Pancreatic cyst surveillance imposes low psychological burden

Kasper A. Overbeek [a, *], Anne Kamps [a], Priscilla A. van Riet [a], Mariacristina Di Marco [b], Giulia Zerboni [c], Jeanin E. van Hooft [d], Silvia Carrara [e], Claudio Ricci [f], Tamas A. Gonda [g], Erik Schoon [h], Marcin Polkowski [i, j], Georg Beyer [k], Pieter Honkoop [l], Laurens A. van der Waaij [m], Riccardo Casadei [b], Gabriele Capurso [c, n], Nicole S. Erler [o], Marco J. Bruno [a], Eveline M.A. Bleiker [p], Djuna L. Cahen [a], On behalf of the PACYFIC study group

[a] Department of Gastroenterology & Hepatology, Erasmus University Medical Center, Rotterdam, the Netherlands
[b] Department of Specialized, Experimental and Diagnostic Medicine, Sant'Orsola-Malpighi Hospital, University of Bologna, Bologna, Italy
[c] Digestive and Liver Disease Unit, Sant'Andrea Hospital, Sapienza University of Rome, Rome, Italy
[d] Department of Gastroenterology & Hepatology, Amsterdam UMC, University of Amsterdam, Amsterdam, the Netherlands
[e] Department of Gastroenterology, Digestive Endoscopy Unit, Humanitas Clinical and Research Center, IRCCS, Rozzano, Italy
[f] Department of Medical Science and Surgery, Alma Mater Studiorum-University of Bologna, Bologna, Italy
[g] Division of Digestive and Liver Diseases, Department of Medicine, Columbia University Medical Center, New York, USA
[h] Department of Gastroenterology & Hepatology, Catharina Hospital, Eindhoven, the Netherlands
[i] Department of Gastroenterological Oncology, The M. Skłodowska-Curie Memorial Cancer Centre, Warsaw, Poland
[j] Department of Gastroenterology, Center of Postgraduate Medical Education, Warsaw, Poland
[k] Department of Medicine II, University Hospital, LMU Munich, Germany
[l] Department of Gastroenterology, Albert Schweitzer Hospital, Dordrecht, the Netherlands
[m] Department of Gastroenterology & Hepatology, Martini Hospital, Groningen, the Netherlands
[n] PancreatoBiliary Endoscopy and EUS Division, Pancreas Translational and Clinical Research Center, San Raffaele Scientific Institute IRCCS, Milan, Italy
[o] Department of Biostatistics, Erasmus University Medical Center, Rotterdam, the Netherlands
[p] Division of Psychosocial Research and Epidemiology & Family Cancer Clinic, The Netherlands Cancer Institute, Amsterdam, the Netherlands

ARTICLE INFO

ABSTRACT

Background/Objectives: For the currently recommended pancreatic cyst surveillance to be feasible, participant adherence is a prerequisite. Our objective was to evaluate the psychological burden of pancreatic cyst surveillance from a participant's perspective.
Methods: The present participant survey is part of an international cohort study (PACYFIC study, www.pacyfic.net), which prospectively records the outcome of surveillance of asymptomatic pancreatic cysts. Participants are invited to complete questionnaires before and during cyst surveillance.
Results: 109 participants, 31 enrolled before and 78 during surveillance (median time since cyst diagnosis 16.5 (IQR 36) months), returned a total of 179 questionnaires. The majority indicated that surveillance reduces concerns of developing pancreatic cancer (82%), gives a sense of certainty (81%) and is a good method to detect cancer (91%). Participants already undergoing surveillance reported more negative aspects than those still to commence, like sleeping worse (30% vs 13%, P = 0.035), postponing plans (32% vs 13%, P = 0.031), and finding the follow-up burdensome (33% vs 13%, P = 0.044). Overall, the vast majority (94%) deemed advantages to outweigh disadvantages. Anxiety and depression scores were low (median Hospital Anxiety and Depression Scale 4 for anxiety (IQR 6), 2 for depression (IQR 5)).
Conclusion: The psychological burden of pancreatic cyst surveillance is low. Therefore, participant adherence is expected to be high and annual surveillance seems feasible.
© 2019 IAP and EPC. Published by Elsevier B.V. All rights reserved.

