Peer Review File

Article Information: https://dx.doi.org/10.21037/jgo-22-863

Reviewer A's comments:

Comment 1: Major 1. The authors state that the study was conducted to find the number of patients that had pancreatic cancer findings on CT scan made for other purposes than pancreatic cancer. However, this is not accurate as: 1 patient had a CT scan for a pancreatic mass incidentally found on abdominal ultrasound; 1 patient for the follow-up of acute pancreatitis; and 1 patient for incidental serum amylase and lipase elevation. Furthermore, 16 patients were scanned because of symptoms that could be attributed to pancreatic cancer (7 patients with jaundice, 9 patients with abdominal pain). All of these patients underwent a diagnostic CT scan, where pancreatic cancer should be ruled out by this scan. Therefore only 8 patients had no clinical suspicion for pancreatic cancer. This is the true number of patients that underwent a CT scan prediagnosis for other purposes. The authors should make this appropriate changes in the article to make it more relevant for the clinical practice.

Response: We would like to thank the reviewer for evaluating our manuscript and for their insightful comments. At the time of prediagnostic CT examination, all of the subjects in this study had undergone CT for a purpose other than pancreatic cancer diagnosis, and there was no report of findings suspicious of pancreatic cancer. All cases where CT was performed to diagnose pancreatic cancer with suspected symptoms of pancreatic cancer were excluded. The reasons for prediagnostic CT were already described on page 7, lines 11–15 and in Table 1. In summary, the reasons are presented below:

Reasons for undergoing prediagnostic CT

Regular follow-up of previously diagnosed other cancers	11
Acute pancreatitis	3
Regular follow-up of chronic pancreatitis	3

Fever	2
Abdominal pain	2
Regular follow-up of liver cirrhosis	1
Lower back pain	1
Liver abscess	1
Common bile duct stone with cholangitis	1
Abdominal trauma	1

All of the cases that the reviewer pointed out explain why CT was performed when pancreatic cancer was diagnosed. Eleven patients were asymptomatic and sixteen patients had symptoms due to pancreatic cancer. The reasons why CT was performed at the time of diagnosis of pancreatic cancer are detailed in the following table.

Reasons for undergoing CT at the time of pancreatic cancer diagnosis

Asymptomatic	
Regular follow-up of previously diagnosed other cancers	6
A pancreatic mass incidentally found on abdominal ultrasound	1
Follow-up of acute pancreatitis	1
Ischemic colitis	1
Upper gastrointestinal bleeding	1
Incidental serum amylase/lipase elevation	1
Symptomatic	
Jaundice	7
Abdominal pain	9

Therefore, all subjects in this study were patients who had no clinical symptoms or CT findings to suspect pancreatic cancer when prediagnostic CT examination was performed.

Comment 2: Minor 1. Patients with pancreatic cancer were selected and prediagnostic CT scan were evaluated. How was this process done? Are all patients with pancreatic cancer in this center included or only that had pancreatic cancer on CT scan?

Response: We would like to thank the reviewer for the insightful comment. Between 2008 and 2019, 736 patients were diagnosed with pancreatic cancer and hospitalized at our hospital. We reviewed all their CT scans and selected patients who had undergone CT within 1 year of a

pancreatic cancer diagnosis. In general, many patients are referred to our hospital after being diagnosed with pancreatic cancer or if suspicious findings are noted at other hospitals. Therefore, there were few patients who underwent CT at our hospital within 1 year of a pancreatic cancer diagnosis. A total of 27 patients were included in this study, excluding patients who were suspected of pancreatic cancer in prediagnostic CT and diagnosed with pancreatic cancer in follow-up.

To avoid misunderstanding, we have revised the corresponding part in the main text as follows: "Between January 2008 and December 2019, patients who were diagnosed with pancreatic cancer and hospitalized at the National Health Insurance Service Ilsan Hospital (Goyang, Korea) were selected. We reviewed all the CT scans of the selected patients. Among them, those who underwent contrast-enhanced abdominal CT or chest CT, including the images of the pancreas within 1 year of a pancreatic cancer diagnosis, were enrolled in this study." (page 4, lines 19–23)

Comment 3: Minor 2. In light of the above-mentioned point: could the authors offer how many patients were included with pancreatic cancer. This information will offer more insight on how many patients were missed on the prediagnostic CT scan.

