

Undetected Pancreatic Adenocarcinoma on CT: Frequency According to CT Scan Protocol

Moran Drucker Iarovich (✉ morandru@gmail.com)

1 - Department of Radiology, Chaim Sheba Medical Center, Tel Aviv University.

Sara Apter

1 - Department of Radiology, Chaim Sheba Medical Center, Tel Aviv University.

Eli Konen

1 - Department of Radiology, Chaim Sheba Medical Center, Tel Aviv University.

Yael Inbar

1 - Department of Radiology, Chaim Sheba Medical Center, Tel Aviv University.

Marrienne Amitai

1 - Department of Radiology, Chaim Sheba Medical Center, Tel Aviv University.

Eyal Klang

1 - Department of Radiology, Chaim Sheba Medical Center, Tel Aviv University.

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Abstract

Purpose: CT is a main diagnostic modality for detecting pancreatic adenocarcinoma. This study aims to assess the frequency of missed pancreatic adenocarcinoma on CT scans according to different CT protocols.

Methods: Consecutive pancreatic adenocarcinoma patients were retrospectively collected (12/2011-12/2015). Patients with abdominal CT scans performed up-to a year prior to cancer diagnosis were included. Two radiologists registered in consensus the presence and radiological signs of missed cancers. The frequency of missed cancers was compared between portal and pancreatic/triphasic CT protocols.

Results: Overall, 180 CT scans of pancreatic adenocarcinoma patients were retrieved. 126/180 (70.0%) were pancreatic/triphasic protocols and 54/180 (30.0%) were portal protocols. The overall frequency of missed cancers was 6/180 (3.3%). The frequency of missed cancers was higher in portal CT protocols compared to pancreatic/triphasic protocols: 5/54 (9.3%) vs. 1/126 (0.8%), $p=0.01$.

CT signs of missed cancers included: 3 cases of small hypodense lesions, 2 cases with peri-pancreatic fat stranding, 1 case of dilated pancreatic duct with a cut-off sign.

Conclusion: The frequency of missed pancreatic adenocarcinoma is higher on portal CT protocols. Physicians should consider the cancer miss rate on different CT protocols.

Key Points

- The frequency of missed pancreatic adenocarcinoma on CT scans is 3.3%
- The frequency of missed cancers was higher in portal CT protocols compared to pancreatic/triphasic protocols
- Subtle CT signs of undetected tumors include: small hypodense lesions, peri-pancreatic fat stranding and dilated pancreatic duct with a cut-off sign

Introduction

Pancreatic cancer is a highly lethal malignancy, considered to be the fourth leading cause of cancer-related death in the western world [1-5]. Initial symptoms are often nonspecific, and include abdominal pain, weight loss, asthenia, anorexia and jaundice [5-9].

Abdominal computed tomography (CT) is a main diagnostic tool for various gastrointestinal complaints, with millions of scans performed worldwide every year. CT commonly serves as a primary imaging modality for the detection of pancreatic malignancy, and considered the gold-standard for determining staging.

Demonstration of pancreatic adenocarcinoma (PDAC) is optimal using a dedicated biphasic CT protocol, comprised of a pancreatic phase scan (starting 35-45 seconds after intravenous contrast iodine-based injection), and a portal phase (performing another scan 65-70 seconds from contrast material injection) [10-15].

Pancreatic phase is optimal for PDAC detection, making this desmoplastic tumor conspicuous compared to the normally enhancing pancreatic parenchyma. Portal phase is superior for assessing regional and distant spreading to peritoneum and liver.

Survival from PDAC depends on early detection, with surgical resection being the only potentially curative therapy [3, 5]. Therefore, Clinicians must be aware of the reliability and potential pitfalls of different CT protocols when diagnosing pancreatic malignancy.

Despite the importance of avoiding delayed diagnosis, there are only a scant number of publications regarding the rate of missed pancreatic adenocarcinoma.

This study aims to assess the frequency of missed pancreatic adenocarcinoma on CT scans according to different CT protocols.

Materials And Methods

Study design

The Chaim Sheba Medical Center at Tel-Hashomer Hospital Institutional review board committee (IRB) approval was granted for this retrospective study. Informed consent was waived by The Chaim Sheba Medical Center at Tel-Hashomer Hospital Institutional review board committee. All research methods were performed in accordance with relevant guidelines and regulations in accordance with the [Declaration of Helsinki](#).

