—Original Article—

Quality of life impact of EUS in patients at risk for developing pancreatic cancer

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ABSTRACT

Background and Objectives: The current knowledge about the psychological impact of pancreatic cancer (PC) screening is limited. We aimed to assess the changes in quality of life (QOL) and level of distress after undergoing EUS in individuals with pancreatic cystic lesions (PCLs) and in patients at high risk for PC based on genetic and familial factors. **Methods:** Eighty patients with PCL and/or increased genetic or familial risk for PC who had undergone EUS were contacted. Fifty percent of those patients successfully completed the brief profile of mood states (POMS) and the linear analog scale assessment (LASA) QOL questionnaires to evaluate their pre/post-EUS overall QOL. The effect size (ES) method was used to assess clinically meaningful changes in the scores. **Results:** There was a significant difference in patients' overall QOL scores before and after the EUS procedure (LASA, mean difference 0.73, standard deviation (SD) 1.76, ES 0.58, $P < 0.01$; brief POMS, mean difference −5.46, SD −6.72, ES 0.81, $P < 0.01$). **Conclusions:** QOL of patients with PCL or increased risk factors for PC is significantly improved after a EUS/EUS-guided fine-needle aspiration (FNA) negative for malignancy.

Key words: EUS, EUS-FNA, pancreatic cancer screening, pancreatic cystic lesions, quality of life

INTRODUCTION

Pancreatic cancer (PC) is one of the leading causes of cancer-related mortality.[1] The estimated incidence and mortality of this disease are almost equivalent, and the 5-year survival rate is <10%.[2]

There is an increasing global interest in screening programs aimed to detect precursor lesions or PC in an early and potentially curable stage. Most screening programs are currently based on EUS and magnetic

Access this article online

Quick Response Code:

Website: www.eusjournal.com

DOI: 10.4103/eus.eus_56_19

How to cite this article: Cazacu IM, Luzuriaga Chavez AA, Mendoza TR, Qiao W, Singh BS, Bokhari RH, *et al*. Quality of life impact of EUS in patients at risk for developing pancreatic cancer. Endosc Ultrasound 2020;9:53-8.

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Received: 2019-03-29; **Accepted:** 2019-07-10; **Published online:** 2019-09-25

resonance imaging (MRI). EUS is a minimally invasive imaging technique that allows for the examination of the gastrointestinal tract and organs in its proximity, and it plays a major role in the diagnosis of pancreatobiliary malignancies.[3] General population screening by any currently accessible method would imply an increased cost with a low yield. However, selective screening of high-risk individuals may be beneficial. 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.[4] Moreover, individuals with PC-associated gene mutations (such as STK11, p16, or BRCA1/2, ATM, PALB2, and PRSS1 gene) are also considered at increased risk. An international consensus recommended that these patients should be screened for PC.[4] A recent study showed improved short-term outcomes, including increased resectability and improved survival rates for patients with screening-detected PC.[5] However, an important concern is that a long-term survival benefit of the screening programs has not yet been proven and there is a limited number of progressors in large high-risk cohorts. These programs are therefore only available in a research setting and/or in specialized centers with high-volume pancreatic surgery, multidisciplinary teams, and well-defined screening protocols.[6]

Pancreatic cystic lesions (PCLs) are being detected in higher frequency due to the technological advances and the widespread use of cross-sectional imaging. The prevalence of pancreatic cysts detected incidentally varies from 2% on computed tomography scans[7] to 9.3% on 3T MRI of the abdomen.[8] With this increased rate of detection, comes the challenge of managing incidentally discovered PCLs. There are various proposed guidelines regarding the management and surveillance of these lesions.[9-13] Given the lethality of PC, the detection of a pancreatic cyst and awareness of its' associated cancer risk may create a significant amount of anxiety and fear.

The reduction of cancer-mortality rate is the primary determinant of benefits for any screening test. When assessing the success of a screening program, one should not only focus on clinical results but also on psychological aspects. Although the impact of EUS screening on survival is not yet fully known, participating in a screening program may yield positive outcomes including reductions in cancer fear or increase in feelings of reassurance, well-being, and improved quality of life (QOL).

