



## Pre-diagnostic delays caused by gastrointestinal investigations do not affect outcomes in pancreatic cancer



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### ABSTRACT

**Background:** Pancreatic ductal adenocarcinomas are poor prognostic cancers accounting for 3% of all cancer cases in the UK. They often present late in the course of the disease process with non-specific symptoms, including gastro-intestinal (GI) symptoms. Delays in diagnosis occur when investigations are carried out in a primary care setting for GI symptoms. The aim of this study was to assess delays in pancreatic cancer diagnosis when patients were referred for GI investigations and evaluate its effect on survival.

**Methods:** Retrospective cohort study of all patients diagnosed with pancreatic adenocarcinoma in a Scottish district general hospital over a seven year period from January 2010 to December 2016. Patients were divided into two groups, those who had a GI investigation 18 months prior to the pancreatic cancer diagnosis and those who did not have GI investigations. Data on demographics, symptoms on referral, stage of disease at diagnosis, treatment undergone and length of survival collected and analysed.

**Results:** One hundred and fifty-three patients were diagnosed with pancreatic cancer in the study period. Forty (26%) of the 153 underwent gastrointestinal investigations in the 18 months prior to diagnosis. The remaining 113 (74%) had no gastro-intestinal investigations in the same time period. Demographic data were comparable. Significant delays occurred from referral to diagnosis in the GI investigated group compared to those who did not have GI investigations. (64.5 days vs 9 days,  $p = 0.001$ ). No difference was noted in disease stage or treatments undergone between the groups. There was no difference in the average survival after diagnosis between the two groups with median of 108 days for those who underwent GI investigations to 97 days for those who did not. ( $U = 2079.5$ ,  $p = 0.454$ ).

**Conclusion:** Delays caused by pre-diagnostic GI investigations do not appear to contribute to the poor prognosis of pancreatic cancer. Recently updated NICE Guidelines recommends early ultrasound or CT in patients with GI symptoms and weight loss which may reduce delays in diagnosis. Screening tests in future may become cost effective and diagnose this condition at a curable stage which in turn may improve survival rates.

## 1. Introduction

Pancreatic ductal adenocarcinoma (PDAC) accounts for 3% of all cancer cases in the UK with 9618 new cases recorded in 2014. This condition has a poor prognosis with less than 4% of patients surviving 5 years following diagnosis and treatment [1]. At the time of diagnosis, almost 80% of patients have stage III or IV disease [2,3]. Median survival is stage dependent; metastatic disease has a median survival of 2–6 months, locally advanced disease 6 to 11 months and resectable disease 11 to 20 months [1,4]. Gastrointestinal (GI) symptoms are frequent in pancreatic cancer [5,6] and patients are often referred for

endoscopic investigations that may delay diagnosis.

## 2. Aims

The aim of this study was to assess delays in pancreatic cancer diagnosis when patients were referred for GI investigations from primary care, either by open access or through gastroenterology clinics and evaluate its impact on survival outcomes.

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### 3. Patients and methods

This retrospective cohort study was conducted in a Scottish District General Hospital (Dumfries and Galloway Royal Infirmary) and approved by the local Quality Improvement department. All patients diagnosed with pancreatic cancer between January 2010 and December 2016 were identified from a prospective cancer database maintained by the local Cancer Audit team. Demographic details, dates of referral and diagnosis, site of tumour, stage at diagnosis and treatment details were collected. Data on principal symptoms triggering referral, GI investigations (endoscopy, colonoscopy or CT Colonogram) in the 18 months prior to diagnosis, treatment details and date of death were obtained by cross referencing each patient's unique Community Health Index (CHI) number with electronic patient records (SCI Store, Information Services Division, NHS Scotland) and our department's gastro-intestinal endoscopy reporting software database (GI Reporting Tool, Unisoft Medical Systems, UK). Patients were allocated to two groups - those who underwent GI investigations in the 18 months prior to their pancreatic cancer diagnosis and those who had no GI investigations in the same period.

Data were anonymised and statistical analysis was performed using IBM SPSS v24.0. Testing between groups was performed using the chi-square test for categorical variables and, either the two independent sample *t*-test or Mann-Whitney *U* test for other measurements, depending on checks for normal distributions. STROCSS (Strengthening the Reporting of Cohort Studies in Surgery) guidelines were followed in the reporting of this study [7].

### 4. Results

One hundred and fifty-three patients were diagnosed with pancreatic cancer between January 2010 and December 2016. Forty (26%) of the 153 underwent gastro-intestinal investigation with endoscopy, colonoscopy, endoscopy and colonoscopy or CT colonography in the 18 months prior to diagnosis. The remaining 113 (74%) had no gastro-intestinal investigations performed in the same period.

