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## Value of pelvis CT during follow-up of patients with pancreatic adenocarcinoma

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### Abstract

**Purpose**—To determine the frequency in which the pelvis component of an abdominopelvic CT provides information that would influence clinical management in two separate groups of patients: those with previously resected pancreatic ductal adenocarcinoma (PDA) and those with locally advanced unresectable PDA.

**Methods**—This institutional review-board approved, HIPAA compliant retrospective study with waived informed consent included 247 subjects with histologically proven PDA, including 153 subjects post-pancreaticoduodenectomy and 94 subjects with locally advanced unresectable disease. Imaging reports interpreted between January 2005 and December 2013 were obtained from our institution’s Radiology Information System by searching a Cancer Registry database of PDA patients separately for the words “whipple” and “unresectable”. CT findings were separated by location in the abdomen or pelvis, and subsequently reviewed and graded for their likelihood of representing metastatic disease. The probability of pelvic CT influencing clinical management- i.e. of finding isolated pelvic metastatic disease- was determined using 95% binomial proportion confidence intervals for both the post-pancreaticoduodenectomy and locally advanced unresectable groups.

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Compliance with Ethical Standards:

Conflict of Interest: The authors declare that they have no conflict of interest.

Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This article does not contain any studies with animals performed by any of the authors.

Informed Consent: For this type of study, formal consent is not required.

**Results**—No subjects who had undergone pancreaticoduodenectomy had an isolated pelvic metastasis on follow-up imaging (0%; 95% CI 0–2.38,  $p = 0.0004$ ); 33 had metastatic disease in the abdomen, and 120 had no or equivocal evidence of abdominopelvic metastatic disease. One subject with locally advanced unresectable PDA had a possible isolated pelvic metastasis on follow-up imaging (1.1%; 95% CI 0.03–5.79,  $p = 0.048$ ); 20 had metastatic disease in the abdomen, and 73 had no or equivocal evidence of abdominopelvic metastatic disease.

**Conclusion**—Isolated pelvic metastatic disease rarely occurs in patients with PDA who have had prior pancreaticoduodenectomy or have a locally advanced unresectable primary tumor, suggesting routine pelvic CT in follow-up imaging of these patients may not be necessary.

### Keywords

Pancreatic adenocarcinoma; CT protocol; pancreaticoduodenectomy; isolated pelvic metastases

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### Introduction

Most patients diagnosed with pancreatic ductal adenocarcinoma (PDA) present with locally advanced or metastatic disease for which prognosis is very poor and standard treatments, including chemotherapy, radiation, and surgical resection, are only marginally effective. The most common surgery is a pancreaticoduodenectomy, but less than 10% of patients can have a curative resection at the time of diagnosis [1,2].

Cross-sectional imaging is routinely performed in many hospitals to stage patients with PDA before surgery, after surgery, and in patients with borderline locally advanced PDA ineligible for surgery at the time of diagnosis. The most common locations of metastases from PDA, in decreasing order, include the liver, peritoneum, lung/pleura, bones, and adrenal glands; however, PDA has been reported to metastasize virtually anywhere in the body [3,4]. Given the typical metastatic pattern of PDA, the value of routine pelvic follow-up imaging, which depends almost entirely on the detection of isolated pelvic metastases, is unclear. This study was designed to determine the frequency in which the pelvis component of an abdominopelvic CT provides information that would influence clinical management in two separate groups of patients: those with previously resected pancreatic ductal adenocarcinoma (PDA) and those with locally advanced unresectable PDA.

### Materials and Methods

Institutional review board approval was obtained and informed consent waived for this Health Insurance Portability and Accountability Act-compliant retrospective investigation.

### Subjects and Setting

A search of the Comprehensive Cancer Center Registry database maintained at our quaternary care academic medical center yielded 1,474 subjects with histologically or cytologically confirmed PDA evaluated at our institution from January 1, 2005 to December 31, 2013. All abdominal CT reports (with or without a CT of the pelvis) performed in subjects with known PDA were extracted from the Radiology Department Radiology Information System database, resulting in 7,549 total imaging reports, including combined

abdomen and pelvis, separate abdomen, and separate pelvis reports, for 1,474 subjects. All reports were finalized interpretations by board-certified radiologists at our academic medical center, regardless of whether the examination was physically performed at our institution or another facility.

