

Screening for pancreatic cancer in familial high-risk individuals: A systematic review

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Abstract

AIM: To analyze the benefits and harms of pancreatic cancer screening in familial high-risk individuals (HRIs).

METHODS: Studies were identified by searching PubMed, EBSCO, ClinicalTrials.gov and the Cochrane database from database inception to June 2014. We also obtained papers from the reference lists of pertinent studies and systematic reviews. English-language trials and observational studies were searched. The key words used as search terms were "screening" and "surveillance". Cost-effectiveness, diagnostic rate, survival rate, mortality and adverse events were the outcomes of interest. Age, sex, lifestyle and other confounding factors were also considered. However, anticipating only a few of these studies, we also included observational studies with or without control groups. We also included studies concerning the anxiety associated with pancreatic cancer risk and other psychological changes in familial HRIs. We extracted details on study design, objectives, population characteristics, inclusion criteria, year of enrollment, method of screening, adjusted and unadjusted mortality, cost-effectiveness and adverse events from the included studies. Studies were assessed using the Reporting of Observational studies in Epidemiology (STROBE) checklist.

RESULTS: Sixteen studies on pancreatic cancer screening were included. Five studies included control groups, nine were observational studies without control groups, and the other two studies investigated the worry associated with pancreatic cancer risk. We found that pancreatic cancer screening resulted in a high curative resection rate (60% vs 25%, $P = 0.011$), longer median survival time (14.5 mo vs 4 mo, $P < 0.001$), and higher 3-year survival rate (20% vs 15.0%, $P = 0.624$). We also found that familial HRIs had a higher diagnostic rate of pancreatic tumors than controls (34%

vs 7.2%, $P < 0.001$). In patients who underwent regular physical examinations, more stage I pancreatic cancers were observed (19% *vs* 2.6%, $P = 0.001$). In addition, endoscopic ultrasonography, which was the main means of detection, diagnosed 64.3% of pancreatic cancers. In comparison, endoscopic retrograde cannulation of the pancreas, magnetic resonance imaging, and computed tomography diagnosed 28.6%, 42.9%, and 21.4%, respectively. For mass lesions, instant surgery was recommended because of the beneficial effects of post-operative chemotherapy. However, in patients with intraductal papillary mucinous neoplasms, we did not find a significant difference in outcome between surgery and follow-up without treatment. Moreover, pancreatic cancer screening in familial HRIs had a greater perceived risk of pancreatic cancer ($P < 0.0001$), higher levels of anxiety regarding pancreatic cancer ($P < 0.0001$), and increased economic burden.

CONCLUSION: Pancreatic cancer screening in familial HRIs is associated with a higher detection rate and longer survival, although screening may influence psychological function and increase the economic burden.

Key words: Pancreatic cancer; Screening; Benefit; Familial high-risk individuals; Pancreatic tumor

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Core tip: Pancreatic cancer is a fatal disease with a five-year survival rate of less than 5%. The early diagnosis of pancreatic cancer is essential. Individuals with a family history of pancreatic cancer have an increased risk of developing the disease. To date, no study has systematically and comprehensively reported on pancreatic cancer screening in familial high-risk individuals. Here, for the first time, we performed a systematic review to determine whether screening for pancreatic cancer in familial high-risk individuals can detect early stage pancreatic cancer and prolong survival or reduce the negative effects of this disease.

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INTRODUCTION

Pancreatic cancer has become one of the most fatal diseases over the past years. The 5-year survival rate, estimated by the Surveillance Epidemiology and End Results program, is 4% and this figure is the lowest for all types of cancer^[1]. There were 216400 new cases of pancreatic cancer and 213500 deaths worldwide from pancreatic cancer in 2000^[2]. The reasons for

the high mortality rate include a low early diagnostic rate, low eradication rate, and poor radiotherapy and chemotherapy response rates. Almost half of patients with early stage pancreatic cancer are asymptomatic. Once detected, the 4-year survival rate can increase to 78% following resection of pancreatic cancers < 2 cm^[3]. The detection of pancreatic cancer in the early stage affects prognosis in the pancreatic cancer high-risk population, especially familial high-risk individuals (HRIs).