Introduction

Asymptomatic pancreatic cysts are an increasingly common finding in this time of accessible and advanced imaging. Their

* Corresponding author. Doctor Molewaterplein 40, 3015 GD, Rotterdam, the Netherlands.
E-mail address: k.overbeek@erasmusmc.nl (K.A. Overbeek).

prevalence in the general population is reported to be as high as 49% and increases with age [1]. Because neoplastic pancreatic cysts are at risk of progressing into malignancy, European [2], American [3,4], and International [5] guidelines all recommend long-term, yearly surveillance with MRI/MRCP and/or endoscopic ultrasound, although the efficacy in reducing pancreatic cancer-related mortality remains to be established. As a result, a growing number of individuals is subjected to yearly surveillance of unclear benefit and burden.

The World Health Organization has formulated criteria that should be met before a population screening program is instituted. One of the original criteria by Wilson and Jungner, is that a screening test must be acceptable to the population [6]. Another important criterion, that emerged later, is that the overall benefits of surveillance should outweigh any physical and psychological harm, associated with the program [7]. Psychological harm may include the burden of the examination and an increased awareness of being at risk of developing pancreatic cancer, resulting in stress and anxiety.

The psychological impact of pancreatic cyst surveillance is unknown. Pancreatic cancer patients have an over five-fold increased odds of being depressed, as compared to the general population [8]. It is conceivable that the presence of a pancreatic cyst and awareness of its' associated cancer risk similarly lead to increased anxiety and depression. Psychological distress could decrease participants' adherence to surveillance and counterbalance its' possible benefits. Feasibility from a participants' perspective is therefore a prerogative for successful surveillance. The aim of this study is to assess possible positive and negative aspects of cyst surveillance, as perceived by participants, to objectify the effect of surveillance on anxiety and depression, and to determine participants' preferences regarding surveillance frequency and duration.

Methods

Study design and population

The present study is a side study of the PACYFIC study (Pancreatic CYst Follow-up: an International Collaboration, www.pacyfic.net), a multicenter observational cohort study, including 43 university and non-university hospitals worldwide. It prospectively records the outcome of pancreatic cyst surveillance, as performed according to current clinical guidelines [2,3,5]. Eligible are individuals with a pancreatic cyst requiring follow-up according to their treating physician. They are enrolled at the time of cyst diagnosis, during the course of surveillance, or after surgery for an intraductal papillary mucinous neoplasm (IPMN). The primary objective is to establish the yield of pancreatic cyst surveillance and to identify the most effective and cost-effective surveillance strategy. One of the secondary objectives is to assess the psychological impact of cyst surveillance on participants.

The PACYFIC study has been approved by the institutional review board of the Erasmus University Medical Center in 2014 (MEC-2014-021) and participating centers, and is registered in the Dutch Trial Register under NTR4505 (www.trialregister.nl). All participants have given written informed consent prior to enrollment. The study was executed conform the Declaration of Helsinki.

Psychological questionnaires

The PACYFIC study uses an online, electronic system to register patient data and visits. When a physician registers a new participant or a follow-up visit, and the patient has provided their e-mail address, the system automatically sends out a patient questionnaire by e-mail. Participants who fail to respond are reminded by e-mail every 2 weeks up to 3 times. At the time of this study, questionnaires were installed in Dutch and Italian, thus participants from the Netherlands and Italy were invited to complete questionnaires.

Questionnaire

The first part of the questionnaire concerns questions regarding lifestyle, personal history, and familial history on malignancies and pancreatic diseases. Second, participants are asked to review statements on possible positive and negative aspects of surveillance [9]. For example, whether surveillance leads to a reduction of concerns about developing pancreatic cancer, conveys a sense of safety, leads to unnecessary worries, or creates discomfort. Possible answers range on a 5-point scale from 'Strongly agree' to 'Strongly disagree', or on a 4-point scale from 'Not at all' to 'Very much'. Third, participants are asked about their experience with the imaging modalities and their preferred frequency of follow-up visits, as well as their attitude towards duration and discontinuation of surveillance.

Anxiety and depression scales

Patients are asked to fill out the Hospital Anxiety and Depression Scale (HADS). The HADS is a validated and reliable tool that consists of the subscales anxiety (HADS-A) and depression (HADS-D), each with 7 items to be scored from 0 to 3 [10–12]. The total score for each subscale ranges from 0 to 21, and although there is no specific cut-off, a score >8 reflects a high level of general anxiety or depression and is generally considered clinically significant [12]. In this study, Cronbach's alpha showed good internal consistency for both subscales (0.84 for HADS-A and 0.80 for HADS-D).