Subjects with either resected or locally advanced PDA were included in this cohort. Subjects with resectable disease who had not yet had a pancreatectomy were not included in this study. This is because while the actual incidence of finding a solitary pelvic metastasis may be low, a pre-surgical CT pelvis may still have reasonable utility given the high morbidity of pancreaticoduodenectomy [2,5,6].

To create the first study group consisting of subjects who were post-pancreaticoduodenectomy for PDA, all imaging reports were searched for the word “whipple”, providing 237 scans in 218 subjects. The first available CT abdomen scan for each subject performed at least 4 weeks after pancreaticoduodenectomy was selected for review to coincide with the start of chemotherapy and to avoid equivocal immediate post-operative findings; time from surgery to imaging ranged from 1 to 61 months, with a mean of 9.8 months, and a median of 6 months. Of the 218 subjects, 24 (11.0%) were excluded because none of their scans included the pelvis, 29 (13.3%) were excluded because they had pancreatic neuroendocrine tumor despite being originally entered as PDA in the Cancer Registry, and 12 (5.5%) were excluded because none of their scans were performed at least 4 weeks after surgery. This resulted in a group of 153 subjects with 153 CT scans including both abdomen and pelvis performed at least 4 weeks after pancreaticoduodenectomy.

To create the second study group consisting of subjects with locally advanced unresectable disease, all imaging reports were searched for the word “unresectable”, providing 252 scans in 242 subjects. All subjects had a histologic diagnosis of PDA. Of the 242 subjects, 148 (61.2%) were excluded because none of their scans included the pelvis. The first available scan for each subject was selected for review, resulting in a group of 94 subjects with 94 CT scans including both abdomen and pelvis in subjects with locally advanced unresectable primary tumor.

### Data Collection and Terminology

Two board-certified radiologists specializing in abdominal imaging with over 30 years of experience each independently reviewed all the imaging reports. The abdomen portion of the CT was considered to range from the included lung bases to the iliac crests, and the pelvis portion from the iliac crests to the included upper thighs.

Exams for both the abdomen and pelvis portions were graded as follows:

- A positive grade was given if a report indicated a high likelihood that a finding was metastatic, including organ-based lesions, lymph nodes described as enlarged, and omental/mesenteric nodularity.
- An equivocal grade was given if a report indicated indeterminate lesions, lymph nodes described as borderline

enlarged or prominent, or moderate to large volume non-nodular ascites.

- A negative grade was given if a report indicated a normal exam, a small volume of non-nodular ascites, or benign findings only.

The specific locations of equivocal or positive findings were recorded. The abdomen and pelvis scores were assigned based on the highest grade finding within each portion. Exams for which it was unclear if the findings were located in the abdomen, pelvis, or both were marked for direct image review; examples included mesenteric nodules/caking/deposits, lymph nodes described only as mesenteric, peritoneal carcinomatosis, and ascites (limited to moderate to large volume ascites). In the event of a disagreement between the two reviewers in the assessment of the radiology reports, the disputed cases were also marked for direct image review. For all directly reviewed cases, the CT images were reviewed by both reviewing radiologists together, and a consensus grade was applied to the case.

### Statistical Analysis

For statistical analysis, the post-pancreaticoduodenectomy and locally advanced unresectable PDA groups were treated separately because the risk of solitary pelvic metastasis for each group is theoretically different. The proportion of subjects with positive, equivocal, and negative findings in the abdomen and pelvis was recorded. Ninety-five percent binomial confidence intervals were calculated using the binomial exact test for one proportion. The primary outcome measure was the percentage of subjects with positive or equivocal findings in the pelvic CT with negative findings in the abdomen CT. A  $p < 0.05$  was considered significant for all hypothesis tests, and indicated that the prevalence of disease isolated to the pelvis was less than 5%. A cutoff of 5% was chosen as a reasonable value under which the pelvis portion of CT would be considered unnecessary. If more than 5% of exams demonstrated isolated pelvic metastases, the CT pelvis portion would be considered reasonably worthwhile.

