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Patients 65 years and older with incidental pancreatic cysts: Is there a relationship between all-cause mortality and imaging follow-up?

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ABSTRACT

Purpose: To assess the relationship between imaging follow-up and all-cause mortality in subjects ≥65 years with and without incidental pancreatic cysts (IPC).
Methods and materials: Patients ≥65 years with abdominal CT/MR 11/1/01-11/1/11 were included. IPC group included subjects with IPC on CT/MR report; No-IPC group was 3:1 frequency-matched on age decade, imaging modality and year of initial study from the pool without reported IPC. Demographics, date of last encounter, date of death, Charlson scores within 3 months before initial CT/MR and number of abdominal CTs and MRs performed after initial study were recorded. Logistic regression models with binary outcomes of death and having post-index imaging were constructed. Models were adjusted for age, race, sex, Charlson score and follow-up time. Subgroups were created based on interactions between variables.
Results: There were 1320 subjects in IPC group and 3805 in No-IPC group, with mean ages 79.1 (±8.0) and 78.8 (±8.0) years, respectively ($p = 0.293$), and median follow-up times of 3.1 (IQR 0.74–5.26) and 3.0 (0.36–5.23) years, respectively ($p = 0.009$). Adjusted odds ratios of post-index imaging for IPC were 2.18 ($p < 0.001$) in subgroup <84 years and follow-up <4years, 3.37 ($p < 0.001$) in subgroup <84 years and follow-up ≥4 years, and 1.20 ($p = 0.201$) in subgroup ≥84 years. Number of follow-up CTs and MRs was not independently associated with decreased odds of death in any subgroup.
Conclusion: Older subjects with IPC are more likely to undergo imaging follow-up compared to subjects without IPC, yet increasing number of follow-up studies does not decrease the odds of death.

1. Introduction

In recent years, increased utilization and technical improvements in cross-sectional imaging has resulted in increased detection of incidental pancreatic cysts. In particular, a trend towards discovery of smaller cysts and those without overtly worrisome imaging features for malignancy has been reported [1]. Appropriate management of these small incidental pancreatic cysts remains controversial, largely due to the fact that a small but significant number of cystic pancreatic lesions have malignant potential [2,3]. It has also been shown that patients with pancreatic cysts are at an increased risk for developing pancreatic adenocarcinoma throughout the pancreas, not just at the site of existing cysts [4–6]. When appropriate selection criteria are applied, the majority of incidentally discovered pancreatic cysts can usually be followed conservatively, particularly when small [7,8]. The American College of Radiology (ACR) Incidental Findings committee has most recently recommended at least one follow-up imaging study for cysts smaller than 2 cm, and serial follow-up imaging for cysts 2–3 cm in asymptomatic patients [9]. In practice, however, it is not uncommon to see serial follow-up imaging recommended, even for the smallest cysts. This has implications for patient anxiety as well as personal and national health care costs.

Recently, a large cohort study explored the relationship of incidental pancreatic cysts (IPC) found on imaging and all-cause mortality, and found that this relationship varied by age [6]. Patients younger than 65 years with IPC had an increased mortality risk with a hazard ratio of 1.40 compared with patients without IPC, when adjusted for sex, race, and comorbidities [6]. However, patients 65 years or older with IPC were found to have no increased mortality risk compared with patients without IPC when adjusted for the same factors [6]. Since many patients with pancreatic cysts undergo imaging surveillance, regardless of age, the question of whether intensive follow-up imaging contributed to the lack of increased risk of mortality in patients ≥65 years with IPC can be raised. In other words, does surveillance imaging for pancreatic

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cysts lead to early detection and treatment of potentially life-threatening conditions in this older population, therefore negating the increased risk of mortality that is seen in younger patients with pancreatic cysts?

The goals of this study were therefore to compare imaging patterns in patients 65 years and older with and without incidental pancreatic cysts, and to assess the relationship between imaging follow up and all-cause mortality in patients 65 years and older with incidental pancreatic cysts.

2. Materials and methods

This study was approved by the institutional review board, and informed consent was waived. The study was compliant with Health Insurance Portability and Accountability Act regulations.

2.1. Patient selection

This retrospective case-control study included a sub-population of patients from the larger cohort, the selection of which has been previously described in detail [6]. Briefly, an institutional decision support tool (DST) (Clinical Looking Glass; Streamline Health, Atlanta, Ga) was used to identify abdominal CT and MR imaging reports from November 1, 2001 to November 1, 2011 which did (cohort with IPC) or did not (cohort without IPC) contain the words "pancr*" and "cyst" in the same sentence. For the cohort with IPC, reports were manually reviewed and patients with evidence or history of pancreatitis, autosomal dominant polycystic kidney disease, von Hippel-Lindau syndrome, reports not describing a definite cyst arising from the pancreas, and those with a clinical indication of pancreatic lesion or use of pancreatic protocol were excluded. The cohort of patients without IPC was frequency-matched on modality (CT vs. MR imaging), age decade, and year of initial study date, with a ratio of 3:1.