There is a familial aggregation of pancreatic cancer. Familial HRIs are defined as families with at least two first-degree relatives, suggesting an autosomal dominant penetrance^[4]. Some researchers have suggested that individuals with three or more affected family members, one of whom must be a first-degree relative, are considered high-risk individuals and should undergo screening^[5]. Persons who do not fit into this category can be classified as having sporadic pancreatic cancer.

The risk and incidence of pancreatic cancer is exceptionally high in familial pancreatic cancer kindred, where at least three first-degree relatives have already been diagnosed with pancreatic cancer^[6]. There was a 57-fold increased risk of pancreatic cancer in these individuals compared with surveillance findings^[6]. A meta-analysis that included nine studies indicated a significant increase in pancreatic cancer risk associated with having an affected relative, with an overall summary relative risk of 1.80^[7]. Therefore, targeted screening of familial HRIs may detect potential pancreatic neoplasms or precursor lesions, including pancreatic intraepithelial neoplasia (PanIN), intraductal papillary mucinous neoplasms (IPMNs) and mucinous cystic neoplasms (MCNs)^[8]. More and more professional societies recommend pancreatic cancer screening using imaging studies or other methods, primarily in patients at high risk for pancreatic cancer. However, the recommendations for pancreatic cancer screening include some questionable points. The cost-effectiveness, concern regarding pancreatic cancer risk, screening test accuracy, and attitude to cancer screening should be taken into consideration.

In this study, we conducted a systematic review to analyze the benefits and harms of pancreatic cancer screening in familial HRIs.

MATERIALS AND METHODS

Data sources

We searched PubMed, EBSCO, ClinicalTrials.gov and the Cochrane database from database inception to June 2014. We also obtained papers from the reference lists of pertinent studies and systematic reviews.

Study selection

We included English-language controlled clinical trials and observational studies on pancreatic cancer

Table 1 Analytical studies on pancreatic cancer screening

| Study | Type of study (number of subjects) | Country | Duration of follow-up | Measured outcome |
|---|---|---------------|-----------------------|--|
| Canto <i>et al</i> ^[12] , 2006 | Prospective controlled study (n = 227) | United States | About 3 yr | Different diagnostic rate of PC, tumor type and screening complications |
| Kim <i>et al</i> ^[13] , 2011 | Retrospective controlled study (n = 60) | Korea | - | Different tumor type, curative resection, median survival, 3-yr survival rate |
| Potjer <i>et al</i> ^[14] , 2013 | Prospective controlled study (n = 241) | Netherland | A minimum of 1 yr | Different tumor type, frequency and behavior of precursor lesions |
| Lachter <i>et al</i> ^[15] , 2007 | Retrospective controlled study (n = 134) | Israel | - | Different diagnostic rate of PC, the number of operations |
| Zubarik <i>et al</i> ^[16] , 2011 | Prospective controlled study (n = 670) | United States | 1 yr | Different diagnostic rate of PC, tumor type, screening complications and cost of detection |

PC: Pancreatic cancer.

screening in familial HRIs. The key words used as search terms were “screening” and “surveillance”, which included any screening or surveillance programs in which specific tests (imaging studies and tumor markers) were performed to detect pancreatic cancer in familial HRIs. Age, sex, lifestyle and other confounding factors were also considered. RCTs comparing different early diagnostic rates, mortality, or the presence of complications were identified; however, anticipating only a few of these studies, we also included observational studies with or without control groups. We also included studies on anxiety associated with pancreatic cancer risk and other psychological changes in familial HRIs.