Statistical analysis

Descriptive statistics are presented as means with standard deviation or medians with interquartile range, depending on distribution, and as frequencies and percentages in case of categorical data. Participants were divided in three groups, based on the duration of surveillance (before initiation, ≤2 years and >2 years). To assess differences in attitude towards surveillance between groups, we used the Chi-square test. We performed the Cronbach's Alpha on internal consistency on the HADS-A and HADS-D to assure reliability. To compare HADS scores, we used the Mann-Whitney U test for two groups, and the Kruskal Wallis test for more than two. Possible risk factors for increased anxiety or depression were analyzed using a generalized linear mixed model with a Poisson distribution and a log-link function. Factors of possible influence were added as fixed effects, including age, gender, nationality, smoking, alcohol use, diabetes, personal cancer history and familial pancreatic cancer history. A Bonferroni correction was incorporated in the model to correct for multiple testing. For all analyses except the mixed model, we only included the first questionnaire per participant, as only half of participants had already been invited to fill out multiple questionnaires at this time. In the generalized linear mixed model for increased anxiety and depression scores, we analyzed all questionnaires with complete HADS-A and HADS-D subscales, thereby including multiple questionnaires per patient. Correlation between repeated measures within the same patient was taken into account by a random patient-specific intercept, and time since cyst diagnosis was added as a fixed effect covariate. We used SPSS Statistics 22 (IBM Corporation, Armonk, New York, USA) for all statistical analyses.

Results

Study population

By July 2018, 11 Dutch and 2 Italian centers were participating in the psychological questionnaire study-arm. In these centers, 143 participants had provided their e-mail address and 109 returned a total of 179 questionnaires (response rate to first questionnaire 76%, some participants had already returned questionnaires after two or three visits). Their median age was 68 (IQR 13) years, 39 (36%) were male, 68 (62%) Dutch and 41 (38%) Italian. At the moment of the first questionnaire, the median time since cyst diagnosis of the total cohort was 16.5 (IQR 36) months. 31 (28%) participants were included in the study prior to initiation of surveillance (median 5 (IQR 5) months after diagnosis), 39 (36%) within two years of having started surveillance (median 14 (IQR 9) months after diagnosis), and 39 (36%) after having undergone already two or more years of surveillance (median 58 (IQR 38) months after diagnosis).

The median size of the participants' largest cyst was 15 (IQR 13) mm. Most subjects were followed for a presumed branch-duct IPMN (79%), an unspecified cyst (10%), or a mixed-type IPMN (6%). One participant was under surveillance for a presumed mucinous cystic neoplasm, one had a main duct-IPMN, but had refused surgery, and one was under surveillance after surgery for IPMN. Eight (7%) participants reported a family history of pancreatic cancer. There were no differences in demographics between respondents and non-respondents. The complete baseline characteristics are shown in Table 1.

Attitude towards surveillance

Regarding positive effects of cyst surveillance, of the total group of respondents (N = 109), the majority 'Agreed' or 'Strongly agreed' that surveillance reduces their concerns of developing pancreatic cancer (82%), gives them a sense of certainty (81%), and is a good method to detect cancer (91%). 74% stated cyst surveillance 'Rather' or 'Very much' conveys a sense of safety. For these statements, we found no differences in the levels of agreement between individuals who were to commence (N = 31) and those already undergoing surveillance (N = 78). Also, there was no difference between those who underwent less or more than 2 years of surveillance (both groups N = 39, see Fig. 1, all P-values >0.100).

Negative aspects were experienced less often than the positive aspects. Within the overall group of 109 respondents, cyst surveillance created discomfort in 11%, led to worries in 13%, and was burdensome for 28%. The next visit was dreaded by 28%, and 25% slept less well before a visit, 30% were nervous, and 26% postponed plans until after the visit. Compared with participants who had not commenced yet, those already under surveillance reported more often to sleep less well before the visit (30% versus 13%, P = 0.035), to postpone plans until after the visit (32% versus 13%, P = 0.031), and to find the follow-up burdensome (33% versus 13%, P = 0.044). This was uninfluenced by the duration of surveillance, less or more than 2 years (all P-values >0.300).

