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Routine Chest Computed Tomography for Staging of Pancreatic Head Carcinoma

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Objectives: The diagnostic value of routine chest computed tomography (CT) in addition to abdominal CT in workup for pancreatic head carcinoma is unclear. The aim of this study was to determine if routine chest CT revealed significant lesions that altered the management of patients with suspected pancreatic head carcinoma.

Methods: All Dutch pancreatic cancer centers were surveyed on the use of chest CT in preoperative staging. In addition, a single-center retrospective cohort study was performed including all patients referred with suspected pancreatic head malignancy without chest CT between 2005 and 2016. The primary end point was the proportion of patients in which chest CT revealed clinically significant lesions, leading to a change in management.

Results: In 7 of 18 Dutch pancreatic cancer centers (39%), a preoperative chest CT is not routinely performed. In the study cohort, 170 of 848 patients (20%) were referred without chest CT and underwent one by local protocol. Chest CT revealed new suspicious lesions in 17 patients (10%), of whom 6 had metastatic disease (3.5%).

Conclusions: Routine use of chest CT in diagnostic workup for pancreatic head carcinoma reveals clinically significant lesions in 10% of patients, being metastases in up to 4%.

Key Words: multiple pulmonary nodules, pancreas, pancreatic neoplasms, solitary pulmonary nodule, x-ray computed tomography

(*Pancreas* 2020;49: 387–392)

Literature on the additional value of a chest computed tomography (CT) is scarce and inconclusive.^{1–5} Routine use of a chest CT is not included in several current guidelines for standard diagnostic workup,⁶ whereas other guidelines recommend the use of chest CT.^{7,8} Distant metastases most frequently occur in the liver, followed by the peritoneum and the lungs. Despite that the lungs are the third most common site of metastases,^{9–12} only a few studies in selected populations have been performed on the incidence of isolated pulmonary metastases.^{1–5} For patients with isolated pulmonary metastases, chest CT might be of great value.

Cases of patients referred to a tertiary center are discussed by a tumor board, a multidisciplinary team of medical specialists who

regularly meet to determine the best treatment for each individual cancer patient. A considerable proportion of patients with advanced disease are not referred to a tertiary center.¹³ Therefore, we speculate that in an unselected group the incidence of relevant pulmonary findings may be much higher than reflected by tumor board meetings in these centers.

We designed this study to determine the incidence of clinically relevant lesions on chest CT for staging pancreatic head carcinoma. First, we did an online survey to evaluate the perceived incidence of relevant findings and the current perception among all Dutch pancreatic surgery centers about the role of preoperative chest CT. Second, to determine the clinical relevancy of a routine chest CT, we analyzed the consequences for initial management in a large series of patients with suspected pancreatic head malignancy.

MATERIALS AND METHODS

Survey

Using a questionnaire, we surveyed all Dutch pancreatic cancer centers on the use of chest CT in preoperative staging (see Appendix, Supplemental Digital Content 1, <http://links.lww.com/MPA/A782>, which shows all questions included in the survey). All 18 Dutch Pancreatic Cancer Group (DPCG) centers received an invitation to participate in an online survey between March 2017 and August 2017. The survey contained 14 questions on pancreatic head resections, preoperative (chest) imaging, incidence of pulmonary metastases at chest CT, prognosis with solitary and multiple pulmonary metastases, and preclusion of patients from resection. The incidence of finding pulmonary metastases and the incidence of preclusion from resection due to the findings at chest CT were defined as rarely (<5% of patients annually), occasionally (5%–10% of patients annually), or frequently (>10% of patients annually).