Data extraction

We extracted details on study design, objectives, population characteristics (including sex, age and ethnicity), inclusion criteria, year of enrollment, method of screening, adjusted and unadjusted mortality, cost-effectiveness and adverse events. All data were double-checked by one author. Two investigators assessed independently the quality of the studies by adapting the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist^[9] and other existing tools^[10,11]. The observational studies had no validated criteria; therefore, we did not report an overall summary assessment. Finally, we synthesized the evidence on the benefits and harms of pancreatic cancer screening.

Statistical analysis

The χ^2 test was used to compare discrete variables. We also used the χ^2 test to verify the statistical significance regarding the merged data of pancreatic tumors and stage I pancreatic cancer. Statistical analysis was performed using SPSS 16.0 for Windows (SPSS Inc., Chicago, IL, United States).

The statistical methods of this study were reviewed by Professor Zhang Hong of Fudan University.

RESULTS

We included 16 studies in the final analysis. Five studies were case-control studies that included a comparison group^[12-16], nine were observational studies without a comparison group^[17-25], and the other two studies investigated anxiety associated with pancreatic cancer risk.

Analytical controlled studies

Five controlled studies were included^[12-16]. The major characteristics of these studies are summarized in Table 1. In these five studies, the main method used in the detection of pancreatic cancer was endoscopic ultrasonography (EUS). Ultrasonography (USG)^[13] and MRI^[14] were also used in some studies. In two prospective studies, more neoplastic-type lesions were detected in the experimental group (21.8% vs 0.7%, 42% vs 16%, respectively)^[12,14]. In two retrospective studies, the experimental group had more stage I (TNM classification) pancreatic cancer than the control group (15% vs 7.5%, 100% vs 0.9%, respectively)^[13,16]. Pancreatic cancer patients in the experimental group had more curative resections (60% vs 25%, $P = 0.011$), longer median survival time (14.5 mo vs 4 mo, $P < 0.001$), and a higher 3-year survival rate (20% vs 15.0%, $P = 0.624$)^[13]. In the experimental groups with higher asymptomatic or T1 stage patients, the 3-year survival rate was not significantly improved. Precursor lesions were removed by surgery, with no significant postoperative complications^[12]. The average cost involved in detecting a pancreatic neoplastic lesion was \$8430.75 and was \$41132.74 to detect a pancreatic adenocarcinoma^[16].

We merged the diagnostic rate of pancreatic cancer in two studies^[12,14] and the pancreatic cancer TNM classification in another two studies^[13,16], regardless of heterogeneity. We found that familial HRIs had a higher diagnostic rate of pancreatic tumors than

Table 2 Non-controlled studies on pancreatic cancer screening

| Study (author/year) | Country | Study population <i>n</i> (HRIs%) | Period of time | Pancreatic tumor, <i>n</i> (%) | PC/death, <i>n</i> (%) |
|---|---------------|-----------------------------------|----------------|--------------------------------|------------------------|
| Langer <i>et al</i> ^[17] , 2009 | Germany | 76 (100) | 5 yr | 6 (7.9) | 0 (0)/0 (0) |
| Rulyak <i>et al</i> ^[18] , 2001 | United States | 35 (100) | 2 yr | 12 (34.3) | 0 (0)/0 (0) |
| Sud <i>et al</i> ^[19] , 2014 | United States | 30 (63.3) | 3 yr | 3 (10) | 2 (6.7)/0 (0) |
| Al-Sukhni <i>et al</i> ^[20] , 2012 | Canada | 262 (60.9) | 8 yr | 84 (32.1) | 3 (1.1)/2 (0.8%) |
| Verna <i>et al</i> ^[21] , 2010 | United States | 51 (100) | 3 yr | 20 (39.2) | 2 (3.9)/0 (0) |
| Poley <i>et al</i> ^[22] , 2009 | Netherland | 44 (47.7) | 2 yr | 10 (22.7) | 3 (6.8)/2 (4.5) |
| Ludwig <i>et al</i> ^[23] , 2011 | United States | 109 (100) | 7 yr | 9 (8.3) | 1 (0.9)/0 (0) |
| Brentnall <i>et al</i> ^[24] , 1999 | United States | 14 (100) | 15 mo | 7 (50) | 0 (0)/0 (0) |
| Canto <i>et al</i> ^[25] , 2012 | United States | 216 (90) | 28.8 mo | 92 (45.6) | 0 (0)/0 (0) |

