses identified during the expert consensus meeting increased to 97% and 100%, respectively, as compared with 87% and 98% in the overall population.

From the 123 CT scans performed in referring centers, a reassessment report in the referral center was available for 58 patients. Of the remaining 65 CT scans, the original report could be retrieved from the referring center for 48 patients. Subgroup analysis showed no major differences in the diagnostic value of a pancreatic mass between these 2 types of reports, nor compared with the reports from the CT scans performed in the referral centers (n = 217).

DISCUSSION

In this multicenter retrospective cohort study in patients with presumed pancreatic cancer, the diagnostic value of the presence of a pancreatic mass on CT for the identification of malignancy was high, especially in patients with jaundice and weight loss. The absence of a measurable pancreatic mass on CT, however, cannot rule out malignancy because the sensitivity and negative predictive value are low. Surprisingly, the interobserver agreement among 2 experienced abdominal radiologists regarding the presence of a pancreatic mass was only moderate as they disagreed in 29% of cases. However, individually and, especially in consensus using a uniform definition, the experts were superior to the initial assessment since the number of false positively identified pancreatic masses was lower leading to a doubled specificity for malignancy. The use of a uniform definition of a "pancreatic mass" on CT is therefore recommended.

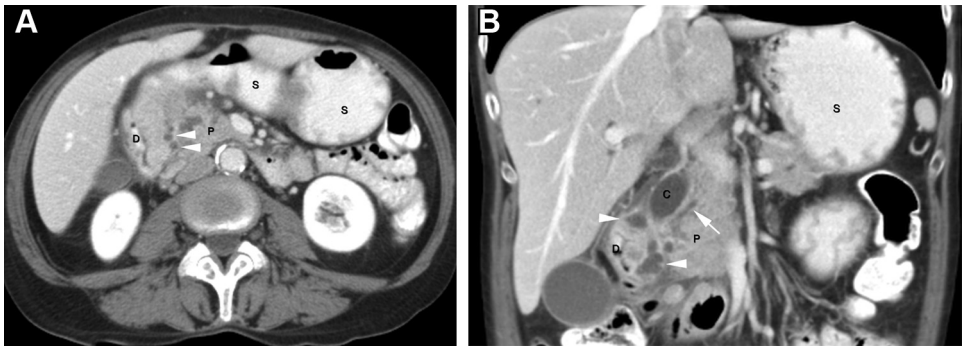

Fig 2. Groove pancreatitis. A 51-year-old woman with groove pancreatitis. The original radiologist described thickening of the duodenal wall with obstruction of the common bile duct, suggestive of malignancy. Both expert radiologists diagnosed groove pancreatitis with typical small cysts in the pancreatic groove (*arrowheads* in *A* and *B*). (*A*) Axial CT image showing thickening of pancreatic groove (D = duodenum, P = pancreatic head, S = stomach). (*B*) Coronal reformatted CT image depicts the markedly dilated common bile duct (C) and normal diameter of pancreatic duct (*arrow*).

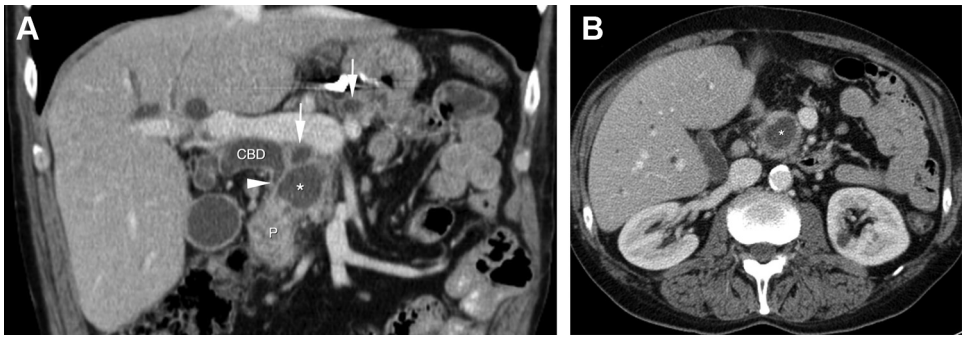

Fig 3. Focal chronic pancreatitis and pseudocyst. A 60-year-old man with focal chronic pancreatitis and pseudocyst. The original radiologist described a cystic pancreatic tumor suspicious for malignancy. Both expert radiologists interpreted this as a pseudocyst in chronic pancreatitis. (*A*) Coronal reformatted CT image depicts a cystic lesion (*asterisk*) in pancreatic head (P) with dilated pancreatic duct (*arrows*) and common bile duct (CBD), which tapers (*arrowhead*) in proximity of the pseudocyst. (*B*) Axial CT image showing the pseudocyst (*asterisk*) in pancreatic head.