When asked if participants felt overall advantages of cyst surveillance outweigh disadvantages, the vast majority (94%) of those already under surveillance agreed 'Somewhat' (17%), 'Rather' (44%) or 'Very much' (33%). This was not different for those still to commence (P = 0.331), and uninfluenced by the duration of surveillance (P = 0.680).

Anxiety and depression

The total group of respondents reported low overall anxiety and depression scores (median 4 (IQR 6) for anxiety, median 2 (IQR 5) for depression, scores stratified by cyst surveillance duration shown

Table 1
Baseline characteristics of respondents and non-respondents.

Patient characteristics	Respondents (N = 109)	Non-respondents (N = 34)	P-value
Age, median (IQR), y	68 (13)	68 (17)	0.661
Male gender	39 (36)	16 (47)	0.238
Caucasian	104 (95)	30 (88)	0.721
Country			0.948
Netherlands	68 (62)	21 (62)	–
Italy	41 (38)	13 (38)	–
Current tobacco use	17 (16)	3 (9)	0.320
Current alcohol use	53 (49)	–	–
Pancreatic symptoms[†]	16 (15)	8 (24)	0.228
Diabetes mellitus	15 (14)	6 (18)	0.590
History of colon, breast, or prostate cancer	16 (15)	5 (15)	0.997
Self-reported medical history			
Pancreatitis	9 (8)	–	–
Family history of pancreatic cancer	8 (7)	–	–
Cyst and surveillance characteristics			
Largest cyst diameter, median (IQR), mm	15.0 (13)	15.5 (9)	0.717
Working diagnosis			0.964
Unspecified cyst	11 (10)	4 (12)	–
Branch-duct IPMN	86 (79)	28 (82)	–
Mixed-type IPMN	6 (6)	2 (6)	–
Main-duct IPMN	1 (1)	0 (0)	–
Operated IPMN, no cysts in remnant pancreas	1 (1)	0 (0)	–
Mucinous cystic neoplasm	1 (1)	0 (0)	–
Unknown	3 (3)	0 (0)	–
Months since diagnosis, median (IQR)	16.5 (36)	10.5 (41)	0.183
Modalities used within 6 months prior to inclusion			
MRI/MRCP	94 (86)	27 (79)	0.335
EUS	53 (49)	18 (53)	0.660

Values presented as n (%) unless otherwise indicated; [†]Possible symptoms included epigastric pain, recurrent acute pancreatitis, steatorrhea, weight loss, or non-specific abdominal pain; SD, standard deviation; IPMN, intraductal papillary mucinous neoplasm; MRI/MRCP, magnetic resonance imaging/magnetic retrograde cholangiopancreatography; CT, computational tomography; EUS, endoscopic ultrasound; FNA, fine needle aspiration.
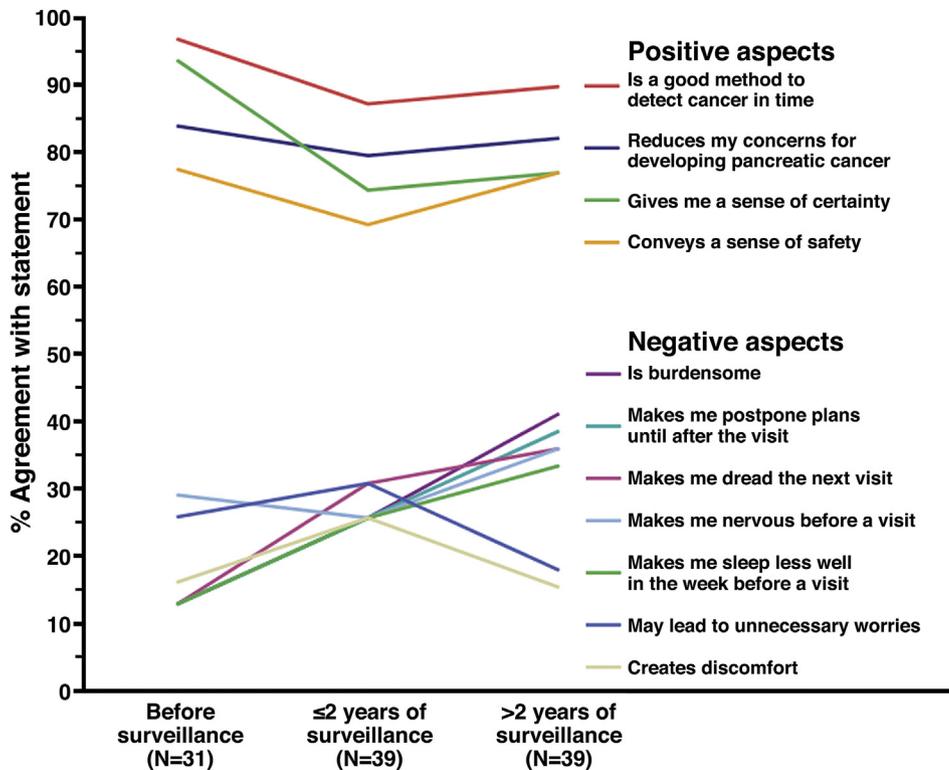
Fig. 1. Attitude towards cyst surveillance, in percentage of respondents who 'Agreed' or 'Strongly agreed' with the statement or experienced the stated effect 'Rather' or 'Very much', stratified by duration of cyst surveillance.

