Psychological impact of pancreatic cancer screening by EUS or magnetic resonance imaging in high-risk individuals: A systematic review

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ABSTRACT

Background and Objectives: There is an increasing global interest in screening programs aiming to detect pancreatic cancer (PC) in an early and potentially curable stage. Concerns still remain as to whether screening would confer any survival benefit. Another approach to evaluate the benefits of the pancreatic screening programs would be to consider its impact on the quality of life of the individuals who at risk of developing cancer. The aim of this systematic review was to investigate the current knowledge regarding the psychological impact of participation in routine screening for PC. Methods: A systematic literature search was carried out in January 2018 in three major databases which are as follows: PubMed, Scopus, and Web of Science. Cross-sectional and prospective studies evaluating the psychological aspects of screening in high-risk individuals were included in the study. For each study, the following data were recorded: name of first author, year of publication, study design, study population, aims, screening protocol, outcomes and instruments, main results, and summary of findings. Results: Six cohort studies and one cross-sectional study that addressed the psychological aspects of PC screening were included in the analysis. Overall, studies have shown that high-risk individuals have positive psychological outcomes from participating in PC screening programs. Conclusions: Although screening might not always be reassuring, it may improve individuals’ quality of life, and this should be an important aspect when considering PC screening.

Key words: EUS, pancreatic cancer, quality of life, screening

INTRODUCTION

By 2030, pancreatic cancer (PC) is expected to become the second leading cause of cancer-related mortality in the United States.¹,² The poor prognosis is mainly related to the late clinical presentation and the rapid progression of the disease. Despite extensive research in the field, the 5-year survival rate is <8%. Most of the patients present with advanced-stage, incurable
Early detection is a key issue for improving the prognosis of this aggressive disease. Patients with early-stage PC have a 5-year survival rate of 31.5%. Since survival rates are strongly related to the stage of PC, there is an increasing global interest in screening programs aiming to detect precursor lesions or PC in an early and potentially curable stage.

Screening of the entire population is not considered feasible because of the low incidence of PC in the general population and the lack of a noninvasive, reliable, sensitive, and inexpensive screening test. General population screening using any currently accessible method would imply an increased cost with a low yield. However, selective screening of high-risk individuals is considered beneficial. Till date, screening has been performed in research settings on high-risk individuals. Based on consensus agreement, individuals with a family history of PC are considered at high risk for developing PC if at least two first degree relatives (FDRs) or any three relatives (including one FDR) have a diagnosis of PC. Moreover, individuals with Peutz-Jeghers Syndrome or Lynch Syndrome and those with p16, or BRCA1/2, ATM, PALB2, and PRSS1 gene mutations are also considered at risk and should be screened.

The first report of pancreatic screening of high-risk individuals was published nearly 20 years ago by Brentnall et al. Since then, several other screening studies have been completed. Most of the studies included familial PC (FPC) individuals, while others involved individuals with PC-associated gene mutations. Screening programs for PC require multidisciplinary teams and different imaging modalities including EUS, magnetic resonance imaging (MRI), magnetic resonance cholangiopancreatography, and computed tomography (CT) to identify early pancreatic lesions. The diagnostic accuracy of screening programs varies from 1.3% to 50%. The most frequently detected pancreatic lesions are cysts.

However, an important concern is that the value of the screening programs has not yet been proven. These programs are therefore only available in a research setting and in specialized centers with high-volume pancreatic surgery, multidisciplinary teams, and well-defined screening protocols.

The reduction of cancer-mortality rate is the most important aspect for the evaluation of the benefits of a particular screening test. However, studies have yet to show survival improvement in PC screening. Another approach to evaluate the benefits of the pancreatic screening would be to consider its impact on the quality of life of the individuals who are at risk for developing cancer. Although rarely considered, undergoing PC screening may have positive impact including decrease in cancer worry or increase in feelings of reassurance and well-being as well as improved quality of life.

