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Association between family cancer history and risk of pancreatic cancer

Annaka Schulte, MBBS[a,b,*], Nirmala Pandeya, PhD[a,c], Jonathan Fawcett, PhD[a], Lin Fritschi, MBBS, PhD[d], Kerenaftali Klein, PhD[a], Harvey A. Risch, MD, PhD[e], Penelope M. Webb, PhD[a], David C. Whiteman, MBBS, PhD[a], Rachel E. Neale, PhD[a,c]

[a] Department of Population Health, QIMR Berghofer Medical Research Institute, 300 Herston Road, Herston, Queensland 4006, Australia
[b] School of Medicine, University of Queensland, 288 Herston Road, Herston, Queensland 4006, Australia
[c] School of Population Health, Level 2, Population Health Building, 887 Mayne Road, University of Queensland, Herston, Queensland 4006, Australia
[d] School of Public Health, Curtin University, Kent Street, Bentley, Perth, Western Australia 6102, Australia
[e] Yale School of Public Health, 60 College St, New Haven, CT 06510, United States

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ABSTRACT

Purpose: Family history of pancreatic adenocarcinoma is an established risk factor for the disease. However, associations of pancreatic cancer with other familial cancers are less clear. We analyzed data from the Queensland Pancreatic Cancer Study (QPCS), an Australian population-based case-control study, to investigate associations between family history of various cancer types and risk of pancreatic cancer.
Materials and methods: Our study included 591 pancreatic cancer patients and 646 controls, all of whom self-reported the histories of cancer in their first-degree relatives. We used logistic regression to estimate adjusted odds ratios (ORs) and their 95% confidence intervals (CIs). Based on our results, we conducted a systematic literature review using the Medline (OVID) database to identify articles pertaining to the association between family history of melanoma and risk of pancreatic cancer. A meta-analysis including associations in five published studies, unpublished results from a study co-author and the QPCS results was then performed using the DerSimonian and Laird random-effects model.
Results: Cases were more likely than controls to report a family history of pancreatic cancer (OR 2.20, 95% CI 1.16–4.19) and melanoma (OR 1.74, 95% CI 1.03–2.95), but not of breast, ovarian, respiratory, other gastrointestinal or prostate cancer. Meta-analysis of melanoma family history and pancreatic cancer risk yielded an OR of 1.22 (95% CI 1.00–1.51).
Conclusions: Our results yield further evidence of increased risk of pancreatic cancer in those with family histories of the disease. We also provide suggestive evidence of an association between family history of melanoma and risk of pancreatic cancer.

1. Introduction

Pancreatic cancer has among the highest mortality-to-incidence ratio of any cancer, and is responsible for approximately four percent of cancer deaths worldwide [1]. Surgical resection is currently the only beneficial treatment modality but is relatively infrequent because the disease is usually too advanced at the time of diagnosis. A number of risk factors for pancreatic cancer have been identified, including older age, tobacco smoking, personal history of chronic pancreatitis, long-term diabetes mellitus, non-O ABO blood group, obesity, and family history of pancreatic cancer [2–5]. However, evidence for a number of these associations has been inconsistent.

Familial pancreatic cancer (FPC),[1] described as a kindred wherein at least two first-degree relatives have been diagnosed with pancreatic cancer, is thought to account for approximately 5–10% of cases [6,7]. Of these, less than 20% are due to carriage of known genetic conditions that predispose to pancreatic cancer [8], including hereditary pancreatitis, hereditary nonpolyposis colorectal cancer (HNPCC or Lynch syndrome), hereditary breast and ovarian cancer (*BRCA1* and *BRCA2* mutations), familial atypical

* Corresponding author at: QIMR Berghofer Medical Research Institute, Locked Bag 2000 Royal Brisbane Hospital, QLD, Australia.
E-mail address: Annaka.Schulte@qimrberghofer.edu.au (A. Schulte).

[1] Abbreviations in order they appear in text: QPCS – Queensland Pancreatic Cancer Study; OR – odds ratio; CI – confidence interval; FPC – familial pancreatic cancer; HNPCC – hereditary nonpolyposis colorectal cancer; FAMMM – familial atypical multiple mole melanoma; QCR – Queensland Cancer Registry; BMI – body mass index; AOR – adjusted odds ratio.

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multiple mole melanoma (FAMMM) syndrome, Peutz-Jeghers syndrome, and ataxia-telangiectasia [6].

Identifying familial cancer patterns may reveal genetic abnormalities that contribute to cancer development. To date, pancreatic cancer has been reported to be associated with family history of cancers of the pancreas, breast, prostate, colon, stomach, liver, kidney, lung, and ovary. However, population-level evidence is scant and results have been inconsistent [9–12]. We therefore analyzed data from the Queensland Pancreatic Cancer Study (QPCS) to determine whether or not a family history of various cancer types is associated with risk of pancreatic cancer.

