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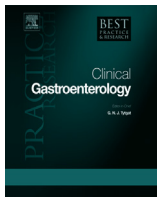

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Surveillance for neoplasia in the pancreas

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A B S T R A C T

Despite its low incidence in the general population, pancreatic cancer is one of the leading causes of cancer-related mortality. Survival greatly depends on operability, but most patients present with unresectable disease. Therefore, there is great interest in the early detection of pancreatic cancer and its precursor lesions by surveillance. Worldwide, several programs have been initiated for individuals at high risk for pancreatic cancer. Their first results suggest that surveillance in high-risk individuals is feasible, but their effectiveness in decreasing mortality remains to be proven. This review will discuss which individuals are eligible for surveillance, which lesions are aimed to be detected, and which surveillance modalities are being used in current clinical practice. Furthermore, it addresses the management of abnormalities found during surveillance and topics for future research.

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Introduction

Pancreatic cancer (PC) has a low age-adjusted incidence of 13.5 per 100,000 per year [1], yet is the fourth leading cause of cancer-related death in the United States, with an estimated 50,000 deaths in 2016. Mortality has been increasing by 0.4% each year, and in 2030, it is projected to be the second leading cause of cancer-related death [2,3]. PC has a dismal prognosis, with a 5-year survival rate of 7%. Because surgery provides the only cure, survival greatly depends on operability at diagnosis. After surgery, the 5-year survival rate increases to 27%. However, only 15–20% of patients present with resectable disease and even in resected cases, 24% experience recurrence [4]. Earlier detection of PC would increase the chances of survival. It is estimated that precursor lesions require an average of 11.7 years to evolve into a malignant clone, and that metastatic subclones occur 6.8 years later [5]. This creates a window for early detection of PC cases through a surveillance program for high-risk individuals (HRIs).

Who is at risk for pancreatic cancer?

The lifetime risk of PC in the United States' general population is estimated at 1.5% [6]. Most PC cases are sporadic. Hereditary PC makes up for 10% of cases, but only in 3%, this can be related to known genetic cancer susceptibility syndromes or inherited disease (described below). In the remainder 7%, no underlying cause is found to explain the familial aggregation. This group is commonly referred to as familial PC (FPC) [7–9]. FPC family members and carriers of known hereditary cancer syndromes are at a higher risk than the general population to develop PC. Therefore, they are designated candidates for surveillance.

Modifiable risk factors

Smoking is the most important modifiable risk factor for PC and doubles the risk (ORs range 1.74–2.2) [10,11]. This effect is dose-dependent, but even second-hand tobacco exposure increases the risk to develop PC (OR 1.2) [12]. After cessation, the risk decreases, but it remains elevated for 10–20 years (OR 1.2) [10,11]. Alcohol use has long been associated with PC [13,14]. A recent meta-analysis of 19 prospective studies showed that low-to-moderate alcohol intake has little effect on PC risk, but high alcohol intake increases the risk (RR 1.15) [15]. As this analysis showed the highest risk in the subgroup with a follow-up greater than 10 years, the long-term impact of alcohol use may have even been underestimated. Also, overweight or obesity at any age increases the risk of PC (HRs range 1.12–1.25 for different age cohorts at the time of BMI measurement) [16]. A pooled analysis of 14 cohort studies showed a 47% increased risk in obese persons (BMI $\geq$30 kg/m^2) [17]. Another meta-analysis showed a higher PC-related mortality for overweight (BMI 25–29.9 kg/m^2, adjusted HR 1.06) and obese (BMI $\geq$30 kg/m^2, adjusted HR 1.31) patients [18]. Many dietary factors have been suggested to influence PC risk, but evidence is inconclusive on this matter, partly due to confounding factors and the lack of randomized trials [19,20]. Fruits, vegetables, and whole grain intake are thought to have a protective effect [21–23] whereas the consumption of red meat in men, unsaturated fatty acids, and some saturated fatty acids were found to increase PC risk [24–26]. It has been suggested high serum Vitamin D levels have a protective effect, but case-control studies have not been able to support this [27,28].

Non-modifiable risk factors

Men are more often affected than women, but this difference is minimal [2]. African–Americans and persons of Ashkenazi Jewish descent are found to be at higher risk [29,30]. Furthermore, the incidence of PC increases with age. Most diagnoses are made between 60 and 80 years [31,32]. Blood types A, B and AB are at modestly increased risk compared to type O (ORs 1.60, 1.09, and 1.14, respectively) [30,33]. Both recent diagnosis of chronic pancreatitis and long-standing chronic pancreatitis of any origin are identified risk factors [30,34,35].