The current knowledge about the impact of PC screening on patients' QOL is limited. Our group conducted a systematic review that addressed the psychological aspects of PC screening.[14] Most of the studies have evaluated the effects of screening on cancer-related distress and cancer worry in a high-risk population.[15-18] The findings indicated that the psychological burden of pancreatic surveillance is low, and participation in a PC screening program does not lead to an increase in risk perception, cancer fear, or general distress. However, some studies used study-specific, nonvalidated scales. Moreover, there is no data regarding changes in the overall QOL of the patients at high-risk for PC after undergoing invasive procedures such as EUS as a part of the screening program.

Thus, we conducted a cross-sectional survey study to clarify the psychological impact of EUS in patients with cystic lesions and individuals at risk for developing PC. We hypothesized that a benign EUS examination in these patients may result in less distress and improved QOL.

METHODS

Study population/sample

This single-center, cross-sectional study was approved by The University of Texas MD Anderson Cancer Center Institutional Review Board. Individuals at risk for developing PC who underwent EUS performed by a single endosonographer (Manoop S. Bhutani) at our institution between 05/2008 and 04/2018 were invited to participate in a survey study. All participants had genetic or familial factors that implicated elevated PC risk, as verified by medical records review. Specifically, asymptomatic individuals with (1) a family history of PC, (2) carriers of PC-prone germline mutations (BRCA1/2, PALB2, MMR, CDKN2A, STK11, PRSS1, TP53), and (3) EUS/EUS-FNA results negative for malignancy were included in the study.

Individuals with a known PCL who underwent EUS-FNA performed by a single endosonographer (MSB) between 01/2016 and 4/2018 were also included in the study. Eligible study participants were over the age of 18 years, did not have a previous PC diagnosis, the cystic lesions did not have any malignant features (such as mural nodules, solid component, or a dilated main pancreatic duct [PD] >10 mm) and EUS-FNA results were negative for malignancy.

Outcomes and instruments

Sociodemographic and clinical data

Data were obtained from medical records on age, sex, marital status, level of education, employment status, cancer history, family PC history, and genetic background.

Quality of life assessment

Participants were administered the brief profile of mood states (POMS) and the single-item linear analog scale assessment (LASA) QOL. The scale and questionnaire were chosen based on their known psychometric properties and clinical usefulness in evaluating distress and overall QOL.

The POMS was developed to assess affective traits, mood, and emotions. The POMS scale is the summary of 11-item questions, and each question is rated from 1 to 4. A higher score means a worse psychological output. The brief POMS-11 has demonstrated reliability and validity for assessing distress in cancer patients. There is evidence that supports the use of the brief form when general distress, an important aspect of QOL, is being investigated.[19]

Single-item questions LASA are the simplest approach to measure QOL. The LASA QOL is a single-item, subjective, and seven-point QOL measure. It is based on one item, and the score ranges from 1 to 7. The higher score means a better psychological outcome. It has been shown to be reliable and valid.[20]

Participants were contacted by phone and invited to take part in the study. After giving consent, they were asked to complete the above-mentioned measures regarding their pre- and post-EUS status for distress and QOL.

Statistical analysis

Signed-rank test (nonparametric statistical method for paired data) was used to assess differences between QOL scores before and after the EUS procedure. The difference was defined as the score after EUS subtracted by the score before the procedure. Wilcoxon rank-sum test was used to assess if there is any significant discrepancy between subgroups (*e.g.*, education subgroup, gender, family history, and employment status) regarding the score difference. All tests were two-sided and $P \leq 0.05$ was considered statistically significant. However, statistically significant results may not be clinically significant. In order to assess clinically meaningful changes in QOL scores, we have used the effect size (ES) method that expresses the magnitude of effect in terms of the distributional standard deviation (SD). It has been shown that a change of 0.5 of the SD of any health-related QOL tool can be considered clinically significant.[21] Statistical analysis was carried out using SAS version 9.4 (SAS Institute, Cary, NC, USA).

RESULTS

Characteristics of the study population

Of the 83 eligible individuals identified by reviewing medical records, only 40 individuals were successfully contacted by phone. All of them gave their consent to take part in the study.