Current knowledge about the psychological impact of PC screening is limited. Although extensive data are lacking for PC, several studies have evaluated the psychological impact of other cancers screening, particularly hereditary breast and ovarian cancer, and mixed results were reported. The overall psychological impact of undergoing breast MRI and mammographic screening by women at high-risk for breast cancer was positive. Furthermore, a study comprising 4,153 individuals examined the psychological impact of participating in screening for colorectal cancer. Perceived risk, colorectal cancer-related worries, and overall anxiety were significantly reduced postscreening. By contrast, a systematic review of the psychological aspects of screening in hereditary cancer syndromes found that screening was associated with higher distress and a reduced quality of life.

Individuals with a family history of PC and carriers of PC-associated gene mutations may overestimate their personal cancer risk and report increased cancer-related worries or concerns, leading to a reduced quality of life. In such scenario, even though the impact of PC screening on survival is not yet known, its psychological benefit should be taken into consideration. The aim of this systematic review was to investigate the current knowledge regarding the psychological impact of participation in routine screening for PC.

METHODS

Data sources and searches
The present study was conducted following the principles of the preferred reporting items for systematic review and meta-analysis protocol statements.

A systematic literature search was carried out in three major databases which are as follows: PubMed, Scopus, and Web of Science. The data search was performed in January 2018, and the following search terms were...
used: “pancreatic cancer,” “screening,” “surveillance,” “psychological,” and “quality of life.” No restriction was set on study design, year of publication, or publication status. References from the retrieved articles were reviewed to identify other potentially eligible publications.

**Study selection**

The studies included in this systematic-review were required to meet the following criteria: (1) studies written in English; (2) studies including individuals being at risk for PC based on their family history or the presence of a PC-associated gene mutation, and undergoing PC screening programs; (3) studies evaluating the psychological aspects related to screening in those patients; (4) cross-sectional and prospective studies were included in the study. Studies regarding the psychological impact of genetic testing only were excluded from the study.

**Data extraction and quality assessment**

Two reviewers (IMC and AALC) independently performed data extraction, in accordance with the inclusion and exclusion criteria listed above. Disagreements were resolved by consensus. For each study, the following data were recorded: name of first author, year of publication, study design, study population, aims, screening protocol, outcomes and instruments, main results, and summary of findings.

The Newcastle–Ottawa quality assessment scale (NOS) was used to assess the quality of the studies.\(^\text{[17]}\) NOS evaluated studies by taking into consideration three aspects as follows: selection, comparability, and exposure. The score range of NOS is from 0 to 8, and studies with a score higher than six are assumed to be of high-quality. The quality assessment was conducted by two investigators independently and any disagreement between the investigators was resolved by a discussion with the third investigator.

**RESULTS**

**Searching results and study characteristics**

The process for the study inclusion is summarized in Figure 1. Altogether, we identified seven articles\(^\text{[15,18 - 23]}\) that reported on psychological aspects of participating in screening programs for PC and met our inclusion criteria. These seven manuscripts covered five studies.

The studies were heterogeneous in their study design, with six cohort studies\(^\text{[15,18,20-23]}\) and one cross-sectional study\(^\text{[19]}\) included. The studies were also heterogeneous in their outcome measures (PC perceived risk, participants’ view on screening, cancer worries, anxiety, depression, cancer-related distress, and general distress) and differed in their duration of follow-up (1 month to 3 years) and number of assessments (1–6). Validated standardized questionnaires were used to measure the psychological outcomes, but some authors\(^\text{[15,19,20]}\) used nonvalidated, study-specific questionnaires. There were also differences regarding screening protocols. Some studies used both MRI and EUS\(^\text{[19-21]}\) or EUS only\(^\text{[23]}\) as screening examinations. In other studies,\(^\text{[15]}\) screening protocols consisted of transabdominal ultrasound, MRI, and blood collection, once a year for 5 years. Due to the heterogeneity in outcome measures and study designs, it was not possible to undertake a quantitative synthesis of outcome measures.

The average NOS score of the included studies was 6.28, ranging from 5 to 7 [Supplementary Table 1].