in Fig. 2). Independently associated with a higher anxiety score were female gender (coefficient 0.426, 95% CI 0.063–0.789) and Italian nationality (coefficient 0.524, 95% CI 0.149–0.898). Time since cyst diagnosis was not associated with higher anxiety or depression, neither were age, smoking, alcohol use, diabetes, a history of cancer, or a family history of pancreatic cancer (Table 2).
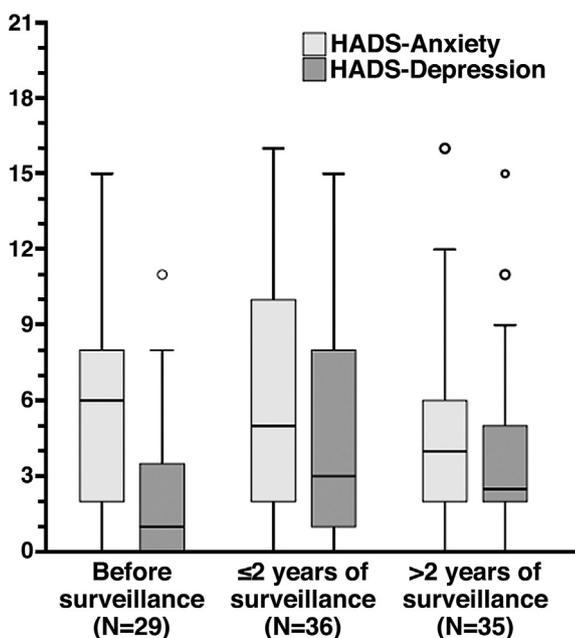

Fig. 2. Median Hospital Anxiety and Depression Scale (HADS) scores stratified by duration of cyst surveillance.

Attitude and preferences regarding follow-up

Of those who had undergone endoscopic ultrasound (EUS, N = 53), 19% reported to dread the next EUS 'Quite' or 'Very much'. The opinion on MRI was similar; of the 94 participants who had undergone MRI, 13% dreaded the next MRI. For both modalities, opinions were no different before or during surveillance (P = 0.488 for EUS, and P = 0.334 for MRI).

When asked about their preferred surveillance interval, 86 (80%) participants chose to be followed every 6 or 12 months. Fig. 3 shows the distribution of desired surveillance intervals. With regard to surveillance duration, 75 (69%) participants wish to undergo life-long surveillance. The other participants prefer to undergo surveillance for 10 years (9%), 5 years (10%), 2 years (8%), or another duration (3%). There was no difference in preferred surveillance interval (P = 0.335) or surveillance duration (P = 0.720) between the three surveillance duration groups. When asked how they would feel if cyst follow-up would no longer be advised, because their risk of developing pancreatic cancer was too low, 19 (18%) participants answered they would no longer be worried or wish to be checked. A larger group of 46 (43%) would remain worried and would like to continue follow-up, and 43 (40%) did not know how they would feel.

Discussion

In our study, the vast majority of participants reported a positive attitude towards surveillance and objectively measured general anxiety and depression scores were low and remained unchanged. At the same time, a substantial part of up to 33% of participants also experienced negative aspects of surveillance. For several negative aspects, this was significantly higher than what participants expected before the start of surveillance. Despite these negative

Table 2
Risk factors for increased anxiety and depression scores.