Pancreatic tumors include cystic adenoma, PC, IPMN, PanIN, neuroendocrine tumor. PC: Pancreatic cancer; HRIs: Familial high-risk individuals.

controls (34% vs 7.2%, $P < 0.001$). In patients who underwent regular physical examinations, more stage I pancreatic cancers were observed (19% vs 2.6%, $P = 0.001$).

Non-controlled studies

Nine non-controlled studies screening for pancreatic cancer in familial HRIs were included^[17-25]. These studies were all carried out in developed countries (Table 2). Most individuals included in these studies were asymptomatic, with the exception of two studies that did not mention this factor^[18,19]. The patients in five studies were familial HRIs, whereas the remaining HRIs also had gene mutations^[19,20,22,25]. EUS combined with fine-needle aspiration (FNA) and pathological examination were the main screening and diagnostic methods used, with the exception of one study that used MRI as the primary detection and diagnosis tool^[20]. In addition, of these nine studies, genetic testing during surveillance was performed in one study^[21].

In general, familial HRIs who underwent screening had more early-stage pancreatic dysplasia or pancreatic cancer. In these nine studies, the pancreatic tumor detection rate ranged from 7.9% to 50%; however, the detection rate of pancreatic cancer only ranged from 0% to 6.8% (in four studies pancreatic cancer was not detected)^[17,18,24,25]. In addition, in the three controlled studies mentioned above^[12,14,15], the detection rate of pancreatic tumors in the experimental group was 21.8%, 41.6%, and 47.2%, respectively, compared with 0.9%, 15.5%, and 32.3% in the control groups, respectively. Five studies with pancreatic cancer cases (0.9%-6.8%) had a higher diagnostic rate than the estimated risk of 0.082% reported by a previous study^[20]. Of the pancreatic tumors, the percentage of pancreatic cancer was less than 30%, except for one study, which was 66.7%^[19]. This was likely affected by the characteristics of the selected population. The presence of pancreatic cancer was higher than that in the general population, and regular screening detected more precursor lesions. In addition, pancreatic cancer patients in four studies^[19-22] also had *BRCA2* gene mutations, which were frequently

demonstrated during pancreatic cancer screening^[26]. In the above controlled studies, one^[14] also included patients with a gene mutation of the p16-Leiden germline. In our analysis, five papers mentioned that the study population included familial HRIs with gene mutations. We found that these patients had a higher rate of pancreatic cancer diagnosis than other patients (Table 2). Thus, those familial HRIs with gene mutations may have a higher susceptibility. EUS was the main means of detecting pancreatic cancer, and diagnosed 64.3% of pancreatic cancers. In comparison, Endoscopic retrograde cannulation of the pancreas (ERCP), magnetic resonance imaging (MRI), and computed tomography (CT) detected 28.6%, 42.9%, and 21.4% of pancreatic cancers, respectively. Therefore, EUS is superior to the other methods.

In addition, 1.4% to 50% of screened patients received preventive or curative resection. Mortality from the time of pancreatic cancer diagnosis was mentioned in two studies^[20,22], and were 0.8% and 4.5%, which was lower than that in the general population (about 75% within one year after diagnosis)^[27]. Patients with precursor lesions underwent preventive surgery, which can result in a clear diagnosis following pathological examination and a curative resection. However, a previous study reported that one person died after prophylactic pancreas surgery^[28]. In the present analysis, ten studies mentioned complications or perioperative morbidity related to surgery for precursor lesions^[12,16-22,24,25]. We merged these studies, which are described in detail in Table 3. For mass lesions, instant surgery was recommended because of the beneficial effect of post-operative chemotherapy. However, for IPMNs, we did not find a difference in outcome between surgery and follow-up without treatment. Follow-up might be a better choice instead of surgical trauma. Only one study^[12] highlighted the complications of screening tests using ERCP. Thirteen patients (10.3%) developed acute pancreatitis. Other methods such as EUS and MRI are relatively safe.