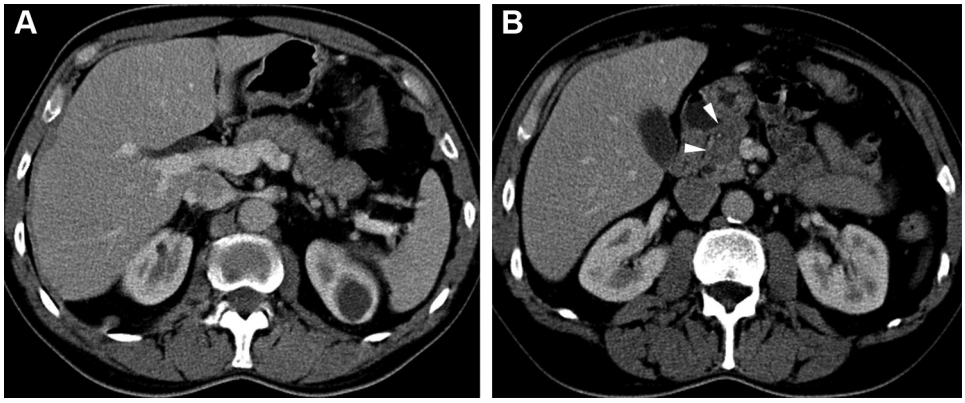

Fig 4. Focal steatosis. A 60-year-old man with focal steatosis of the pancreatic head. The original radiologist reported a pancreatic mass in the head of the pancreas suspicious for malignancy. Both expert radiologists found normal findings with focal pancreatic steatosis as normal variant. (*A*) Normal appearance of pancreatic body and tail, no visible pancreatic duct. (*B*) Focal pancreatic steatosis in the head (*arrowheads*) without mass-effect on surrounding structures.

This is the first study to specifically determine the diagnostic value of a pancreatic mass on CT in the differentiation between malignant and benign disease. Although several studies have assessed the diagnostic accuracy for the detection, staging, and prediction of resectability of pancreatic cancer,[11,16]

Table III. Diagnostic value of a pancreatic mass on CT for the identification of malignancy

	Sensitivity (95% CI)	*Specificity (95% CI)*	*PPV (95% CI)*	*NPV (95% CI)*
Original CT report, $n = 323$	68% (65–71)	42% (31–54)	95% (93–96)	8% (6–11)
Expert 1, $n = 344$	58% (55–61)	80% (70–88)	98% (96–99)	12% (9–15)
Expert 2, $n = 344$	58% (53–61)	72% (61–81)	97% (95–98)	11% (8–14)
Expert consensus, $n = 344$	54% (51–56)	87% (78–93)	98% (97–99)	12% (9–15)

CI, Confidence interval; *CT*, computed tomography; *NPV*, negative predictive value; *PPV*, positive predictive value.

Table IV. Subgroup analysis of the diagnostic value of a pancreatic mass on CT for the identification of malignancy according to the number of symptoms

	Sensitivity (95% CI)	*Specificity (95% CI)*	*PPV (95% CI)*	*NPV (95% CI)*
Asymptomatic patients				
Original CT report, $n = 27$	79% (69–87)	25% (4–64)	92% (83–97)	10% (2–32)
Expert consensus, $n = 27$	68% (43–86)	75% (36–96)	97% (58–98)	17% (22–78)
Patients with either jaundice or weight loss				
Original CT report, $n = 129$	67% (62–71)	33% (19–51)	92% (89–95)	8% (4–13)
Expert consensus, $n = 139$	51% (46–56)	85% (69–94)	98% (95–99)	12% (9–17)
Patients with both jaundice and weight loss				
Original CT report, $n = 139$	66% (62–70)	62% (41–79)	97% (95–99)	8% (5–13)
Expert consensus, $n = 149$	52% (48–56)	97% (81–100)	100% (98–100)	10% (7–14)

CI, Confidence interval; *CT*, computed tomography; *NPV*, negative predictive value; *PPV*, positive predictive value.