Risk factor	Anxiety (N = 164[a])			Depression (N = 172[b])		
	Coefficient	95% CI	P-value[c]	Coefficient	95% CI	P-value[c]
Age	0.000	−0.021−0.021	0.999	0.025	−0.001−0.052	0.063
Female gender	**0.426**	**0.063−0.789**	**0.022**	0.210	−0.244−0.663	0.362
Italian origin	**0.524**	**0.149−0.898**	**0.006**	0.430	−0.040−0.900	0.073
Current smoker	0.143	−0.318−0.604	0.541	0.296	−0.295−0.887	0.323
Current alcohol use	0.086	−0.259−0.431	0.624	−0.111	−0.551−0.329	0.619
Diabetes mellitus	−0.184	−0.710−0.341	0.490	−0.042	−0.663−0.579	0.894
History of colon, breast, or prostate cancer	−0.019	−0.464−0.427	0.934	−0.311	−0.886−0.263	0.286
Family history of pancreatic cancer	−0.162	−0.818−0.493	0.626	−0.540	−1.386−0.306	0.209
Time since cyst diagnosis	−0.003	−0.009−0.002	0.210	−0.000	−0.007−0.006	0.942

Bold text indicates a statistically significant independent association with increased anxiety scores.
[a] 15 questionnaires excluded due to incomplete HADS-A subscale.
[b] 7 questionnaires excluded due to incomplete HADS-D subscale.
[c] P-values adjusted for multiple testing. CI, Confidence Interval.
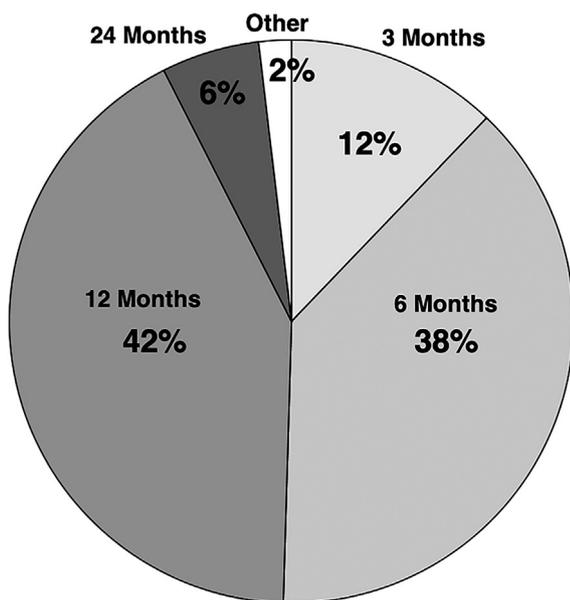

Fig. 3. Preferred surveillance intervals (N = 109).

aspects, 94% of those undergoing surveillance deemed advantages to outweigh disadvantages, and participants were willing to be checked frequently and for a long period of time. Therefore, we deem the psychological burden of pancreatic cyst surveillance to be relatively low and acceptable from a participant's perspective.

To our knowledge, this is the first study to assess the psychological impact of surveillance on patients with a pancreatic cyst. Two previous, cross-sectional studies investigated a pancreatic cyst population, but did not assess the impact of surveillance. Verma et al. [13] measured HADS scores in 100 cyst patients, and found the same, low median scores (4 (range 1−6) for anxiety and 2 (range 1−4) for depression). However, it was unclear if their patients were enrolled in a surveillance program, as 13% was even unaware they had a cyst, 31% was not evaluated by a specialist, and 5% had already undergone surgery. The second study concerned 47 individuals referred to a tertiary referral center for EUS evaluation. Using the State-Trait Anxiety Inventory, they found 23% experienced "a lot" of stress due to their cyst [14]. However, their population had a mean cyst size of 18.6 mm, and >30% of them reported abdominal pain. Thus, this may represent a selection of patients with higher-risk lesions. It is unsure if these results can be extrapolated to the general pancreatic cyst population, of which the majority has a

small, asymptomatic, presumed low-risk cyst.

Similar studies have been performed in asymptomatic individuals with an inherited high risk of pancreatic cancer, some of them by our own group. Although the estimated cancer risk is much higher in these individuals, they provided similar low and unaffected HADS scores (mean 4.5 (SD 3.7) for anxiety and 2.8 (SD 3.2) for depression) [9,15]. Another study showed that in these individuals with inherited high risk, the detection of a pancreatic cystic lesion did not lead to a significant increase in cancer worries [16].