Psychological function and the harms of screening

Familial HRIs have a higher risk of pancreatic cancer, and will receive many examinations during the

Table 3 Studies on precursor lesions

| Category | Surgery, <i>n</i> | Follow-up, <i>n</i> | Complications and prognosis |
|-----------------|-------------------|---------------------|--|
| PanIN | 17 | 0 | Just one patient had a fistula after surgery |
| IPMN | 11 | 97 | No relapse or canceration after surgery or follow-up |
| IPMN + PanIN | 6 | 0 | No relapse or canceration after surgery |
| Mass lesions | 3 | 0 | One patient died after surgery; two patients relapsed then treated with chemotherapy |
| Cytological HGD | 7 | 0 | No relapse or canceration after surgery; one patient had hemorrhage 13 mo later |

Table 4 Prospective studies on psychological function

| Study | Country | Type of study (number of subjects) | Result |
|---|---------------|--|---|
| Maheu <i>et al</i> ^[29] , 2010 | Canada | Prospective controlled study (<i>n</i> = 198) | Non-significant increase in risk perception, cancer worry, or general distress |
| Breitkopf <i>et al</i> ^[30] , 2012 | United States | Prospective controlled study (<i>n</i> = 1406) | HRIs had a greater perceived risk of PC and higher levels of PC worry than controls |

PC: Pancreatic cancer.

screening period. Mental changes in these patients are also worthy of attention. We included two studies that investigated risk perception, cancer-related anxiety or emotional distress during the screening period^[29,30] (Table 4). One study compared familial HRIs with individuals with BRCA2 mutations. However, no statistical difference in psychological function was observed between the two groups. Another study compared familial HRIs with general individuals, and observed that familial HRIs had a higher perceived risk of pancreatic cancer ($P < 0.0001$) and higher levels of anxiety associated with pancreatic cancer risk ($P < 0.0001$) during the screening period^[30].

Patients receiving invasive examinations such as EUS or ERCP did not report severe adverse events in the studies included. In one study, 13 patients developed acute pancreatitis after ERCP (eight requiring hospitalization), 7% in the high-risk group and 13% in the control group ($P = 0.38$)^[12]. One study reported that the cost of screening may be expensive for the general population^[16]. A previous study reported that one-time EUS screening for pancreatic dysplasia had an incremental cost-effectiveness ratio of \$16885/life-year saved, compared with the no screening group^[31]. However, the cost-effectiveness of repeated screening is unknown. Another study performed a clinical and economic evaluation using a Markov model, and the author concluded that doing nothing resulted in the greatest remaining years of life, the lowest cost, and the greatest remaining quality-adjusted life years^[32]. He believed that the most effective strategy was to do nothing if we could not further quantify the risk^[32].

DISCUSSION

We reviewed and evaluated controlled and non-controlled studies systematically, and examined the

benefits and harms of pancreatic cancer screening in familial HRIs. EUS combined with FNA testing was the most common screening method evaluated. Although only two studies^[20,22] reported mortality, and many precursor lesions did well with curative or preventive therapy, there was also very-low-strength evidence to draw conclusions on the benefits and harms of pancreatic cancer screening in HRIs.