only a few studies reported the presence of a pancreatic mass on CT only and even less mentioned whether there was a pancreatic mass visible in patients with benign disease. In a prospective cohort study, DeWitt et al[17] compared EUS with CT and found that 43 of 53 patients with cancer who were treated operatively had a pancreatic mass on CT (sensitivity 81%); however, 8 of 10 patients with benign disease who underwent surgery for suspected malignancy also had a pancreatic mass on CT (specificity 20%). Agarwal et al[18] performed a similar comparison in a retrospective cohort and reported a sensitivity of CT of 75% (53/71) and specificity of 70% (7/10). The sensitivity in these studies was (similar to the original reports in our study) greater than the expert assessment in the current study, which can be explained by the lesser but more specific identification rate of pancreatic masses by our experts. Both studies had a relatively high incidence of benign disease of 16% (10/63 patients) and 12% (10/81). This result is likely attributable to selection bias because only patients who underwent a combination of CT and EUS were included. Probably, some patients with a clear pancreatic mass and high suspicion of malignancy directly proceeded to surgery. Other limitations of these studies are the absence of histopathologic proof in some cases, and the relatively small study populations.[17,18] In addition, the CT scans in these studies were assessed by a single radiologist only. In the present study, we showed that variability among radiologists about the presence of a pancreatic mass is quite large, with only moderate agreement, even between experts. Although the interobserver agreement among radiologists has been investigated for vascular involvement, malignant features of intraductal papillary mucinous neoplasm, and signs of autoimmune pancreatitis,[19-21] data on the presence of a pancreatic mass were thus far unknown. The fair-to-moderate agreement among radiologists may be the consequence of an apparent lack of a clear definition of a "pancreatic mass." A "pancreatic mass" often is referred to as a hypo- or hyperattenuating ill-defined lesion, but sometimes also indirect signs of tumor invasion, such as the presence of the double duct sign, atrophy of the pancreatic tail, or fullness of the pancreatic head, are interpreted as a "pancreatic mass" and reported as such. Moreover, in some cases, a "benign" pancreatic mass is identified on CT, because malignancy can be excluded with a high level of certainty based on additional findings, such as classical findings of autoimmune or groove pancreatitis. Thus, the presence of a pancreatic mass does not always imply malignant disease. This study has shown that the use of a clear definition of a "pancreatic mass"

can improve the diagnostic value of this finding on CT, even among expert radiologists. Future prospective studies are, therefore, required to determine a uniform definition of a "pancreatic mass," which allows differentiation between malignant and benign diseases with a high level of certainty and, can easily be applied in clinical practice, and incorporated in standardized CT reports.[15]

To our knowledge, the value of reassessment of CT scans by radiologists specialized in pancreatic imaging, specifically for the presence of a pancreatic mass, has never been investigated before. Tilleman et al[22] did look at the clinical importance of reinterpretation of radiological investigations performed in a referral hospital. They concluded that reinterpretation of ultrasound and CT resulted in a change of treatment strategy in 9% of patients. The specific CT findings causing the change in strategy were, however, not described.

In our study, the number of patients with a false-positive pancreatic mass was decreased from 45 (3% of the entire cohort) in the original report to 11 (1%) in expert consensus. Especially for the 25 patients (29% of patients with unexpected benign disease) in whom features of autoimmune or groove pancreatitis, pseudocysts, or focal steatosis were mistaken for a pancreatic mass suspicious for malignancy by the original radiologists, a resection could potentially have been prevented, based on the assessment by an expert radiologist, since they identified no ($n = 21$) or a "benign" ($n = 4$) mass. Also in the current era of emerging neoadjuvant treatment options, it is important to assure a correct CT diagnosis before proceeding to investigations to yield histopathologic proof and commence treatment.

Because our experts generally identified fewer pancreatic masses, the amount of false-negative results increased from 78 (30% of the entire cohort after correction for the sampling fraction) to 119 (43%), resulting in a low sensitivity and NPV. It is, however, well known that CT is unable to rule out malignancy. Especially for small (<2 cm) lesions the diagnostic accuracy of CT is limited.[16,23,24] In our previous study, we showed that the absence of a pancreatic mass or double duct sign on CT, in combination with the presence of pain and the absence of jaundice, were strongly associated with the presence of benign disease, albeit with insufficient discriminatory value to exclude malignancy.[8]