Female gender and Italian nationality were identified as risk factors for increased anxiety. However, these effects are not confined to patients under pancreatic cyst surveillance. Female gender has been identified as a risk factor for distress in individuals with a specific inherited risk for gastrointestinal cancers [17], but also for anxiety in the general population [18,19], and can therefore be considered a common demographic factor. Italian nationality being a risk factor could very well be a reflection of a difference in reference data of the general population. Normative data of the Netherlands shows a mean anxiety score of 3.9 in this age category [11], whereas in Italy this is 8.0[19]. It may be seen as a strength that we identified these known risk factors, as it shows that our data had enough power to identify multiple risk factors. This is not surprising, because we used a statistical method that is appropriate for investigating multiple factors and that incorporates repeated measurements, utilizing the full potential of our dataset.

When we evaluated participants' opinion of imaging modalities, we found that some dreaded to undergo the examination (19% for EUS, 13% for MRI). These percentages are somewhat higher than those found by Konings et al. in a high-risk population (6−9% for EUS, 0−8% for MRI) [9]. We have no obvious explanation for this, but it could be that a high-risk population experiences the examinations as less burdensome, because of their willingness to undergo surveillance, often based on the experience of first-degree family members dying of pancreatic cancer. Also, Konings et al. found that dreading the test decreased with each subsequent visit. Because our cohorts' median time since cyst diagnosis is 16.5 (IQR 36) months, we may find similar percentages after longer follow-up. Longer follow-up will also enable us to investigate if participants prefer EUS or MRI. Currently this was not possible, as too few participants had undergone both modalities.

Additionally, with more and longitudinal data, we will be able to assess the cultural differences between a larger number of countries, intra-individual changes over time on all questionnaire aspects, and the impact of worrisome features on the psychological burden. Also, in time, we will be able to determine the long-term impact of cyst surveillance, including if the experience of

negative aspects remains high or will even increase further. Investigation of the long-term impact is of great importance, because cysts are highly prevalent in the general population and the currently recommended surveillance entails a life-long program with repeated investigations.

Strengths of this study are its' prospective and international design, and the use of an extensive questionnaire that includes a validated instrument, has a focus on the participants' preferences, and was written in their native language. Additionally, the response rate was high, which resulted in a large study population that is likely to be representative of pancreatic cyst patients, as encountered in regular clinical practice.

A pitfall, intrinsic to questionnaire research, is selection bias. In this study, we were unable to assess the attitude towards surveillance of those patients who did not participate in the PACYFIC study or did not provide their e-mail address. A selection bias within those invited to complete questionnaires can be deemed unlikely, because of our high response rate, and because we did not find meaningful differences in demographics between responders and non-responders. A second possible limitation is that, as with all psychological studies, it is difficult to objectify the psychological burden in numbers and it is influenced by many factors we could not take into account, such as participants' knowledge of their cyst. A previous study demonstrated there may be a substantial gap in patients' knowledge of their type of cyst and its' potential consequences and implications [13], which could lead to a different perception of the necessity or advantages of surveillance. To incorporate this in the future, the PACYFIC questionnaire has been adjusted and now also assesses what patients know of their cyst type and associated potential consequences. In addition, there are other possibly influential factors that require evaluation. The prevalence of anxiety disorders, for instance, varies depending on gender, age, culture, and economic status [20]. We corrected our anxiety and depression model for gender, age and country, but factors like socioeconomic status, individual resilience and the used coping strategies have not been accounted for, while they are important to consider participants in their entirety. Although, it must be noted that the anxiety and depression scores in our study were low and showed little variety, thereby decreasing the possible effect size of these confounders.

In summary, we consider the psychological burden of cyst surveillance to be low. Participants report a highly positive attitude towards surveillance, desire to undergo regular and long-term follow-up, and demonstrate low anxiety and depression scores, despite the experience of negative aspects. Therefore, based on these results, pancreatic cyst surveillance seems feasible from a participants' perspective, and adherence is predicted to be high.