Consecutive subjects with histopathological diagnosis of pancreatic adenocarcinoma were retrospectively retrieved using a computerized search in our department's Radiological Information System (RIS) (12/2011-12/2015).

Search parameters included the words "pancreatic adenocarcinoma"; "pancreatic tumor"; "pancreatic mass"; "pancreatic malignancy" or "pancreatic cancer".

Only subjects with a new diagnosis of PDAC were included. Other pathologies, such as pancreatic neuroendocrine tumors, were excluded.

Demographic, clinical data and CT referral indications were retrieved from the electronic medical records.

For each patient, we collected the CT scan in which PDAC was first radiologically observed. These scans were considered the gold standard in the study.

For each patient, we collected all CT scans performed up to a year prior the gold standard. For each scan, we checked whether signs of pancreatic cancer have been missed by the original reporting radiologist. All missed cases were re-evaluated in consensus by two senior radiologists.

Missed PDAC was defined as either a pancreatic mass that was not reported, or as secondary radiological findings of malignancy (peri-pancreatic fat stranding, dilatation of pancreatic duct with or without a cut-off sign and peri-pancreatic lymphadenopathy) that were not reported. Small tumors were defined as having a diameter of less than 20 mm as in Yoon et al. paper [20].

The study cohort inclusion process is presented in **Chart 1**.

Imaging technique

CT scans were performed in several institutes. The scans were categorized according to the CT protocol that was used:

1) A dual phase *pancreatic-protocol* CT, which comprises a pancreatic phase performed with a scan delay of 35–45s following a bolus of intravenous contrast agent, and a portal venous phase, performed with a scan delay of 65–70 s. 2) A *triphasic CT protocol* with late arterial (scan delay 30-45 s) and portal phases (scan delay 65-70 s) followed by an additional delayed scan 3 - 5 minutes following intra-venous (IV) contrast bolus. 3) A *portal CT protocol* (scan delay 65-70 s). All protocols were conducted with non-contrast scan prior to injection of intra venous contrast. The various protocols examined in the study were summarized in **Table 1**.

Statistical analysis

Descriptive statistics was used to summarize the study's characteristics. All analyses were conducted with SPSS (Version 20 Armonk, NY, US). Statistical significance was established at a 2-sided $P < .05$. Differences in miss rates were compared between the portal CT protocol group and the pancreatic/triphasic CT protocols (Fisher's exact test). We also compared differences in miss rates between university hospitals and outpatient clinics and between portal CT scans and pancreatic/triphasic CT scans (Fisher's exact test).

Results

Overall, we retrieved 193 PDAC patients with CT scans. 126/193 (65.3%) of the scans were pancreatic or tri-phasic CT protocols, 54/193 (28.0%) were portal CT protocols. 13/193 (6.7%) of the scans were non-contrast only CTs, and were excluded.

Thus, 180 patients were included in the study. **Table 2** summarizes the study cohort according to CT protocol. The age range was 12-90 years, as there was a single case of a child with Fanconi anemia related tumor.

The referral indications for performing CT scans were retrieved and were grouped into fourteen categories (**Table 3**). Patients could have more than one referral indication. The most frequent indication was abdominal pain (96/180 patients, 53.3%), followed by weight loss (63/180, 35.0%). The "other" category included lower limb thrombosis, ischemia or edema, heartburn, splenomegaly, elevated liver enzymes, shoulder, flank or chest pain. Most incidental masses were detected on CT surveillance for previous malignancy (breast, prostate and lymphoma) or pancreatic/liver cyst follow-up. Two incidental masses were found during a work-up for bleeding ulcer and trauma.

The overall frequency of missed tumors was 6/180 (3.3%).

The miss rate was significantly higher in portal CT protocols. Five cancers were missed on portal scans, and a single tumor missed in a pancreatic protocol [portal protocol: 5/54 (9.3%) vs. pancreatic/triphasic protocol: 1/126 (0.8%), $p=0.01$, OR 12.8].