2. Materials and methods

2.1. Study population

The QPCS is a population-based case-control study [13,14]. Eligible patients were Queensland (Australia) residents of age at least 18 years diagnosed with histologically or clinically confirmed pancreatic adenocarcinoma between 1 January 2007 and 31 June 2011. Potentially eligible patients were identified and recruited through a state-wide network of clinicians. We also routinely reviewed notifications to the population-based Queensland Cancer Registry (QCR), and patients who had not been identified through our clinical network were contacted through the QCR and invited to participate. We recruited 705 cases, approximately 37% of all those notified to the QCR during the study period. Reasons for nonparticipation were: patient died before we were able to invite their participation – 35%; patient's doctor refused permission to contact the patient – 8%; patient refused – 11%; patient was unable to be contacted – 8%; cognitive impairment – 1%.

Potential controls were randomly selected from the Australian Electoral Roll (voting is compulsory for Australians of age 18 years and above) and frequency-matched to cases by state (Queensland), sex and age (5-year groups). We approached 1543 potential controls. Of these, 6% were ineligible (unable to give informed consent in English or dead), 39% declined, 8% had no contact information and 1% failed to complete the study interview satisfactorily. Of eligible controls, 711 (49%) completed interviews. The study was approved by the Human Research Ethics Committees of the QIMR Berghofer Medical Research Institute and participating hospitals in Queensland and each participant provided written informed consent.

2.2. Data collection

Participants completed face-to-face (84% of cases; 29% of controls) or telephone interviews, during which we asked about socio-demographic and lifestyle factors, medical and occupational history and family history of cancer in parents and siblings. Cases were also asked for consent to review medical records.

Participants were asked about height and weight at a reference date of one year before diagnosis (cases) or one year before interview (controls) and these data were used to calculate body mass index (BMI, kg/m^2). Participants who had smoked more than 100 cigarettes, cigars, or pipes were asked detailed questions about their smoking histories, and were then classified as never smokers, ex-smokers, or current smokers based on smoking status at one year prior to reference date. We also calculated lifetime pack-years of smoking. We asked about the number of alcoholic drinks consumed during each decade of life and calculated average weekly alcohol consumption as the total number of standard drinks over the lifetime divided by the number of weeks in adulthood (age 20 to age at reference date). We asked about history of diabetes and age at diagnosis. Attained education level was elicited by asking participants at what age they had left school, and about post-school study and qualifications. All participants were asked about their countries of birth. Subject-reported ancestries of grandparents were used to classify participants as Caucasian or non-Caucasian.

2.3. Family cancer history

We asked participants detailed questions about cancer history in parents, full and half siblings, and children. Questions included the current age of relatives or age at death, whether the relative had ever had cancer, and if so, their age at cancer diagnosis and type of cancer. A positive family cancer history was defined as one or more first-degree relatives diagnosed with the relevant cancer type. We did not otherwise validate self-reported family cancer history.

2.4. Statistical techniques

Unconditional logistic regression methods were used to estimate odds ratios (ORs) and 95% confidence intervals (CIs). All analyses were adjusted for age, sex, education, and smoking status. No other variables were included in the final models as none, including BMI, alcohol intake, and history of pancreatitis,

Table 1
Characteristics of controls and pancreatic adenocarcinoma cases included in QPCS analysis.

	N (%)	
Characteristic	Controls (646)	Cases (591)
Sex		
Male	384 (59.4)	352 (59.6)
Female	262 (40.6)	239 (40.4)
Age at interview (years)		
<55	91 (14.1)	85 (14.4)
55–<65	182 (28.2)	171 (28.9)
65–<75	199 (30.8)	178 (30.1)
≥75	174 (26.9)	157 (26.6)
Smoking status		
Never smoker	321 (49.8)	222 (37.6)
Ex-smoker	266 (41.2)	232 (39.3)
Current smoker	58 (9.0)	136 (23.1)
Missing	1	1
Education		
No education past high school	271 (42.3)	272 (46.6)
Technical training or qualification	260 (40.6)	243 (41.6)
University degree	110 (17.2)	69 (11.8)
Missing	5	7
Body mass index 1-year prior to diagnosis (kg/m^2)		
<25	232 (36.4)	181 (32.4)
25–<30	249 (39.1)	221 (39.6)
≥30	156 (24.5)	156 (28.0)
Missing	9	33
Alcohol consumption (drinks/week) in adulthood		
Non-drinker	142 (22.1)	126 (21.8)
<1	47 (7.3)	29 (5.0)
1–<7	215 (33.5)	138 (23.9)
7–<21	135 (21.0)	134 (23.2)
≥21	103 (16.0)	150 (26)
History of Diabetes mellitus		
Yes	82 (12.7)	109 (18.5)
No	564 (87.3)	481 (81.5)
Missing	–	1
History of Pancreatitis		
Yes	8 (1.2)	19 (3.3)
No	637 (98.8)	558 (96.7)
Missing	1	14