In this systematic review, we obtained useful information. In general, screening familial HRIs can identify early pancreatic tumors resulting in early intervention. One retrospective study^[13] indicated subjecting individuals to regular examinations could result in the detection of early-stage pancreatic cancer leading to curative resection, and a greater median survival time. Nearly all the included studies reported precursor lesions and in some studies early treatment was carried out, which decreased the total mortality. The merged data showed a significantly higher diagnostic rate and more stage I pancreatic cancer in the experimental group. Although heterogeneity was present, these findings provide a reference point. Methodological flaws such as selection bias, lead-time bias, length-time bias and the lack of RCTs on pancreatic cancer screening were also observed. Although EUS is used widely, other methods such as MRI can also be useful in pancreatic cancer screening. Therefore, we were unsure whether survival rate would be affected by the detection of pancreatic cancer using this method. In addition, interval cancers should be taken into consideration. Interval cancers can be interpreted as those that present symptomatically between screening episodes and can skew the results of screening studies. Considering the latent period of early pancreatic tumors, when the tumor is detected will affect the survival rate.

Most studies were single-center and participants were from the same center, which avoided many biases.

Only four studies^[20,21,24,25] determined the smoking status of patients. Smoking is an established risk factor for pancreatic cancer^[33]. Therefore, it must be taken into consideration. In addition, hypercholesterolemia and alcohol consumption represent significant and independent risk factors for pancreatic cancer^[34]. Pannala *et al.*^[35] indicated that new-onset diabetes was a potential clue to the early diagnosis of pancreatic cancer. These factors may have influenced the final results. We did not know how much they affected the outcomes of these studies.

We chose familial HRIs as research subjects. In this population, there are also individuals with high risks for other diseases. Peutz-Jeghers syndrome with *STK11/LKB1* gene mutation^[36], hereditary pancreatitis with *PRSS1* gene^[37,38] or *SPINK1* gene mutation^[39], familial atypical multiple mole melanoma syndrome with *CDKN2A* or *p16* gene mutations^[40], hereditary breast ovarian cancer syndrome with *BRCA2* and *BRCA1* gene mutations^[41,42], and Lynch syndrome with mismatch repair genes^[43] are found in high risk populations, who should also receive attention. Nevertheless, these are not completely independent. Familial HRIs may also have gene mutations. The *PRSS1* gene mutation is the main influencing factor in hereditary pancreatitis, an autosomal dominant disease. *BRCA2* is one of the most common mutations, and was as high as 17% in one study^[44]. Future studies on HRIs with gene mutations should be carried out to determine if they have a higher risk than HRIs without gene mutations. In addition, because of the complex nature of the pedigrees in pancreatic cancer, Wang *et al.*^[45] designed a tool known as PancPRO to identify familial HRIs, which was used for selecting and screening.

Patients with precursor lesions or early-stage pancreatic cancer are mainly asymptomatic. Therefore, the detection method is very important. Biomarkers and imaging tests are both optional. In view of the existence of gene mutations, genetic testing is also a feasible method. Through this method, early intervention can avoid the occurrence of pancreatic cancer. However, because of the cost and difficulty of implementation, some methods may only apply to certain populations. CA199 is the most widely used biomarker. However, it has a very low positive predictive value^[46]; therefore, it is mainly used in the follow-up and surveillance of pancreatic cancer. Abdominal ultrasound is also rarely used for pancreatic cancer screening because of its low sensitivity. One study using abdominal ultrasound as the initial detection method reported a diagnostic rate of 7.5%-15% in stage I pancreatic cancer^[13]; however, this method was unable to confirm the findings in patients with negative results using other methods. As the main screening tool, the accuracy of EUS can reach 87.1%-92%^[47,48], and it also showed a high diagnostic rate of precursor lesions (PanINs and IPMN) (Table 2) in our included studies. Thus, EUS is an ideal detection method. However, EUS is an invasive procedure that

is easily affected by the operator, has a comparatively high cost and cannot be used for screening the general population. However, EUS is necessary in HRIs. MRI as a screening tool also has excellent results^[20,25], and is a non-invasive procedure without exposure to radiation. However, the lack of relevant papers, meant that we could not conclude that EUS is superior to MRI. CT and ERCP are rarely used because of radiation exposure and the risk of acute pancreatitis.