**Outcomes**

**Cancer-specific distress**

All seven articles reported on cancer-specific distress by using the Cancer Worry Scale (CWS)\(^\text{[15,18 - 22]}\) or the Impact of Event Scale (IES).\(^\text{[19,23]}\) The CWS was initially used to evaluate breast and ovarian cancer-related worries.\(^\text{[24]}\) It measures the frequency of cancer worries and their impact on daily life. The score range is from 3 to 32. There is no clinical cutoff score for the CWS.\(^\text{[23]}\) The IES assesses intrusive thoughts and
avoidant behavior. Either the sum of the subscales “intrusion” (0–35) and “avoidance” (0–40) or the total score (0–75) can be used.[26,27]

Overall, studies revealed low-to-moderate levels of PC-related distress. Detailed information is shown in Table 1.

Studies included in our systematic review showed that, for individuals undergoing PC screening, worries about cancer decreased significantly over time. Moreover, participants rated their risk of developing PC significantly lower when they underwent annual screening than when they did not; this might explain the decreasing worries over time. These are interesting findings because all participants were informed about the unproved efficacy of PC screening in improving survival.

Only one study showed a slight, but significant increase in cancer worries for high-risk individuals undergoing PC screening at 1-year assessment. It is important to identify these individuals because they should benefit from psychosocial support. Konings et al.[21] identified the following factors associated with increased PC-worries: elevated perceived-risk of developing cancer and having a family member affected by PC before 50-year old. Surprisingly, a personal history of cancer was not associated with high cancer worries. This was previously described as associated with increased cancer worries,[28] because individuals with the previous history of cancer may be more anxious about developing the disease again.

General distress
Three studies[19,20,22] measured generalized anxiety and depression with two seven-item subscales of the hospital anxiety and depression scale (HADS) as follows: HADS-A and HADS-D. A score higher than 11 on a subscale indicates an increased level of anxiety or depression.[29,30] Studies included in our systematic review reported that only a few individuals undergoing PC screening showed scores indicating anxiety or depression disorder [Table 1]. Anxiety and depression levels scored above cutoff values in nearly 10% of the participants. This is similar to the proportion of individuals in the general population[31] and suggests that the anxiety and depression levels are not related to the participation in the PC screening programs, but may have other causes. McBride et al.[22] showed a significant mean decrease of scores of 1.2 points in short-term anxiety.

One study[18] measured general distress with the Global Severity Index (GSI) of the Brief Symptom Inventory-18[32] and showed that <20% of the participants scored above the cutoff on the GSI. The present study[18] further revealed that distressed individuals at baseline reported significantly lower intrusive thoughts after the intervention.

General quality of life
Only one study[23] reported on the general quality of life of individuals undergoing PC screening. The Psychological Consequences Questionnaire (PCQ) was used to measure negative and positive psychological aspects of screening.[33] A significant reduction in the negative emotional consequences subscale score of the PCQ was found in high-risk individuals at 1-year postscreening.

Pancreatic cancer risk perception
Three studies[15,19,20] reported on PC risk perception using study-specific questionnaires. Overall, low-to-moderate levels of perceived risk were revealed [Table 1].

Aspects of screening in familial pancreatic cancer
Maheu et al.[15] found that individuals at the highest risk for psychological disturbances are younger individuals with a family history of PC. A descriptive study[34] indicated that a family experience of cancer-related death was an important component of how a person addressed PC risk. Despite the uncertain efficacy of the procedures, individuals chose to participate in PC screening programs to avoid an experience similar to that of their family members.[35,36] Lawson and Flocke described this as a “teachable moment” where individuals witnessing a family member die of cancer are more likely to make a personal change.[37] Radecki Breitkopf et al. further sustained this concept in a study including family members of patients with colorectal cancer and found that they are more willing to participate in a cancer screening program.[38]