The original study included 8052 patients, with analysis of the relationship between incidental pancreatic cysts, the development of pancreatic adenocarcinoma, and all-cause mortality [6]. The current study included all patients from the original cohort ≥65 years; patients with IPC were considered cases, and patients without IPC were considered controls. While this study included a subset of the original cohort, the analyzed data were different. First, the aim of this study was to explore whether the lack of increased mortality in patients over 65 years with IPC compared to those without IPC seen in the original study [6] could be explained by differences in the number of imaging studies obtained after the index CT or MRI. Additionally, since the data analysis for this study was performed approximately 18 months after completion of the original study, the clinical data were all updated to reflect the most recent available information.

2.2. Clinical data

Demographic data, location of index imaging study (outpatient, inpatient, or Emergency Department), and number and type of cross-sectional abdominal imaging studies (CT or MR) performed for each patient in the period from the initial study through the date of latest encounter were extracted from DST. The date of the latest encounter was defined as the date of the most recent laboratory test, imaging study, or patient encounter (outpatient, inpatient, or Emergency Department). Date of death was also extracted when applicable; this included deaths based on Social Security data through 11/1/11, and hospital system deaths after 11/1/11. The modified Charlson comorbidity index was calculated by DST for each patient using data from the outpatient, inpatient, and Emergency Department encounters over the period from the index study until the date of the latest encounter. The Charlson comorbidity index is a validated tool for comorbidity adjustment and mortality prognosis [10–12].

2.3. Statistical analysis

STATA version 13.1 (StataCorp, LP, College Station TX) was used. Statistical significance was considered at p value <0.05.

Bivariate associations of the continuous variables were compared using Student's *t*-test or Wilcoxon rank-sum test, as appropriate. Bivariate associations of the categorical variables were compared using chi square test or Fisher's exact test, as appropriate.

For the purposes of statistical analysis, the follow-up interval was defined as the time interval between date of index study and date of latest encounter, and post-index imaging was defined as having at least one study (abdominal CT or MR) during the follow-up interval. Multivariate logistic regression models with binary outcomes of post-index imaging and death were constructed using manual backward stepwise selection approach. Variables with p values of <0.1 on bivariate associations were entered into the model. The exit criteria were defined as p value of a covariate's coefficient greater than 0.05 and change in coefficient of variable of interest (case/control status) of less than 10%. Age, sex and race were to be included in the final model a priori. Interactions with variable of interest (case/control status) were explored in all models. Interaction had a standard definition of a relationship between the outcome and the predictor variables being dependent on a value of a third variable. The models were stratified when interaction term had p value less than 0.10, and the stratification point was chosen so that the interaction within each strata would be eliminated.

3. Results

From the initially identified study population, there were 5125 patients ≥65 years who were included in this analysis. Of these 5125 patients, 1320 (25.8%) had IPC (cases) and 3804 (74.2%) had no IPC (controls). Of 1320 patients with IPC, cysts were solitary in 972 (73.6%) and multiple in 348 (26.4%). For 1178 cases with documented cyst size, the mean cyst diameter was 14.3 ± 13.1 mm, and was less than 3 cm in 1122 (95.2%) cases.

Table 1 summarizes demographic characteristics of cases and controls. There was no significant difference in mean age or mortality between the cases and controls. Compared with controls, cases had more women (66.9% vs. 60.7%, respectively; $p < 0.001$), more white patients (39.8% vs. 31.3%, respectively; $p < 0.001$), and patients with higher mean modified Charlson comorbidity indices (9.1 ± 4.3 vs. 7.8 ± 4, respectively; $p < 0.001$). Compared with controls, more cases had their index imaging performed in the outpatient setting (50.2% vs. 39.2%, respectively; $p < 0.001$). The median follow up intervals were 3.1 (IQR 0.74–5.26) and 3.0 (IQR 0.36–5.23) years for cases and controls, respectively ($p = 0.009$).

62.0% of patients with IPC (cases) underwent at least one post-index imaging study as compared to 42.5% patients without IPC (controls) ($p < 0.001$). In those with post-index imaging, the mean numbers of post-index CT scans were 2.7 (±2.3) in cases and 2.2 (±2.1) in controls ($p < 0.001$), and the mean numbers of post-index MR scans were 2.5 (±2.6) in cases and 1.8 (±1.9) in controls ($p < 0.001$).

Of 5125 total patients included in this analysis, 2434 (47.5%) had post-index imaging, and 2691 (52.5%) did not. Table 2 summarizes the demographic characteristics of patients with and without post-index imaging. Patients with post-index imaging were younger than those without (mean age 77.7 ±7.4 years vs. 80.0 ± 8.5 years, $p < 0.001$), and more likely to have been initially scanned in the outpatient setting (49.1% vs. 35.6%, $p < 0.001$). Patients with IPC (cases)