Acknowledgements

References

[1] Kromrey ML, Bulow R, Hubner J, Paperlein C, Lerch MM, Ittermann T, et al. Prospective study on the incidence, prevalence and 5-year pancreatic-related mortality of pancreatic cysts in a population-based study. Gut 2018;67: 138–45.
[2] European evidence-based guidelines on pancreatic cystic neoplasms. Gut 2018;67:789–804.
[3] Vege SS, Ziring B, Jain R, Moayyedi P. Clinical Guidelines C, American Gastroenterology A. American gastroenterological association institute guideline on the diagnosis and management of asymptomatic neoplastic pancreatic cysts. Gastroenterology 2015;148:819–22.
[4] Elta GH, Enestvedt BK, Sauer BG, Marie Lennon A. Acg clinical guideline: diagnosis and management of pancreatic cysts. Am J Gastroenterol 2018;113: 464–79.
[5] Tanaka M, Fernandez-Del Castillo C, Kamisawa T, Jang JY, Levy P, Ohtsuka T, et al. Revisions of international consensus fukuoka guidelines for the management of ipmn of the pancreas. Pancreatology : Off J Int Assoc Pancreatol (IAP) [et al] 2017;17:738–53.
[6] Wilson JMG, Jungner G. Geneva. In: WHO, editor. Principles and practice of screening for disease; 1966. Available from: http://apps.who.int/iris/handle/10665/208882.
[7] Andermann A, Blancquaert I, Beauchamp S, Dery V. Revisiting wilson and jungner in the genomic age: a review of screening criteria over the past 40 years. Bull World Health Organ 2008;86:317–9.
[8] Hartung TJ, Brahler E, Faller H, Harter M, Hinz A, Johansen C, et al. The risk of being depressed is significantly higher in cancer patients than in the general population: prevalence and severity of depressive symptoms across major cancer types. Eur J Cancer 2017;72:46–53 (Oxford, England : 1990).
[9] Konings IC, Sidharta GN, Harinck F, Aalfs CM, Poley JW, Kieffer JM, et al. Repeated participation in pancreatic cancer surveillance by high-risk individuals imposes low psychological burden. Psycho Oncol 2016;25:971–8.
[10] Zigmond AS, Snaith RP. The hospital anxiety and depression scale. Acta Psychiatr Scand 1983;67:361–70.
[11] Spinhoven P, Ormel J, Sloekers PP, Kempen GI, Speckens AE, Van Hemert AM. A validation study of the hospital anxiety and depression scale (hads) in different groups of Dutch subjects. Psychol Med 1997;27:363–70.
[12] Bjelland I, Dahl AA, Haug TT, Neckelmann D. The validity of the hospital anxiety and depression scale. An updated literature review. J Psychosom Res 2002;52:69–77.
[13] Verma D, Kwok KK, Wu BU. Patient preferences for management of cystic neoplasms of the pancreas: a cross-sectional survey study. Pancreas 2017;46: 352–7.
[14] Shieh FK, Siddiqui UD, Padda M, Dharan M, Rossi F, Aslanian HR. Anxiety and perception of cancer risk in patients undergoing endoscopic ultrasonography for pancreas cystic lesions. Pancreas 2013;42:548–9.
[15] Cazacu IM, Luzuriaga Chavez AA, Saftoiu A, Bhutani MS. Psychological impact of pancreatic cancer screening by eus or magnetic resonance imaging in high-risk individuals: a systematic review. Endosc Ultrasound 2019 Jan-Feb;8(1): 17–24. https://doi.org/10.4103/eus.eus_25_18. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6400091/.
[16] Konings IC, Harinck F, Kuenen MA, Sidharta GN, Kieffer JM, Aalfs CM, et al. Factors associated with cancer worries in individuals participating in annual pancreatic cancer surveillance. Fam Cancer 2017;16:143–51.
[17] Gopie JP, Vasen HF, Tibben A. Surveillance for hereditary cancer: does the benefit outweigh the psychological burden?–a systematic review. Crit Rev Oncol-Hematol 2012;83:329–40.
[18] Faravelli C, Alessandra Scarpato M, Castellini G, Lo Sauro C. Gender differences in depression and anxiety: the role of age. Psychiatry Res 2013;210: 1301–3.
[19] Iani L, Lauriola M, Costantini M. A confirmatory bifactor analysis of the hospital anxiety and depression scale in an Italian community sample. Health Qual Life Outcomes 2014;12:84.
[20] Baxter AJ, Scott KM, Vos T, Whiteford HA. Global prevalence of anxiety disorders: a systematic review and meta-regression. Psychol Med 2013;43: 897–910.