Cohort

A single-center retrospective analysis was performed including all patients who were assessed for suspected pancreatic head cancer at the University Medical Center Groningen, the Netherlands, between January 2005 and April 2016. The University Medical Center Groningen is the main tertiary and quaternary referral center in a large managed clinical oncological network covering the whole northeast of the Netherlands. Patients were identified using the internal database for pancreatic cancer in our center. All cases were discussed in our weekly tumor board meeting by a multidisciplinary group of hepatopancreatobiliary surgeons, radiologists, nuclear physicians, gastroenterologists, pathologists, and oncologists. The vast majority of patients with evident pulmonary metastasis will probably not be referred for surgical treatment. In order to prevent selection bias, only patients referred to our center without a chest CT were included in the analysis. Patients with neuroendocrine tumors, with cystic benign or premalignant lesions, with insufficient documentation, or without reviewable imaging were excluded. When abdominal metastases or locally unresectable tumors were present at abdominal CT, patients were also excluded from the

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FIGURE 1. Flowchart of the study cohort. Outcomes of patients referred to our multidisciplinary tumor board meeting with potentially resectable pancreatic head cancer, who underwent a first-time preoperative chest CT at our institution.

analysis (Fig. 1). The study was approved by the ethics committee of the University Medical Center Groningen (METc 2017430). All patients' personal data have been secured.

The primary end point was the proportion of patients in which clinically relevant lesions, defined as suspicious by an experienced radiologist, were found, leading to a change in initial management. A change in management was defined as performing additional diagnostic procedures or precluding surgery due to the

findings on chest CT. Secondary end points were the additional procedures performed due to the findings on chest CT, the final pathology of these lesions, the delay caused by additional diagnostic procedures, and the number of patients who were excluded from surgical exploration due to these findings. Chest CT documentation, documentation of the tumor board meeting, pathology reports, and further management were reviewed for each patient. Statistical analysis was performed with SPSS (version 23.0; SPSS Inc, Armonk, NY). Normality of distribution was assessed and checked for skewness. Continuous data were expressed in medians with interquartile ranges (IQRs) and categorical variables in numbers with percentages.

RESULTS

Survey

Our survey was completed and returned by all 18 DPCG centers (100%). In these centers, a median number of 40 (IQR, 25–51) pancreaticoduodenectomies were performed in 2016. In 11 of 18 centers (61%), a preoperative chest CT is done routinely. In 5 of the 7 remaining centers (71%), a preoperative chest x-ray is mandatory. In case of suspicious lesions on chest x-ray, a subsequent chest CT will be performed.

Among all Dutch centers where chest CT is routinely performed, 4 (36%) report to find pulmonary metastases of pancreatic head cancer rarely, 5 (46%) occasionally, and 2 (18%) frequently. In 11 of 16 centers (69%), histopathologic confirmation for any suspicious lesion seen on chest CT is mandatory.

In almost two-thirds of centers (11/18), the responding surgeons presumed that patients with advanced-stage disease, as judged by the referral centers, were not routinely referred for discussion in their multidisciplinary tumor board meeting. The majority of all centers indicate that only a minority of patients are precluded from surgical exploration based on the findings on chest CT. From all respondents, 15 of 17 (88%) believe that a solitary pulmonary metastasis will influence prognosis, whereas all believe that multiple metastases do. However, 12 (67%) of all centers indicate that chest CT should be included in the preoperative diagnostic staging protocol (Fig. 2).

Cohort

In our series, a total of 848 patients with suspected pancreatic head cancer were discussed in the multidisciplinary tumor board meeting between January 2005 and April 2016. Of these, 203 patients (24%) were referred without any CT imaging or without chest CT and routinely underwent one by local protocol. Eighty-four of 203 patients (41%) were referred to our center by

FIGURE 2. Survey results. Results from a national survey among all Dutch pancreatic cancer group centers (100% response rate). Survey questions are depicted at the y axis. *This question was answered only by centers where chest CT is routinely performed. MDT indicates multidisciplinary tumor board meeting.

TABLE 1. Clinical Characteristics of the Study Population

Characteristic	n = 170
Age at diagnosis, median (IQR), y	67 (57–73)
Sex, males, n (%)	100 (59)
BMI, median (IQR), kg/m ²	24 (22–27)
ASA score, n (%)	
Class I	24 (14)
Class II	97 (57)
Class III	48 (28)
Class IV	1 (1)
Largest pancreatic tumor diameter on CT, median (IQR), mm	30 (20–39)
History of prior malignancy, n (%)	33 (19)
History of prior lung malignancy, n (%)	0 (0)
History of smoking, n (%)	69 (41)
Missing, n (%)	34 (20)
History of diabetes mellitus, n (%)	41 (24)
Missing, n (%)	3 (2)
Preoperative CEA, median (IQR), µg/L	2.7 (1.6–5.2)
Missing, n (%)	100 (59)
Preoperative CA 19-9, median (IQR), kU/L	204 (27–1389)
Missing, n (%)	38 (22)

ASA indicates American Society of Anesthesiologists; BMI: body mass index; CA, carbohydrate antigen.

a general practitioner, admitted through the emergency department, or internally referred. One hundred nineteen patients (59%) were referred by peripheral centers. Clinical characteristics of the study population are displayed in Table 1. Based on the abdominal CT scan, 170 of 203 patients (84%) were found eligible for surgical exploration.