Experience with the screening procedures
Two studies[19,20] reported on participants’ experience with PC screening. EUS and MRI were described as equally burdensome. About 11% of individuals undergoing PC screening reported that the MRI was
### Table 1. Studies evaluating psychological aspects of pancreatic cancer screening

| Reference          | Study population | Study design | Screening protocol | Outcome and instruments | Main results                                                                                             |
|--------------------|------------------|--------------|--------------------|-------------------------|---------------------------------------------------------------------------------------------------------|
| Maheu et al., 2010 | n=198: 131 with FPC; 67 with BRCA2 | Cohort study, prospective; 2 assessments: Baseline and after 3 months | Genetic counselling, transabdominal ultrasound, blood collection, MRI; once a year for 5 years | 1. Risk perception - study specific questionnaire, 2. Cancer worry - the CWS (4 items), 3. General distress: BSI-18 | Baseline: Low to moderate levels of risk perception, cancer worry and general distress; FPC group showed higher perceived PC risk than BRCA group; for general distress: 22.9% men and 18.9% women scored above the cutoff for BSI; 3 months: No significant change in perceived PC risk-still higher in the FPC group; significant decrease in cancer worry over time within the FPC group; significant decrease of BSI in those scoring above cutoff for clinical distress |
| Hart et al., 2012  | Baseline: n=198; 3 months follow up: n=129 | Cohort study, prospective; 3 assessments: Baseline; 3 months; 12 months | Genetic counselling; transabdominal ultrasound, MRI, blood collection; once a year for 5 years | 1. Cancer worry: CWS; 2. Cancer-related distress: IES (intrusion scale + avoidance scale); 3. General distress: BSI-18 (GSI) | Cancer worry: Increased by 0.2 points over time (decreased from baseline to 3 months, but increased from 3 months to 12 months) Contd... |
| Harinck et al., 2011 | n=69: 31 FPC; 21 P16-mutation; 4 STK11; 1 BRCA1; 10 BRCA2; 2 PS3 | Cross sectional; one assessment: 4 weeks after receiving screening results | Genetic counselling; annual MRI and EUS | 1. Participants’ view on screening: Study - specific questionnaire; 2. Psychological distress: Cancer worries - CWS (8 items); Anxiety and depression - HADS-A and HADS-D | Cancer worry: 29% worried frequently about getting cancer, but this is not related to the screening outcomes; HADS: Only 9% with significant clinical level of anxiety and depression; Contd...
Table 1. Contd...

| Reference | Study population | Study design | Screening protocol | Outcome and instruments | Main results |
|-----------|------------------|--------------|--------------------|-------------------------|--------------|
| Konings et al., 2016 | n=140: 71 FPC; 69 syndromic PC (38 CDKN2A; 2 BRCA1; 19 BRCA2; 7 STK11/LKB1; 3 p53) | Cohort study, prospective; Assessments: T0 (after genetic counselling); T1 (after intake for participation); T2 (after the first MRI and EUS) and after the MRI and EUS 1 (T3), 2 (T4) and 3 years (T5) after first surveillance | Genetic counselling; annual MRI and EUS | 1. PC perceived risk - study-specific questionnaire; 2. Cancer worries: CWS (8 items); 3. Anxiety and Depression: HADS-A and HADS-D | no statistically significant association between screening results and levels of anxiety; in 99% no influence on mood or daily activities PC perceived risk: Lower when undergoing annual surveillance compared with not undergoing screening; Cancer worry: Decreased from baseline (14.4, SD 4.3) by 0.5 points each year; Anxiety and depression: Low (mean HADS-A=4.5, SD 3.7; mean HADS-D=2.8, SD 3.2); only 7% showed HADS-A >10 and 5% showed HADS-S >10; no significant changes over time Overall average CWS-score=13; significant intra-individual decrease in CWS over time (P<0.001); factors associated with cancer worries at the 2nd year follow up: Having a family member diagnosed with PC below the age of 50 and an elevated perceived PC risk at baseline. In 56% of participants a pancreatic cystic lesion was detected; no impact on cancer worries. In 4% of participants pancreatic surgery was performed; no impact on cancer worries Baseline HADS: 3 participants had borderline anxiety, 2 had clinical anxiety and 1 met clinical cutoff for depression; significant mean decrease of scores of 1.2 in short-term anxiety at 2 w postscreening. Baseline CWS: 47% had frequent cancer worries; reduction in the mean CWS after screening, but no statistically significant. IES scores decreased slightly over time, but no statistically significant |
| Konings et al., 2017 | n=166: 84 FPC; 44 CDKN2A; 2 BRCA1; 25 BRCA2; 7 LKB1; 4 P53 | Cohort study, prospective; Assessments: T0 (after genetic counselling); T1 (after intake for participation); T2 (after the first MRI and EUS) and after the MRI and EUS 1 (T3), 2 (T4) and 3 years (T5) after first surveillance | Genetic counselling; annual MRI and EUS | Cancer worries: CWS (8 items) | |
| McBride et al., 2017 | n=17; TP53 mutation carriers | Cohort study; prospective; Assessments: Baseline; 2 weeks, 12 weeks, 26 weeks and 52 weeks post-WB-MRI | Annual screening with WB-MRI/ annual physical exam, breast MRI and colonoscopy/endoscopy dependent on family history | 1. Anxiety and depression-HADS-A and HADS-D; 2. Cancer worry-CWS; 3. Cancer-related distress: IES (intrusion and avoidance) | |