## Results

### Post-Pancreaticoduodenectomy Group

The specific distribution of equivocal and positive findings in the abdomen and pelvis for the post-pancreaticoduodenectomy group is summarized in Table 1. The most frequent site of positive metastatic disease was the liver ( $n = 17$ , 11%).

The results for the post-pancreaticoduodenectomy group are summarized in Table 2. Of the 153 subjects, 33 (21.6%) had positive evidence of metastatic disease in the abdomen; of these, 3 (2.0%) had positive and 2 (1.3%) had equivocal findings of pelvic metastases. The remaining 120 (78.4%) subjects had either a) no evidence of a metastasis in the abdomen or pelvis ( $n=90$ , 58.8%), or b) equivocal evidence of an abdominal metastasis with equivocal or no evidence of a pelvic metastasis ( $n=30$ , 20.0%). No subjects had equivocal or positive evidence of an isolated pelvic metastasis with negative abdominal images, and no subjects had positive evidence of a pelvic metastasis with equivocal evidence for an abdominal metastasis. Thus, in no case did the pelvis component show a higher level of disease than the

abdomen component. Furthermore, in all 8 (5.2%) subjects in which both the abdomen and pelvis were scored as equivocal, both the abdomen and pelvis were involved with the same process and it was not definitive whether this was due to metastases; specifically, all 8 subjects had either moderate/large volume non-nodular ascites or enlarged abdominopelvic lymph nodes. Thus, the pelvis portion of the scan was uniquely suspicious for metastatic disease in 0/153 examinations (0%; 95% CI 0–2.38,  $p = 0.0004$ ).

### Locally Advanced Unresectable Group

The specific distribution of equivocal and positive findings in the abdomen and pelvis for the locally advanced unresectable group are summarized in Table 3. The most frequent sites of positive metastatic disease were the liver ( $n = 10$ , 10.6%) and abdominal peritoneum/mesentery ( $n = 10$ , 10.6%).

The results for the locally advanced unresectable group are summarized in Table 4. Of the 94 subjects, 20 (21.3%) had positive evidence of metastatic disease in the abdomen; of these, 6 (6.4%) had positive and 1 (1.1%) had equivocal findings of pelvic metastases. Of the remaining 74 (78.7%) subjects, 73 (77.7%) had either a) no evidence of a metastasis in the abdomen or pelvis ( $n=55$ , 58.5%) or b) equivocal evidence of an abdominal metastasis with equivocal or no evidence of a pelvic metastasis ( $n=18$ , 19.1%). Furthermore, in all 8 cases in which both the abdomen and pelvis were scored as equivocal, both the abdomen and pelvis were involved with the same process and it was not definitive whether this was due to metastases; specifically, all 8 subjects had either moderate/large volume non-nodular ascites or enlarged abdominopelvic lymph nodes. One subject had equivocal evidence for a pelvic metastasis with negative abdominal findings, and no subjects had positive evidence for a pelvic metastasis with equivocal evidence for an abdominal metastasis. Thus, in one case the pelvis component showed a higher level of disease than the abdomen component (1.1%; 95% CI 0.03–5.79,  $p = 0.048$ ).

The one scan that was negative for metastatic disease in the abdomen but equivocal in the pelvis was reported as “a (new) 5 cm long malignant appearing stricture of the sigmoid colon... potentially colonic neoplasm or a metastasis from pancreatic malignancy.” The subject entered palliative care without a definitive pathologic diagnosis. In consensus review, this was counted as an equivocal pancreatic cancer metastasis.