Response: We would like to thank the reviewer for the insightful comment. Initially, 736 patients were selected. Some revisions have been made to clarify this part. In our hospital, many patients were incidentally diagnosed with pancreatic cancer on CT performed for purposes other than pancreatic cancer diagnosis. In this retrospective study, it was not possible to evaluate how many patients were incidentally diagnosed with pancreatic cancer, and how many cases of pancreatic cancer were missed on CT performed for other purposes. This has been described in detail in the limitation part of the Discussion section. (page 14, lines 14–19)

Please note that we have made the following changes in the Results section:
"Between January 2008 and December 2019, 736 patients were diagnosed with pancreatic cancer at the National Health Insurance Service Ilsan Hospital and hospitalized. Among them, 27 patients who underwent prediagnostic CT within 1 year of a pancreatic cancer diagnosis and had no reports of suspected pancreatic cancer lesion on CT were finally enrolled in this study." (page 7, lines 1–4)

Comment 4: Minor 3. Two independent radiologists reviewed the CT scans with the knowledge of all patients had eventually pancreatic cancer. All disagreements between the two radiologists were resolved by discussion. Could the authors offer numbers on how many cases the radiologists did not reach an agreement on the first time. If this data is available the authors could show the interobserver variability. This would help to understand the clinical value of this study.

Response: We would like to thank the reviewer for these comments. We performed an additional analysis of the interobserver variability between two radiologists. We quantified interobserver agreement with Cohen's kappa. Undoubtedly, Cohen's kappa is the most popular method to assess agreement between two raters. We have provided this information in the revised manuscript as follows:

"The agreements between two radiologists for findings of pancreatic parenchyma and pancreatic duct were calculated using Cohen's kappa." (page 6, lines 15–17)
"Interobserver agreements between two radiologists for pancreatic parenchyma and pancreatic duct findings were good (Cohen's kappa=0.74, $P<0.001$) and strong (Cohen's kappa=0.88, $P<0.001$), respectively." (page 7 and 8, line 24 and lines 1–2, respectively)

Comment 5: Minor 4. The patient's clinical features are made for symptomatic and asymptomatic. One could argue that acute pancreatitis is symptomatic patient, as sometimes pancreatitis is the first symptom for pancreatic cancer.

Response: We would like to thank the reviewer for the constructive comments. Eleven patients were asymptomatic at the time of diagnosis of pancreatic cancer, and one of them underwent CT examination as a follow-up examination for acute pancreatitis. This patient had abdominal pain due to acute pancreatitis 2 months earlier, but at the time of follow-up CT examination, he had no symptoms associated with acute pancreatitis or pancreatic cancer. Therefore, we classified this patient as asymptomatic for pancreatic cancer at the time of pancreatic cancer diagnosis.

Reviewer B's comments:

Comment 6: Major 1. Continuous variables were presented as the mean ± the standard deviation. However, all values must be expressed as medians (range) of the small number of cases and the no-Gaussian distribution. The principle is that the mean should be used only when the set is the Gauss distribution.

Response: We would like to thank the reviewer for evaluating our manuscript and for their insightful comments. We agree with the reviewer's comment. According to reviewer's recommendation, we have expressed the values as median values and modified the text accordingly. The revised parts are presented below.

Changes in the text:

(1) "a median size of 1.2 cm" (page 2, line 14)

(2) "Continuous variables are presented as median values" (page 6, line 13)

(3) "The median age of the patients was 73.6 (range, 47–87) years, and the group included nineteen men and eight women. The median time interval between the prediagnostic CT and pancreatic cancer diagnosis was 6.6 (range, 1.9–12.0) months." (page 7, lines 5–7)

(4) "The median size of the retrospectively detected mass-like lesion was 1.2 (range, 0.8–1.9) cm." (page 8, lines 12–13)

(5) "The median size of pancreatic cancer was 3.0 (range, 1.2–8.7) cm (Table 4)." (page 9, line 7)

(6) "During the follow-up period, 24 patients died, and their median survival was 10.6 (range, 1.2–61.5) months." (page 9, lines 16–17)

(7) "In this study, nine mass-like lesions had a median size of 1.2 cm, and all showed hypoattenuation with contrast enhancement." (page 11, lines 18–19)

(8) "Age (median) (years)" in Table 1.

(9) "Size of pancreas cancer (median) (cm)" in Table 4.

Comment 7: Major 2. In the discussion section, authors mentioned about focal pancreatic

atrophy (page 12, line13). You need to add a statement that localized pancreatic atrophy can occur in non-cancerous patients and should be noted. References should also be added(Kurita et al. Abdom Radiol 2021;46:4817-4827).

Response: We would like to thank the reviewer for the constructive comment. We agree with the reviewer's comment. In accordance with the reviewer's suggestion, we have stated that distal parenchymal atrophy can be found in benign conditions and cited two new references (References #35,36). And we added the reference of Kurita et al's paper in discussion (Reference #33). The revised parts are as follows:

"However, distal parenchymal atrophy can be observed sometimes even in benign conditions. Distal parenchymal atrophy was present in 4% of controls without pancreatic diseases (11,35) and in 7.1–15.8% of patients with benign main pancreatic duct stricture (32,34,36)." (page 12, lines 20–23)

"In three case series studies of localized main pancreatic duct structure without a detectable mass, 47%–54% of cases were actually diagnosed with pancreatic cancer (31,32,33)." (page 12, lines 10–11)