Dyspepsia, abdominal pain, weight loss, bloating, diarrhoea or constipation and unexplained iron deficiency anaemia were the main triggers for referral for GI investigation. One patient had an upper GI endoscopy for Barrett's surveillance and was asymptomatic. Three symptomatic patients had colorectal cancer on colonoscopy; the pancreatic lesion being identified on staging CT scans. Two patients had pancreatic cancers invading the stomach and duodenum allowing tissue biopsy at the time of endoscopy. A pancreatic lesion was not identifiable in one of three patients who underwent a CT colonogram but became apparent in a subsequent CT scan 8 months later. Patients undergoing surgery or chemotherapy had biopsy or cytology proven pancreatic ductal adenocarcinoma.

There were no significant difference in the average age between the group that underwent GI investigations and the group that did not have GI investigations, 72 (range 43–84) vs 72 (range 39–94) respectively [*t* = 0.811, *p* = 0.419; 95% CI -5.49, 2.29] or gender profiles, M:F % = 57.5:42.5 vs 50.4:49.6 respectively [ $\chi^2$  = 0.341, *p* = 0.559] (Table 1).

Patients who underwent GI investigations had a significantly higher

**Table 1**  
Demographics.

	GENDER		AGE	
	Male 80 (52.3%)	Female 73 (47.7%)	Mean	Median (Range)
GI Investigation n = 40	23 (57.5%)	17 (42.5%)	70	72 (43–84)
No GI investigation n = 113	57 (50.4%)	56 (49.6%)	72	72 (39–94)

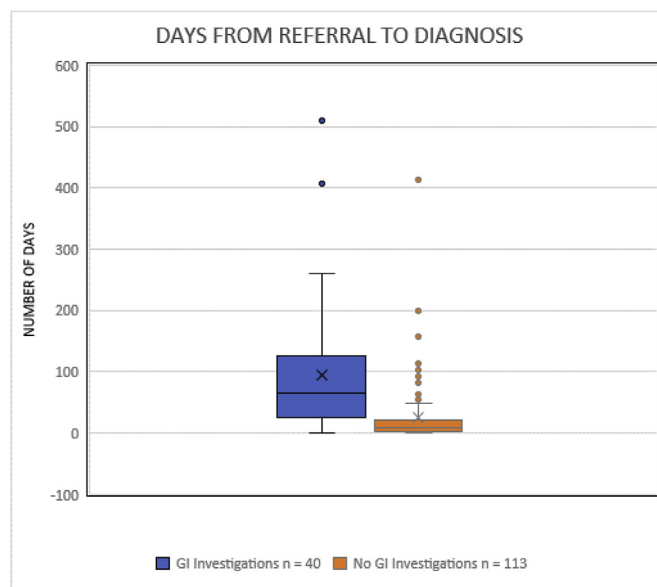
**Table 2**  
Presenting symptoms of both groups.

Symptoms	GI Investigation group n = 40	No GI investigation group n = 113	
GI Symptoms	24 (60%)	27 (23.9%)	$\chi^2 = 15.74$ <i>P</i> < 0.001
Abdominal pain	29 (72.5%)	58 (51.3%)	$\chi^2 = 4.57$ <i>P</i> = 0.033
Weight loss	31 (77.5%)	48 (42.5%)	$\chi^2 = 13.14$ <i>P</i> < 0.001
Jaundice	5 (12.5%)	54 (47.8%)	$\chi^2 = 14.07$ <i>P</i> < 0.001
New onset diabetes	3 (7.5%)	10 (6.5%)	$\chi^2 = 0.0$ <i>P</i> = 1.0
Other symptoms	16 (40%)	31 (27.4%)	$\chi^2 = 1.64$ <i>P</i> = 0.200

occurrence of GI symptoms such as nausea, early satiety, bloating, altered bowel habits, constipation or diarrhoea. Abdominal pain and weight loss were reported more frequently in this group [72.5% v 51.3% and 77.5% v 42.5% respectively]. Presentation with obstructive jaundice was more common in the group that did not undergo GI investigations [12.5% v 47.8%]. There was no difference in other symptoms such as shortness of breath, cough, tiredness and new onset diabetes (Table 2).

We found significant delays from referral to diagnosis in the group that underwent GI investigations with a median delay of 64.5 days (range 1–509) compared to 9 days (range 0–414) for the group not undergoing GI investigation, (*U* = 768.5, *p* < 0.001) (Fig. 1).

Head of pancreas tumours were more frequent in patients who did not have GI investigations (65.5% vs 32.5%), body of pancreas tumours were more frequent in the group that underwent GI investigations (42.5% vs 17.7%) and tail of pancreas was involved more frequently in the GI investigation group also (25% vs 16.8%) (Fig. 2). There was no significant association between the groups and the stages of disease. Similarly, there was no significant difference between the groups in treatments undergone. [ $\chi^2$  = 5.834, *p* = 0.212] (Table 3). Of the 19 patients with potentially operable lesions, only 3 were from the group that had GI investigations. Seven of these nineteen patients (36%) went on to have a Whipple's resection (4/19) or distal pancreatectomy with splenectomy (3/19) and adjuvant chemo therapy. Only one patient of the three potentially operable patients from the GI investigations group



**Fig. 1.** Days from referral to diagnosis.

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