### Discussion

There are no clear national recommendations on how to utilize pelvic imaging for pancreatic adenocarcinoma. The National Comprehensive Cancer Network (NCCN) guidelines, for example, state only that imaging the chest or pelvis during follow-up of patients with PDA should reflect institutional preference [7]. Given that 148 (61.2%) out of 242 subjects in the locally advanced unresectable group and 24 (11.0%) out of 218 subjects in the post-pancreaticoduodenectomy group were excluded from the study because none of their CT scans included the pelvis, it appears many referring physicians already suspect the pelvis portion of a follow-up CT may not provide important information, despite the lack of published evidence on this topic.

Our study found that the pelvic portion of abdominopelvic CT raised suspicion of metastatic disease not already suggested by the abdomen portion in 0% of subjects after pancreaticoduodenectomy and 1.1% of subjects with locally advanced unresectable disease, and that these frequencies were statistically significantly less than 5% (p values of 0.0004 and 0.048, respectively). The one subject with equivocal evidence of pelvic metastatic disease in the absence of abdominal metastatic disease had a 5-cm-long malignant-appearing stricture in the sigmoid colon that may have been a PDA metastasis or a primary colonic neoplasm.

The most obvious potential benefit of imaging the pelvis is the identification of a solitary pelvic metastasis, as such a finding could change disease stage, prognosis, or treatment. However, we show that metastatic disease in the pelvis in the absence of abdominal metastases is rare in subjects following pancreaticoduodenectomy and in subjects with locally advanced unresectable PDA, suggesting that the pelvic component of CT imaging in these cohorts is of limited utility.

The major drawback to including the pelvis in routine CT scanning is cost. The Medicare payment of a CT abdomen & pelvis with contrast is \$314.06\* compared to \$232.13\* for a CT abdomen with contrast; this translates into \$81.93 saved per scan per subject [1,8]. The average subject with pancreatic cancer in our Cancer Registry database received 4.6 scans, translating into a potential average savings of \$376.88 per subject.

Another debatable drawback of the additional pelvic CT includes increased radiation exposure. Radiation exposure for most pancreatic cancer subjects is of doubtful significance, given that these subjects already have a malignancy with a high mortality rate; however, a small fraction of the post-pancreaticoduodenectomy subjects will be cured with surgery.

Subjects with potentially resectable but not yet resected disease also presumably have a low likelihood of solitary pelvic metastatic disease, likely in a similar range as the post-pancreaticoduodenectomy and locally advanced unresectable groups. However, the threshold value for which pelvic CT is worthwhile in this cohort is lower. Even if only 1% of pre-surgery subjects have a solitary pelvic metastasis, many referring physicians may reasonably argue that it is worth scanning 99 pelvises without benefit in order to avoid one inappropriate pancreatic resection.

Our study is limited by its retrospective design, as well as its single institution/single database subject pool. Our institution is a quaternary cancer center, which may have a subject population that differs from the community setting. A substantial number of subjects were excluded because none of their CT scans included the pelvis, an exclusion that might result in selection bias; however, if the pelvis were included in the scan range in our included study subjects because of clinical suspicion of pelvic metastatic disease, this would bias our study toward finding more pelvic disease rather than less. For the post-operative cohort, while the mean time between surgery and imaging was 9.8 months, some exams had a

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\*Values were obtained using the physician fee schedule search provided by [cms.gov](https://www.cms.gov) and reflect fees based on both technical and diagnostic fees using the "Global Service" prices based on a national payment amount for Medicare enrolled providers for procedure codes 74177 and 74160.

shorter interval between surgery and imaging, the shortest being 4 weeks, which may have decreased the likelihood of finding isolated pelvic metastatic disease in these subjects. Because only a single imaging report was reviewed for each case, lesions that were not suspicious unless determined to change over time- for example, a prominent lymph node that later grew larger- were not captured as positive. The reviewers were not blinded to the purpose of the study, which may represent a source of bias in their grading. Finally, while we recognize that there could be errors in the original radiologic interpretations themselves, we elected not to review all current images, follow up imaging reports, or histology because this would not mimic the clinical scenarios where oncologists make treatment decisions in real time.