Chest CT revealed suspicious lesions in 17 patients (10%) (Fig. 1). Of these, 10 had pulmonary lesions, 5 had extrapulmonary lesions, and 2 had both (Fig. 3). The character (multiple/solitary), type, and the size of the lesions are displayed in Table 2. In all

17 patients, these findings had consequences for the initial management. In 15 patients, extra imaging was performed by means of an additional chest CT, positron emission tomography scan, bronchoscopy, mammography, chest x-ray, or ultrasound. In 8 patients, histopathology was obtained by biopsy or bronchial wash cytology for pathologic confirmation. In 6 patients, resection of the suspicious lesion was performed using wedge resection (n = 5), lobectomy (n = 1), and/or mastectomy (n = 1; the same patient who also underwent a wedge resection) (Fig. 3). Additional diagnostic procedures revealed a second primary tumor in 3 patients. In 6 patients (3.5%), metastases of pancreatic origin were found (Fig. 4).

Two primary lung cancers and 1 primary breast cancer were found (Fig. 3; no. 1, 2, 11). One of these lung cancers (Fig. 3; no. 2) was proven by biopsy of the adrenal gland, which also demonstrated suspicious enlargement on abdominal CT. The other case (Fig. 3; no. 1) proved to be a T2 pulmonary squamous cell carcinoma. The patients with breast cancer and pulmonary squamous cell carcinoma were treated with curative intent and subsequently underwent pancreatic exploration.

Of the 6 patients in whom pancreatic metastases were found, 4 were located in the lungs, 1 in the mediastinal nodes, and 1 in the cervical nodes (Fig. 3; no. 3–6, 16, 17). Two finally underwent surgical exploration; however, no resection was performed due to metastatic disease. The chest lesions in the remaining 8 patients proved to be benign (Fig. 3; no. 7–10, 12–15). Of these, 7 underwent surgical exploration; the final patient underwent a positron emission tomography scan that proved abdominal metastases. The positive predictive value for the diagnostic utility of a preoperative chest CT for pulmonary metastasis was 53% (95% confidence interval, 36%–69%).

Eleven patients eventually underwent surgical exploration, of which 5 underwent resection. Additional diagnostic procedures caused a median delay of 62 days (IQR, 29–86 days) from chest CT to exploration. Six patients were precluded from exploratory surgery due to the findings on chest CT (Fig. 3; no. 2, 4, 6, 8, 16, 17).

DISCUSSION

The clinical relevance of a preoperative chest CT in the diagnostic workup for suspected pancreatic head cancer is unclear because of insufficient evidence. This is illustrated by the fact that

FIGURE 3. Follow-up of patients with suspicious lesions. Swimmers plot to visualize follow-up of all patients with suspicious lesions at chest CT. Follow-up started at time of chest CT until date of resection or date of incurable disease. The legend under the figure shows the location of the lesion, final diagnosis, and final management of the primary tumor. If a patient is not displayed in a pattern, the lesion proved to be benign. The legend right from the figure displays all additional procedures performed due to the findings at chest CT.