Contd...
uncomfortable mostly because of claustrophobia and 10% stated that EUS was uncomfortable because of inadequate sedation.\cite{19}

Till date, EUS and MRI are the most promising PC screening procedures.\cite{39,40} Compared to MRI, EUS is an invasive technique, and it can be assumed that its acceptability is lower. Surprisingly, studies have shown that EUS and MRI were described as equally burdensome. One explanation might be the use of sedation for EUS. Another point of view was given by Lewis et al.\cite{41} who reported that individuals with a family or personal history of cancer often prefer the more invasive screening procedures.

**Participation in pancreatic cancer screening programs**

PC screening is different from other cancers screening programs regarding the poor prognosis, the lack of reliable screening procedures, and the clinical costs of potential preventive surgery. Although the survival benefits associated with regular screening remain the subject of debate, it may offer a sense of control over the disease for high-risk individuals. A Dutch study\cite{42} evaluated the reasons to participate in a screening program as well as psychological benefits and barriers to screening. Most individuals reported that advantages of screening surpassed disadvantages. On the other hand, data from the German FPC registry showed that only 40% of the individuals at risk participated in the recommended screening program.\cite{43} Thus, it would be interesting to also assess the high-risk individuals who decided not to participate in a screening program.

**Limitations**

Several limitations of our study should be noted. All included studies were published in English; therefore, some qualified articles in other languages may have been missed. Moreover, a meta-analysis of the studies to evaluate the overall psychological impact of screening was not suitable because of the heterogeneous data. The studies used different measures and different time intervals.

The studies included in the present review have some limitations as well. Although most studies used validated questionnaires, some studies used study-specific, and nonvalidated scales, which made the comparability of the study findings difficult. Moreover, the impact of PC screening on the quality of life of participants has not been investigated and should be an issue of interest for future research. All studies lacked a control group. Future research should also aim to include those individuals not attending surveillance as a control group.

**CONCLUSIONS**

To the best of our knowledge, this is the first systematic review regarding the psychological impact of PC screening on high-risk individuals. Six cohort studies and one cross-sectional study that addressed the psychological aspects of PC screening were included in the study. Overall, studies have shown that high-risk individuals have positive psychological outcomes from participating in PC screening programs. Although screening might not always be reassuring, it may improve individuals’ quality of life, and this should be an important aspect when considering PC screening. Moreover, to cope with anxiety, it would be useful for patients to be in contact with professionals and rely on medical progress. Further studies are needed to obtain more information on possible connections between PC screening programs and participants’ quality of life.
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Conflicts of interest
There are no conflicts of interest.

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