The natural history of early-stage pancreatic cancer or precursor lesions has not been well-characterized. Therefore, long-term surveillance or preventative surgery is controversial. Preventative surgery may be risky, as mentioned above. The current viewpoint is that IPMNs have the potential for malignant transformation^[49] and may result in early-stage pancreatic cancer. Unfortunately, we do not know the frequency and rate of progression of early-stage pancreatic cancer or precursor lesions. Tanno *et al.*^[50] performed a prospective study that included 82 patients with branch duct IPMN. Five patients (6.1%) developed adenoma, one (1.2%) had carcinoma *in situ*, one (1.2%) was borderline, six (7.3%) had cystic dilatation, and 69 (84.1%) had no change at a median follow-up of 59 mo. Tanno *et al.*^[50] confirmed the possibility of canceration of IPMNs during 59 mo. Therefore, IPMNs or other precursor lesions detected in the included studies had the potential to develop into adenomas. Although the IPMNs were stable during the follow-up period, it was possible that they could change to adenomas beyond the follow-up period. The results of the remaining patients with precursor lesions, which were recovery or death from cancer, would influence the final mortality and cost-effectiveness measures.

Some limitations were present in our systematic review. Firstly, we excluded non-English-language studies, but mitigated the risk by searching more databases. One study indicated that language restrictions did not appear to bias estimates of the effectiveness of a conventional intervention^[51], which also supported our evidence. Secondly, the lack of RCTs, and the existence of selection bias, lead-time bias and length-time bias were limitations in our included studies. These reduced the credibility of the review. Thirdly, although we identified some information regarding the harms of screening, we did not determine the cost-effectiveness of screening. Some studies referred to the cost or cost-effectiveness^[16,31]; however, a large RCT would be the most definitive way to estimate the cost-effectiveness of pancreatic cancer screening.

In conclusion, the current results showed that pancreatic cancer screening in familial HRIs is associated with a higher detection rate and longer survival. For precursor lesions, follow-up or surgery is controversial. However, screening may influence psychological function and increase economic burden. Thus, in developed countries, pancreatic cancer screening should be promoted. In addition, further

RCTs on pancreatic cancer screening in familial HRIs should be performed to provide more conclusive evidence.

COMMENTS

Background

Pancreatic cancer has become one of the most fatal diseases over the past years. The 5-year survival rate is estimated to be about 4% and this figure is the lowest for all types of cancer. In addition, pancreatic cancer has a familial aggregation. Familial high-risk individuals have a higher risk of pancreatic cancer. The early diagnosis of pancreatic cancer remains a challenge.

Research frontiers

Many relevant studies have been published on pancreatic cancer screening in familial high-risk individuals. The results of screening did not provide a consistent view. The current research involves a comprehensive review of these studies to analysis the benefits and harms of pancreatic cancer screening in familial high-risk individuals.

Innovations and breakthroughs

This is the first systematic review to determine the benefits and harms of pancreatic cancer screening in familial high-risk individuals. PubMed, PsycINFO, ClinicalTrials.gov and the Cochrane database were searched from database inception to June 2014.

Applications

This study shows that pancreatic cancer screening in familial high-risk individuals (HRIs) is associated with a higher detection rate and longer survival, and screening may also influence psychological function and increase the economic burden.

Terminology

Pancreatic cancer is the growth of cancer cells in the pancreas. Symptoms include abdominal pain or back pain, jaundice, unexplained weight loss, pale, light colored feces, dark urine color and lack of appetite. Early stage pancreatic cancer usually has no symptoms. When pancreatic cancer is diagnosed, it has usually metastasized to other organs.

Peer-review

This is a good systematic review in which the authors analyzed the benefits and harms of pancreatic cancer screening in familial high-risk individuals. The results are interesting, and suggest that pancreatic cancer screening in familial HRIs can improve detection rate and prolong lifetime. In addition, it can influence psychological functions and increase the economic burden.

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