There was a similar distribution of missed tumors between university hospitals and outpatient centers [university hospitals: 3/96 (3.1%) vs. outpatient centers 3/77 (3.9%), $p=1$].

The following CT signs were retrospectively identified in missed cancers: Three patients demonstrated small (diameter ≤ 20 mm) hypodense lesions (**Figure 1**). Three additional patients did not reveal a detectable pancreatic mass, but exhibited the following radiological findings: two cases of peri-pancreatic fat stranding (**Figure 2**) and one case of dilated pancreatic duct with a cut-off sign (**Figure 3**).

Discussion

In this study, we have evaluated the failure to diagnose PDAC in different CT protocols. Our cohort included 180 patients, and found a miss rate of 9.3% of PDAC in portal CT scans. To the authors' knowledge, this is the largest cohort to investigate missed PDAC in abdominal CT scans, with reference to different CT protocols.

Kielar et al. described 13 errors that involved the pancreas out of 222 imaging errors, one of which was due to a missed pancreatic mass [16], and Donald et al. presented 558 diagnostic imaging errors, of which CT scans accounted for 43%, including 4 patients with missed pancreatic tumors [17]. These studies, however, did not analyze the rate of missed pancreatic tumors solely, and did not separate results according to CT protocols.

This study demonstrated significantly higher miss rate (9.3%) of PDAC in portal CT scans. Our findings are supported by current literature stating that pancreatic phase is superior in demonstrating pancreatic adenocarcinoma, due to better tumor-to-pancreas contrast [10-15]. In addition, the lower rate of missed pancreatic tumors on pancreatic and triphasic scans may also be attributable to radiologists being more conscious of subtle imaging findings when interpreting pancreatic/triphasic CT scans, which usually hold a stronger relation to the clinical question of tumor detection [18]. Since pancreatic adenocarcinoma is a

lethal malignancy and early detection is the main chance of survival, physicians' knowledge of CT techniques is of crucial importance.

Several previous studies investigated the imaging findings of insidious pancreatic tumors [20-25]. Yoon *et al.* showed in their study of small (≤ 20 mm) PDAC, that approximately one-fourth of the small pancreatic masses were iso-attenuating. In that study, most of the small iso-attenuating tumors showed secondary signs; of which the most frequent were pancreatic duct abnormalities, including cut-off or dilatation [20]. Ahn *et al.* demonstrated that focal hypo-attenuation and pancreatic duct dilation with or without interruption were the most useful findings for avoiding delayed diagnosis of pancreatic cancer [21].

In our study, undetected tumors registered the following radiological signs: i) small (≤ 20 mm) hypodense lesions only retrospectively identified, ii) peri-pancreatic fat stranding and iii) dilated pancreatic duct with cut-off sign. We further recommend that these signs be emphasized in physician's training.

Errors in cancer diagnosis are likely the most harmful and expensive types of diagnostic errors [18-19]. Physicians should take into account the appropriate CT technique when there is clinical suspicion of pancreatic malignancy.

Our study has several limitations. This is a retrospective study, but only a retrospective study can present an accurate estimation of the miss rate of PDAC. Secondly, CT scans included in our work were done in several institutes, which reflect real life variability. Thirdly, the number of missed cases is small, though statistical significance has been observed.

In conclusion, the frequency of missed PDAC is higher on portal CT protocols. Physicians should consider the cancer miss rate on different CT protocols.

Abbreviations

- Computed Tomography (CT)
- Institutional review board (IRB)
- Radiological Information System (RIS)
- Intra-Venous (IV)
- Odds Ratio (OR)

Declarations

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Conflicts of interest/Competing interests: The authors of this manuscript declare no conflict of interest.

Ethics approval: An institutional review board approval (IRB) was granted for this retrospective study and informed consent was waived by the IRB committee.

Consent to participate: An institutional review board approval (IRB) was granted for this retrospective study and informed consent was waived by the IRB committee.