In conclusion, isolated pelvic metastatic disease rarely occurs in patients with PDA who have had prior pancreaticoduodenectomy or have a locally advanced unresectable primary tumor. This suggests that routine pelvic CT in follow-up imaging of these patients is not necessary.

## Acknowledgments

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**Table I**

Location of abdominopelvic metastases in subjects (n=153) who have undergone prior pancreaticoduodenectomy for pancreatic adenocarcinoma.

Location	Positive	Equivocal
		1
Lung Bases	1 (0.7%)	0 (0%)
Abdomen		
Abdominal Wall	1 (0.7%)	0 (0%)
Bone	0 (0%)	2 (1.3%)
Liver	17 (11.1%)	12 (7.8%)
Lymph Nodes	9 (5.9%)	10 (6.5%)
Muscle	1 (0.7%)	0 (0%)
Peripancreatic	10 (6.5%)	5 (3.3%)
Peritoneum/Mesentery	11 (7.2%)	10 (6.5%)
Pelvis		
Lymph Nodes	1 (0.7%)	1 (0.7%)
Muscle	1 (0.7%)	0 (0%)
Bone	0	1 (0.7%)
Peritoneum/Mesentery	2 (1.3%)	9 (5.9%)

Positive and equivocal refer to the presence of metastatic pancreatic cancer in the given anatomic location based on the radiology report. Subjects may have had suspicious findings in more than one location.

All patients with positive/equivocal findings in lymph nodes, muscle, bone, and peritoneum/mesentery in the pelvis also had positive/equivocal findings in the abdomen.

**Table II**

Presence of abdominopelvic metastases in subjects (n=153) who have undergone prior pancreaticoduodenectomy for pancreatic adenocarcinoma.

	Pelvis			
Abdomen	Positive	Equivocal	Negative	Total
Positive	3 (2.0%)	2 (1.3%)	28 (18.3%)	33 (21.6%)
Equivocal	0	8 (5.9%)	22 (14.4%)	30 (19.6%)
Negative	0	0	90 (58.8%)	90 (58.8%)
Total	3 (2.0%)	10 (6.5%)	140 (91.5%)	153

Positive, negative, and equivocal refer to the presence of metastatic pancreatic cancer in the given anatomic location based on the radiology report.

**Table III**

Location of abdominopelvic metastases in subjects (n=94) with locally advanced unresectable pancreatic adenocarcinoma.

<b>Location</b>	<b>Positive</b>	<b>Equivocal</b>
Lung Bases	0 (0%)	2 (2.1%)
Abdomen		
Liver	10 (10.6%)	5 (5.3%)
Lymph Nodes	3 (3.2%)	2 (2.1%)
Muscle	0 (0%)	1 (1.1%)
Peritoneum/Mesentery	10 (10.6%)	10 (10.6%)
Pelvis		
Lymph Nodes	1 (1.1%)	0 (0%)
Peritoneum/Mesentery	6 (6.4%)	9 (9.6%)
Sigmoid Colon	0 (0%)	1 (1.1%)

Positive and equivocal refer to the presence of metastatic pancreatic cancer in the given anatomic location based on the radiology report. Subjects may have had suspicious findings in more than one location.

All patients with positive/equivocal findings in lymph nodes and peritoneum/mesentery in the pelvis also had positive/equivocal findings in the abdomen.

**Table IV**

Presence of abdominopelvic metastases in subjects (n=94) with locally advanced unresectable pancreatic adenocarcinoma.

	Pelvis			
Abdomen	Positive	Equivocal	Negative	Total
Positive	6 (6.4%)	1 (1.1%)	13 (13.8%)	20 (21.3%)
Equivocal	0	8 (8.5%)	10 (10.6%)	18 (19.1%)
Negative	0	1 (1.1%)	55 (58.5%)	56 (60.0%)
Total	6 (6.4%)	10 (10.6%)	78 (83.0%)	94

Positive, negative, and equivocal refer to presence of metastatic pancreatic cancer in the given anatomic location based on the radiology report.

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