When CT is inconclusive, it is common practice to proceed to EUS with or without fine-needle aspiration biopsy, to confirm or exclude malignancy. EUS is known to be more sensitive than CT in detecting pancreatic lesions, especially when they are small.[25,26] In patients with a visible mass on CT, in contrast, it was previously shown that EUS has no additional diagnostic value and does not influence the decision to proceed to surgery.[27] In the current cohort, a pancreatic mass was identified on EUS in 115 of 162 (71%) patients, of whom 30 (26%) had unexpected benign disease, indicating that also pancreatic masses identified on EUS have limited specificity for malignancy, as reported previously.[18,28,29] Endoscopic retrograde cholangiopancreatography (ERCP; with brush cytology) can provide additional information about the nature of a biliary stricture and was performed in 245 patients of our study cohort. Further details on the EUS, ERCP, and preoperative pathologic findings are reported in the previously published multicenter cohort study.[8] The role of magnetic resonance imaging in the work-up of patients with pancreatic cancer is currently increasing, but magnetic resonance imaging scans were rarely performed during our study period.

The presence of biliary stents (both plastic and metal) may hamper CT assessment because they cause artefacts and post-ERCP inflammatory changes on CT images.[18] A pancreatic mass can, however, be identified in case of a large lesion or duct obstruction at a considerable distance from the stent. In our study, 21 of 90 (23%) cases of disagreement between both expert radiologists could be attributed to the presence of a biliary stent. Sensitivity analysis after exclusion of patients with a biliary stent, however, did not show any differences compared with the whole group, similar to a previous study on the diagnostic value of CT and EUS.[30] Nonetheless, in clinical practice it is preferred to perform CT imaging before placement of a biliary stent in patients with suspected pancreatic cancer.

This study has a number of limitations. First, only patients who underwent pancreatoduodenectomy were included. This resectable subgroup represents only 20% of all patients with pancreatic or periampullary cancer and an even smaller subset of all patients referred for suspected pancreatic cancer. Besides the fact that a definitive histopathologic diagnosis often is unavailable for unresected patients, inclusion of all patients referred for suspected pancreatic cancer would, however, also be practically unfeasible due to the size of this group. Moreover, in the 40% of patients with metastatic disease the question whether a pancreatic mass is present is less relevant. The same applies to a lesser extent to the remaining

40% of patients with extensive vascular involvement leading to local irresectablity. Also, for practical reasons, only a selection of patients with malignant disease was included in the final analysis. To reduce the risk of bias, the included subset of patients with malignant disease was selected randomly from the entire consecutive cohort by using a random number list.

Another limitation is the heterogeneity in diagnoses, because all patients undergoing pancreatoduodenectomy for suspected malignancy were included. However, in clinical practice, the histopathologic diagnosis of the tumor is frequently unclear in the preoperative phase as well. Moreover, sensitivity analysis after exclusion of cystic and ampullary lesions did not show any differences in the results.

In addition, a considerable proportion of false positive pancreatic masses identified in the original CT report can be attributed to unrecognized autoimmune or groove pancreatitis. The knowledge on autoimmune and groove pancreatitis has rapidly increased over the past few years.[2] Therefore, these diseases are likely to be underreported in the early years of our study.

It also must be noted that, in contrast to the original radiologists who were aware of clinical data and imaging that was performed before the CT (eg, ultrasound or ERCP), the expert radiologists were blinded to any clinical data, additional imaging, and the final diagnosis. This is common practice in diagnostic studies and essential to reduce measurement bias, since knowledge of these additional data might influence their interpretation of the CT-scans. The expert radiologist were, however, aware of the fact that all patients had undergone pancreatoduodenectomy for presumed malignancy and the 1:3 benign/malignant ratio.

Finally, only 2 experts performed the reassessment. Ideally, the group of experts would have been larger, but the results of the 2 expert radiologists separately are fairly similar and already show the additional value of experts over the original assessment. Although one might expect that CT reports from the referral centers match the expert-radiologists reports more closely than the reports from the referring center, subgroup analysis did not show this difference, justifying the fact that we clustered them into one group.

In conclusion, this study confirms that the presence of a pancreatic mass on CT has a high specificity and PPV for malignancy, especially in symptomatic patients with jaundice and weight loss. However, the absence of a pancreatic mass does not rule out malignancy. Expert reassessment, especially in consensus using a uniform definition, leads to a lower, but more accurate detection rate of pancreatic masses on CT as compared with the original assessment. Clinicians should be aware of the potential considerable disagreement amongst radiologists about the presence of a pancreatic mass and, hence, the use of a uniform definition of a pancreatic mass is recommended.

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