Availability of data and material: Not applicable

Code availability: Not applicable

Authors' contributions: All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Dr. Moran Drucker Iarovich, Dr. Eyal Klang, and Prof. Sara Apter. The first draft of the manuscript was written by Dr. Moran Drucker Iarovich, and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Tables

Table 1. Different Computed Tomography protocols examined in cohort

CT Protocol	Protocol Phases	Time of scanning (Post IV contrast administration)
Pancreatic protocol	Pancreatic	35-45 seconds
	Portal	65-70 seconds
Triphasic protocol	Late arterial	30-45 seconds
	Portal	65-70 seconds
	Delayed	3-5 minutes
Portal protocol	Portal	65-70 seconds
*All protocols were conducted with non-contrast scan prior to injection of intra-venous contrast		

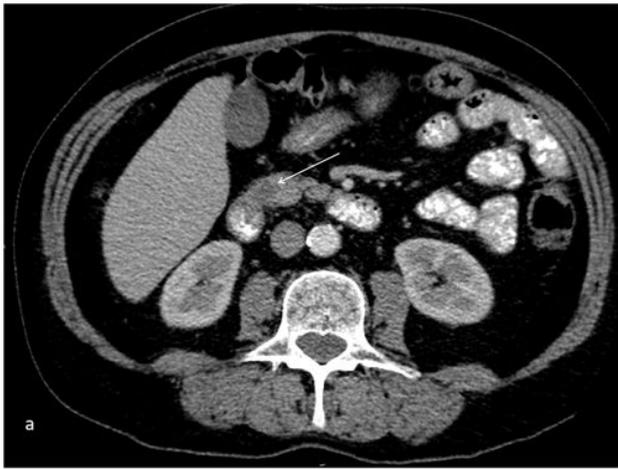
Table 2. Study Cohort Data according to CT Protocol

Data Type	Entire cohort	Portal	Pancreatic/Triphasic
N. Patients	180	54	126
(%)		(30%)	(70%)
M:F Ratio	108:72	39:15	69:57
Age (Mean)	66.4±10.8	66.4±10.0	66.5±11.2
Performing institutes	University hospitals: 94/180 (52%)	University hospitals: 28/54 (52%)	University hospitals: 66/126 (52.4%)
	Outpatient centers: 77/180 (43%)	Outpatient centers: 21/54 (39%)	Outpatient centers: 56/126 (44.4%)
	Unknown: 9/180 (5%)	Unknown: 5/54 (9%)	Unknown: 4/126 (3.2%)
Number of undetected tumors	6	5	1

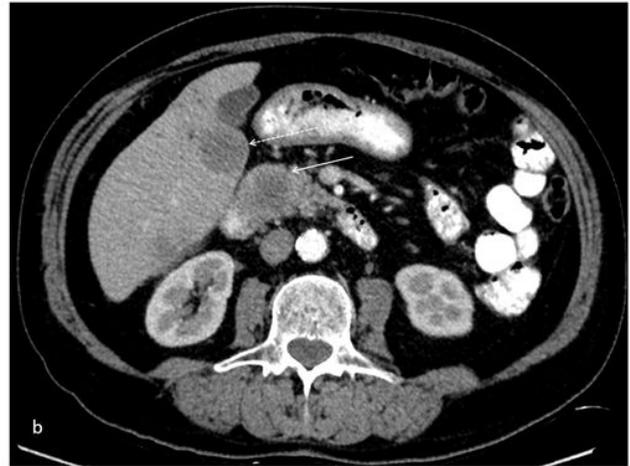
Table 3. Clinical Indications for Performing CT (patient could have more than one indication)

Clinical indication for performing CT	Entire cohort (N.)	Percentage	Portal	Pancreatic/Triphasic	N. of undetected cancers
Obstructive jaundice	36	20%	8	28	0/6
Abdominal pain	96	53.3%	34	62	6/6
Lethargy	15	8.3%	3	12	0/6
Weight loss	63	35%	20	43	2/6
Anorexia	27	15%	9	18	1/6
New onset diabetes	8	4.4%	1	7	0/6
Pancreatitis	5	2.7%	3	2	0/6
Back pain	23	12.8%	8	15	2/6
Nausea/vomiting	24	13.3%	7	17	1/6
Change in bowel habits	16	8.9%	8	8	0/6
Night sweat	5	2.7%	1	4	0/6
Elevated CA19-9 tumor marker	3	1.7%	0	3	0/6
Other	17	9.4%	6	11	1/6
Incidental finding	8	4.4%	2	6	0/6

