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Cigarette smoking and pancreatic cancer risk: More to the story than just pack-years

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KEYWORDS
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Abstract ***Purpose:*** Cigarette smoking is an established risk factor for pancreatic adenocarcinoma. However, few studies have thoroughly investigated the effects of independent smoking dimensions (duration, intensity, cumulative dose and time since quitting) on risk estimates. We analysed data from the Queensland Pancreatic Cancer Study (QPCS), an Australian population-based case-control study, with the aim of determining which smoking component is primarily important to pancreatic cancer risk.
Methods: Our study included 705 pancreatic cancer patients and 711 controls. Logistic regression and generalised additive logistic regression (for non-linear dose effects) were used to determine odds ratios (ORs) and 95% confidence intervals (CIs).
Results: Compared to never-smokers, current smokers had an increased risk of pancreatic cancer (OR = 3.4; 95% CI 2.4–5.0) after adjustment for age, sex, education, alcohol intake and birth country. Of the various smoking dimensions, smoking duration and time since quitting had a greater effect on OR estimates (OR 1.3; 95% CI 1.1–1.4 and OR 0.8; 95% CI 0.7–0.8) than smoking intensity (OR 1.1; 95% CI 0.9–1.2), once ever-smoking was accounted for.
Conclusions: This study confirms the association between cigarette smoking and pancreatic adenocarcinoma, and provides evidence to suggest that smoking pattern, in addition to dose effect, may affect disease risk.

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1. Introduction

Pancreatic cancer is the fourth leading cause of cancer mortality in more-developed countries [1]. Five-year survival rates are less than 5%, giving pancreatic cancer the highest mortality to incidence ratio of any cancer [2]. Currently, 30–40% of cases are attributable to known risk factors, which include tobacco smoking, increasing age, family history of pancreatic cancer, chronic pancreatitis, long-term diabetes mellitus, ABO blood group and obesity [3–6]. Of these, cigarette smoking has been consistently associated with risk of pancreatic cancer [7]. Despite being a well-established risk factor, little is known about which smoking components most strongly affect risk estimates.

The typical approach to reporting the multiple dimensions of smoking data in epidemiological studies is to analyse each dimension independently, such as intensity, duration and time since quitting (for former smokers). However, several recent studies on lung and oesophageal cancer have demonstrated that this method of data interpretation may lead to over- or under-estimation of odds ratios (ORs) due to the complex associations between different smoking components [8–10]. Thus, the primary aim of this analysis was to disentangle the effects of various smoking dimensions on pancreatic cancer risk.

2. Methods

2.1. Participants

The Queensland Pancreatic Cancer Study (QPCS) was a population-based case-control study. Eligible patients were residents of Queensland over 18 years of age who had been diagnosed with histologically- or clinically-confirmed pancreatic cancer between 1st January 2007 and 31st June 2011. Potentially eligible patients for this study 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 by the QCR and invited to participate. We recruited 705 cases, approximately 35% of all those notified to the QCR during the study period. Reasons for non-participation were: patient died before we were able to invite their participation – 51%; patient's doctor refused permission to contact patient – 11%; patient refused – 16%; patient was unable to be contacted – 12%; patient was diagnosed outside of the eligibility period – 9%; cognitive impairment – 1%. In total, 93% of pancreatic cancer patients completed independent interviews, whereas 7% were assisted by proxies. Restricting the analysis to those who completed their own interviews did not materially alter results. The median time interval between date of diagnosis and date of interview was 65 days.

Potential controls were randomly selected from the Australian Electoral Roll (voting is compulsory for Australians above 18 year-olds) and frequency-matched to cases by sex and age (5-year groups). People unable to give informed consent or for whom a telephone number could not be located were excluded from the study. We approached 1543 potential controls. Of these, 6% were ineligible or dead, 39% declined, 8% had no contact and 1% failed to satisfactorily complete the interview. Of eligible controls, 711 (46%) completed interviews. The study was approved by the Human Research Ethics Committees (HRECs) of the QIMR Berghofer Medical Research Institute and participating hospitals in Queensland (Australia) and each participant gave written consent.

2.2. Data collection

Participants completed face-to-face (84% of cases; 29% of controls) or telephone interviews, during which we inquired about socio-demographic and lifestyle factors, medical and occupational history and family history of cancer. Cases were also asked for consent to review medical records. We offered a short version of the interview to participants who were unable or unwilling to complete the long interview. All of the variables used in this analysis were included in both the long and short interviews.

2.2.1. Health and lifestyle factors

Participants were asked about height and weight 1 year before diagnosis (cases) or 1 year before interview (controls) and these data were used to calculate body mass index (BMI, kg/m^2). We asked about the number of alcoholic drinks consumed during each decade 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 current age). We asked about history of diabetes and age at diagnosis if present. Education level was elicited by asking participants at what age they left school, and about post-school study and qualifications. All participants were asked about their country of birth. Self-reported ancestry of grandparents was used to classify participants as Caucasian or non-Caucasian.

2.2.2. Smoking history

Participants who had smoked more than 100 cigarettes, cigars or pipes, over their whole life were asked detailed questions about their smoking history, including the age at which they started smoking, the age at which they stopped smoking permanently (among ex-smokers), the amount they smoked in a typical day and the number of days per week that they smoked.