TABLE 2. Size and Character of the Suspicious Tumors Found With Chest CT

Patient No.	Origin of Lesion	Multiple/Solitary	Size,* mm
1	Lung	Solitary	15
2	Lung	N.A.	N.A.
3	Lung	Solitary	15
4	Lung	Solitary	26
5	Lung	Multiple	6
6	Lung	Multiple	5
7	Lung	Multiple	10
8	Lung	Solitary	3
9	Lung	Multiple	5
10	Lung	Solitary	6
11	Breast	Solitary	13
12	Mediastinal node	Multiple	3
13	Breast	Solitary	14
14	Breast	Multiple	N.A.
15	Thyroid	N.A.	14
16	Mediastinal node	Multiple	12
17	Supraclavicular node	Multiple	12

*In case of multiple tumors, the size of the largest tumor is described.
N.A. indicates not applicable.

chest CT is not routinely performed in 39% of all DPCG centers (Fig. 2). Also, in a recent consensus review of guidelines on the treatment of pancreatic cancer by the International Association of Pancreatology and the European Pancreatic Club, the utility of chest CT in the diagnostic workup was not discussed.¹⁴ Interestingly, in our series, a chest CT revealed significant lesions in 10% of patients, being metastases of pancreatic origin in 4% of patients. In other words, 29 patients need to undergo a preoperative chest CT to reveal 1 pulmonary metastasis. This study is the first to show the relevant diagnostic yield for a preoperative chest CT in a large series of patients who all underwent a chest CT by local protocol.

We sought to determine the current role of a preoperative chest CT in staging patients with suspected pancreatic head malignancy. The literature on this subject is rather scarce. Only the study by Chang et al⁴ specifically analyzed pulmonary lesions in pancreatic head carcinoma, also including patients with solely imaging of the lower lung fields at abdominal CT. All performed studies confirm a limited diagnostic yield for a preoperative chest CT.^{1–5} Arguments for this conclusion are a limited amount of solitary

pulmonary metastases revealed by chest CT.^{1,3,4} Lung metastases seldom appear without other contraindications for resection.⁵ Furthermore, pulmonary nodules do not affect survival,^{1,2,4} even when they develop to metastases²; neither do findings in chest CT generally change management of the primary tumor.^{1,3} Unfortunately, these studies were performed in relatively small, selected, nonidentical populations, without routine use of chest CT, including patients referred from peripheral centers with prior chest CT, permitting some degree of bias. An overview of the available literature is displayed in Table 3.

The variability in advised diagnostic workup between guidelines,^{6–8} reflected by previous literature, is similar to the results from our nationwide survey in which more than half of the DPCG centers (61%) indicate that they routinely perform a preoperative chest CT by local protocol. Although 88% of the pancreatic surgeons consider a solitary pulmonary metastasis to influence prognosis, one-third of the centers (33%) do not indicate that a chest CT should be included in the preoperative staging protocol. This opinion can be explained by our observation of a low rate of patients with upfront metastatic disease during our multidisciplinary tumor board meetings; 33 of 203 patients (16%) proved advanced-stage disease in the abdominal CT, while one would expect approximately 80% to 90%.^{15,16} This suggests that referral centers already filter out most patients with obvious disseminated disease, including patients with evident pulmonary metastasis. This finding is supported by our survey results in which almost two-thirds of DPCG centers indicate that presumably not every patient with advanced-stage disease is referred for discussion in their multidisciplinary tumor board meeting (Fig. 2). This explains our survey result that findings on chest CT mostly preclude only a minority of patients from surgical exploration. With our strategy to include only those patients primarily diagnosed in our center or those patients referred to our center without chest CT, we have tried to outbalance this selection.

Although our study describes current clinical practice, a limitation of our study is that unlike previous studies, no threshold was maintained for the number and size of the lesions to be classified as suspicious. Nevertheless, an experienced radiologist assessed all lesions by a clear and relevant clinical description, and all patients with suspicious lesions were further evaluated.

A major question remains if pulmonary metastases, especially when small and low in number, influence prognosis. A large retrospective study including 13,233 patients has shown a better overall and pancreatic cancer-specific survival for patients with synchronous isolated lung metastases compared with isolated liver metastases. They suggest that surgery of the primary tumor or surgery of metastatic disease does not improve survival.¹⁷ A smaller study by Kruger et al¹⁸ defined a subgroup of 13 patients

FIGURE 4. Three patients with suspicious lesions at chest CT. A, CT shows a metastasis in the base of the right lower lobe. B, CT shows a lesion apical in the right upper lobe. Wedge resection was performed, and the pathology showed a squamous cell carcinoma. C, CT shows a dense nodule in the left breast. Pathology showed an invasive ductal carcinoma.