Figures



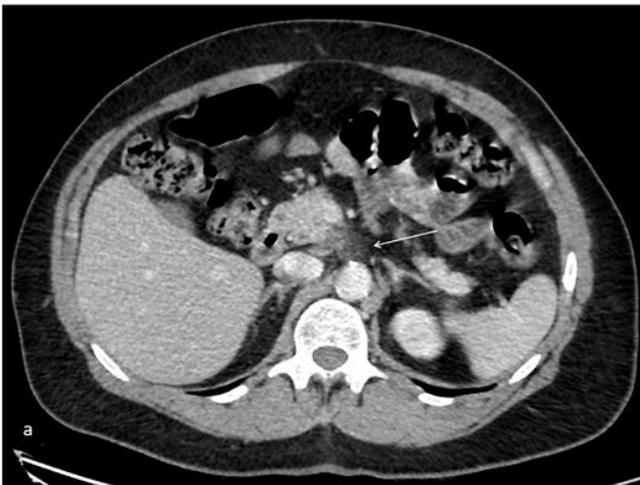
A



B

Figure 1

62 years old male, CT surveillance for previous prostatic cancer (a) undetected small hypodense mass in head of pancreas (b) CT scan six months later, showing enlargement of the hypodense mass, and new liver metastases are detected



A



B

Figure 2

57 years old male, Chest-Abdomen CT scan done for dyspnea (a) undetected peri-pancreatic fat stranding (b) 2 months CT follow-up done for increased abdominal pain, showing increased peri-pancreatic fat

stranding, and new liver metastasis

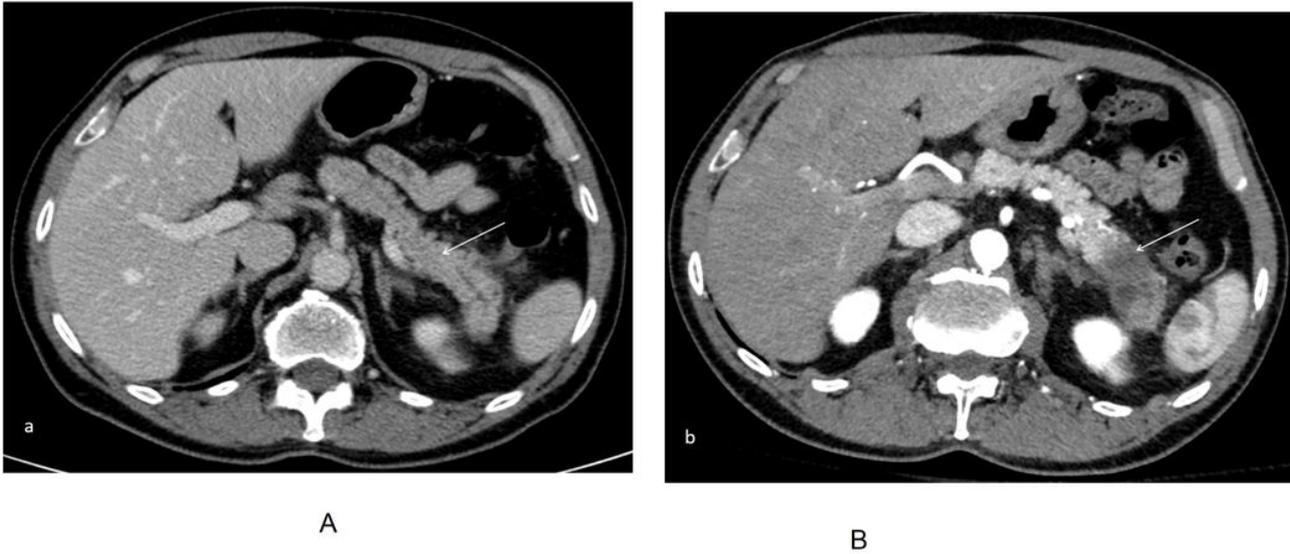


Figure 3

67 years old male, Triphasic CT scan done for ischemic limb (a) Slightly dilated distal pancreatic duct with cut off sign (b) 6 months CT follow-up done for recurrent limb ischemia, showing a large hypodense mass in the tail of pancreas.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [OnlineChart1.png](#)