As shown in Table 1, the mean age of the respondents was 56.40 (±10.91) years. Seventeen patients underwent EUS for the evaluation of a known PCL. Only one patient with a PCL had a mildly dilated main PD of the neck measuring 4.8 mm. All 17 of these patients underwent a EUS-FNA which was negative for malignancy. Twenty-three patients were at high risk for developing PC based on their familial and/or

Table 1. Main characteristics of the study population

	Total (%)
Age, mean±SD (range)	56.4±10.91 (31-76)
Gender	
Male	9 (22.5)
Female	31 (77.5)
Level of education	
Primary school/high school	15 (42.8)
College/university	20 (57.1)
Marital status	
Married/partner	28 (71.7)
Single/divorced/widowed	11 (28.2)
Genetic background	
Familial pancreatic cancer	18 (45)
Hereditary tumor syndromes	17 (55)
Hereditary tumor syndromes individuals	
BRCA2	9 (52.9)
BRCA1	2 (11.7)
P53	3 (17.6)
ATM	1 (5.8)
CDKN2A/p16	2 (11.7)
Personal history of cancer	
Yes	20 (50)
No	20 (50)
EUS indication	
Pancreatic cystic lesion	17 (42.5)
Pancreatic cancer screening	23 (57.5)

SD: Standard deviation

genetic background, and they underwent EUS as part of a PC screening program. No solid/cystic lesions and any potential targets for EUS-FNA were found in these patients. Most participants were female (75.7%), married (70%), employed (64.5%), and about 50% had attained a university degree.

Seventeen participants (43%) carried a proven PC-prone gene mutation and BRCA2 was the most frequently mutated gene (47%). Eighteen individuals (45%) had at least one relative who had been previously diagnosed with PC. Twenty respondents (50%) had a personal history of cancer [Table 1].

Linear analog scale assessment quality of life

There was a significant difference in patients' overall QOL assessed by the LASA QOL scale before and after the EUS procedure (mean difference 0.73, SD 1.76, $P < 0.01$). According to our results, participants tend to have a higher score after undergoing EUS [Table 2]. The ES was 0.58 in our group of patients, suggesting that the changes in QOL score were clinically significant.

Subgroup analysis was also performed. Regarding patients with cystic lesions, we found a significant increase in the LASA QOL scale after EUS (mean difference 0.65, SD 0.70, $P < 0.01$). The ES was 0.92, indicating clinically meaningful changes in the QOL for this particular group of patients. Similarly, individuals who underwent EUS as part of a PC screening program had statistically and clinically significant changes in the LASA QOL scale before and after the procedure (mean difference 0.78, SD 1.57, $P = 0.02$, ES = 0.5).

The brief profile of mood states

A significant difference in the brief POMS score was found before and after the EUS procedure (mean difference −5.46, SD −6.72, $P < 0.01$). According to our results, participants tend to have a lower score after undergoing EUS [Table 2]. The ES was 0.81, indicating that there were clinically meaningful changes in brief POMS score before and after EUS.

The subgroup analysis showed that for patients with cystic lesions, the mean difference in the score before and after the EUS was −6.06, SD 6.14, $P < 0.01$ with the ES of 0.99. In the PC screening group, the mean difference was −5.04, SD 7.22, $P < 0.01$ with an ES of 0.70.

There was no statistically significant association between the change in QOL scores and the participant demographic- and cancer-related characteristics. For example, for individuals, who had graduated university, the average change in single-item QOL score was 0.85 (median 0), while for those with primary education the average change in scores was 0.53 (median = 0). Although participants with college degree had a higher change of scores in average, it was not statistically significant (Wilcoxon rank-sum $P = 0.93$).

DISCUSSION

This study aimed to examine the psychological impact of undergoing EUS in patients at risk for developing PC and in patients with known PCL. The psychological impact was evaluated in terms of QOL and distress, using two validated tools. According to our results, there was a significant difference in QOL scores before and after a benign EUS examination. Although the impact of EUS screening on survival is not yet fully known, our study showed that the participants' QOL and distress improved after the procedure.

Our results are consistent with previous reports showing that participating in a PC screening program may yield positive outcomes including reductions in cancer fear or increase in feelings of reassurance and well-being in patients who are at risk for developing PC.[15,18,22]

Research and scientific evidence that PC screening is worthwhile is far behind compared with screening for other types of malignancies such as prostate, colon, or breast cancer. Another approach to evaluate the benefits of PC screening would be to consider its impact on the QOL of the participants. Individuals with a family

Table 2. Difference in quality of life scores before and after the EUS procedure

Variable	Median	Mean±SD	*P* value based on signed rank test	Effect size
Difference_LASA QOL	0	0.73±1.26	<0.01	0.73/1.26=0.58
Difference_brief-POMS	−3	−5.48±6.72	<0.01	5.48/6.72=0.81