TABLE 3. Literature on Lesions at Preoperative Chest CT in Patients With Suspected PDAC

Study	Population	Patients With Preoperative Chest CT, n (%)	IPN Definition	IPN/Suspicious Lesions, n (%)	Pulmonary Metastases, n (%)	Influence on Survival
Chang et al,* 2015 ⁴	Resectable head PDAC	Undefined; 329 (71) with reviewable chest/abdominal CT	≥1 lung nodule(s) ≤1 cm in diameter	59 (18) [†]	5 (8.5) ^{‡,§}	None
Mehtsun et al,* 2018 ¹	All PDAC	632 (23)	≥1 lung nodule(s) ≤1 cm in diameter	451 (71)	21 (3.3) ^{§,¶}	None
Nordback et al, ^{#**} 2004 ⁵	All PDAC	53 (100)	N.A.	7 (13) ^{††}	3 (43) ^{‡,‡‡}	N.A.
Pappas et al, [#] 2014 ³	Localized PDAC	124 (89)	N.A.	8 (6)	1 (13) ^{‡,§}	N.A.
Poruk et al,* 2015 ²	Resectable PDAC	374 (16)	≥1 lung nodule(s) <3 cm in diameter	183 (49)	29 (16) ^{‡,§}	None

*Study focusing on IPN at preoperative chest CT.

[†]Ten patients with pulmonary nodules of more than 1 cm in diameter were excluded from the analysis.

[‡]Percentage of IPN/suspicious lesions.

[§]Metachronous metastases.

^{||}Two or more 2 chest CT scans obtained.

[¶]Percentage of total cohort.

[#]Study focusing on lesions suggestive of metastases at preoperative chest CT.

^{**}Prospective study.

^{††}Of which 5 (71%) were not seen on chest x-ray.

^{‡‡}In 5 of 7 patients, pulmonary lesions were not further evaluated because of liver metastasis, local invasion, or a poor general condition precluding resection; 1 patient proved to have a pancreatic metastasis of a pulmonary small cell carcinoma.

PDAC indicates pancreatic ductal adenocarcinoma; IPN, indeterminate pulmonary nodules; N.A., not applicable/available.

with synchronous pulmonary metastases who had a 2 times longer survival compared with patients with locally advanced disease.

In addition, in our study, 3 second primary tumors were found. With a median survival of 17 months after pancreatic head resection, the influence of early-stage second primary cancers on survival is doubtful.¹⁹

Possible arguments for not performing a chest CT such as radiation exposure, costs, and delay to surgery should be considered. However, an additional radiation exposure of less than 10 mSv and the low cost of a chest CT are a minor concern for this population.²⁰ Another adverse effect can be an increase in indeterminate findings leading to an increase in downstream costs.²¹ Although literature on indeterminate pulmonary nodules in pancreatic cancer patients is scarce, an incidence has been reported as 18% to 71%.^{1,2,4} In these studies, different definitions of indeterminate pulmonary nodules were used, and only in a minority a chest CT was performed. In our study, significant lesions were found in 10% of patients. Another important finding in our study is that additional diagnostic procedures can lead to delay in time to surgery. A recent study suggested that operation after 32 days of diagnostic imaging doubled the risk of tumor progression to unresectable disease.²² Our results encourage performing chest CT and abdominal CT simultaneously to minimize both radiation exposure and additional delay prior to chest CT. A currently emerging and attractive option could be to offer patients with suspected lesions neoadjuvant chemotherapy during further analysis. However, despite provided support for neoadjuvant chemotherapy,²³ prospective randomized controlled data on pancreatic cancer patients without metastatic disease have not yet been published.²⁴

We conclude that in patients with potentially resectable pancreatic head tumors a routine chest CT has a higher than expected significant diagnostic yield of 10%. Almost half of these patients prove to have malignant lesions, of whom half have a second (treatable) primary and half have metastases. A delay of 2 months

for further diagnostic procedures should be anticipated, and the limited influence of solitary pulmonary metastasis on survival remains doubtful, whereas such a delay of surgery may be more harmful. We therefore advise performing chest CT routinely, but to be very careful to postpone surgery based on these findings.

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