The difference was defined as the score after EUS subtracted by the score before the procedure. QOL: Quality of life, SD: Standard deviation, POMS: Profile of mood states, LASA: Linear Analog Scale Assessment

history of PC and carriers of PC-associated gene mutations may overestimate their personal cancer risk and report increased cancer-related worries, leading to a reduced QOL. Our results showed the EUS procedure had a positive impact on the QOL of these individuals. In order to assess clinically meaningful changes in QOL scores, we have used the ES method. The ES was 0.50 for the single-item QOL scale and 0.70 for brief-POMS ($P = 0.04$) in the group of patients who underwent EUS as part of a PC screening program. Thus, even though the impact of EUS screening on survival is not known yet, there is a psychological benefit that clinicians should be aware of when considering EUS for these patients.

The role of EUS in the evaluation of PCL remains controversial, and various experts and guidelines[9-13] are still debating when to perform EUS-guided FNA. The international consensus guidelines published in 2006 (Sendai)[23] and later revised in 2017 (Fukuoka)[24] recommended EUS-FNA for cystic lesions with worrisome features on imaging (cyst size >3 cm, thickened cyst walls, main PD size of 5–9 mm, abrupt change in caliber of PD with distal pancreatic atrophy, and nonenhancing mural nodule) and surgical resection for cystic lesions with high-risk stigmata on abdominal imaging (main PD >10 mm, enhancing solid component within a cyst). On the other hand, the American Gastroenterological Association guidelines[13] recommended EUS-FNA for cysts with at least two high-risk features (size >3 cm, dilated main PD and the presence of an associated solid component). European guidelines[9] and ACG clinical guidelines[11] on pancreatic cystic neoplasms recommended EUS-FNA only for cases when the results are expected to change clinical management, or the diagnosis is unclear.

Our study is the first one to assess the psychological benefit of EUS-FNA in patients with PCLs. PC is one of the most dreaded diseases and compared to most other cancers, survival rates are much lower, and death occurs at a more rapid pace. Accordingly, having a cystic lesion in the pancreas can be frightening. The possibility of a PC diagnosis can cause significant emotional burden with a detrimental effect on individuals' QOL. Shieh *et al.*[25] investigated the cancer risk perception and anxiety levels in patients undergoing EUS evaluation of PCLs. They showed that 40% of these patients perceive a higher than expected risk of developing PC. Moreover, females and individuals who were highly concerned about their cystic lesion had increased anxiety scores. However, we could not find any prior study assessing the changes in the QOL of patients after undergoing EUS.

Our study found statistically and clinically significant changes in the QOL scores before and after the EUS-FNA, indicating that negative EUS-FNA results have led to an improved QOL and less distress for patients with PCLs undergoing the procedure. This is likely due to the widespread belief in the general and lays community that biopsy is the gold standard to rule out or diagnose malignancy when a lesion is detected.

Several limitations of this study are to be noted. First, the time between the EUS procedure and the date of filling in the questionnaire varied considerably in this study population. Second, the psychological background of the participants is unknown. Furthermore, the majority of participants were well-educated or females who may have more resources to cope with their high-risk status. Therefore, we cannot estimate the psychological impact in a lower educational attainment population. Finally, given the cross-sectional design of the study, the results should be interpreted with caution. However, we have conducted this study as a proof of concept and a starting point for prospective and longitudinal studies.

A particular strength of this study is the use of validated questionnaires to assess the overall QOL of patients at risk for developing PC who underwent a EUS procedure. Furthermore, this is the first study which evaluated the impact of EUS on the QOL of patients with PCLs. PCLs can generate patients' anxiety due to the potential risk of developing PC, perceived as a lethal condition in the general population. Our study has shown the negative EUS-FNA results in patients with PCLs have improved their overall QOL, which was affected by the fear of cancer and the anxiety caused by the cyst.

CONCLUSIONS

Our study showed that the EUS procedure with negative EUS/EUS-FNA results had a positive psychological impact in patients at high risk of developing PC or with PCLs, leading to an improved QOL. Psychological aspects such as fear, anxiety, and decreased QOL of these patients are probably not appreciated by physicians taking care of these patients. Our prospective study is expected to shed further light

on the psychological benefit of EUS as a screening and diagnostic test in these groups of patients.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

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