Challenging dogmas in pancreatic surgery: biliary drainage, outcome and beyond
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Long-Term Outcome after Resection of Pancreatic Cystic Neoplasms; Health-Related Quality of Life, Pancreatic Function and Survival

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Submitted
ABSTRACT

Background
Resection is selectively indicated for pancreatic cystic neoplasia due to malignant potential. Long-term quality of life (QOL) should be considered a vital outcome in patients who underwent resection of primary cystic neoplasia of the pancreas, since difficulty in preoperative differentiation can lead to resection of benign lesions. We investigated these patient reported outcomes, medical outcomes and survival.

Methods
We reviewed 108 consecutive patients who underwent resection of a primary cystic lesion between 1992 and 2007. Questionnaires were sent to participating patients, and function tests were prospectively collected during scheduled home or outpatient clinic visits.

Results
Twenty-nine (27%) patients had undergone resection of (borderline) malignancy, 77 (73%) of a benign lesion. After a median follow-up of 59 (IQR 36-103) months 20 patients had died. Five year overall survival was 94% for benign and 62% for malignant neoplasia. Of 88 remaining patients 65 (74%) completed questionnaires. Physical and mental QoL scores were equal or better compared to healthy references. None of the disease-specific symptom scales were above mean 50, implicating none to mild complaints. Independent predictors for good health at follow-up were young age (P<.05), and resected malignacy (P<.05), while for good gastrointestinal QoL male gender (P<.1), limited resection (P<.05), endocrine insufficiency (P<.05), and employment (P<.05) were significant predictors. Prevalence for endocrine insufficiency was 40%, and 59% for exocrine insufficiency.

Conclusions
After resection of a primary cystic neoplasm of the pancreas patients report long-term QoL outcomes equal to healthy individuals, pancreatic insufficiency is prevalent, but does not impair QoL, and survival relates positive compared to solid adenocarcinoma of the pancreas. This excellent outcome justifies proceeding with surgery once a medical indication for resection has been established.
INTRODUCTION

Pancreatic cystic lesions are increasingly identified due to the use of more advanced cross-sectional imaging. These findings occur frequently by coincidence. The prevalence of pancreatic cysts in an unselected, asymptomatic series of individuals is around 2.4%, and probably rising for the aging of the population. Cystic neoplasia of the pancreas can be congenital, inflammatory, or neoplastic. The large majority of the cystic lesions are benign and deserve no medical attention unless symptomatic, while only a small proportion comprise primary cystic neoplasia with malignant potential. Radical resection is the accepted treatment for this category.

The diagnostic work-up for pancreatic cystic neoplasia is not well defined and poses a clinical challenge; preoperative differentiation with benign lesions is complicated, in particular if solid components are present. Timing of the clinical decision to operate pancreatic cysts, ensuing from difficulty in preoperative differentiation and the low pretest likelihood for malignancy, is another dilemma. The fear for withholding patients with malignant lesions or benign lesions with malignant potential a curative resection is the justification of an aggressive surgical approach. However, an aggressive surgical strategy inevitably results in resected benign lesions. Large contemporary series of patients who underwent resection under the assumption of bearing a (pre)malignant lesion, report figures from around 30 up to 80% of resected lesions appearing to be benign without malignant potential, e.g. serous cystadenoma, pseudocyst, retention cyst, at pathological examination.

Undisputedly surgical morbidity and mortality, as well as long-term survival, are crucial parameters following any surgical procedure carried out for a (suspected) malignancy. However, in a population with an anticipated high rate of resected benign lesions we consider long-term general and disease-specific quality of life (QoL) as another vital outcome measure. Surprisingly, studies that report long-term QoL in addition to survival, specifically following primary pancreatic cyst resection, are scarce. Another, frequently neglected, aspect of operative treatment for cystic pancreatic neoplasia is the iatrogenic consequence of potentially inducing pancreatic insufficiency and its effect on long-term QoL.

Although a number of series report resection rates, malignancy rates, and survival figures following resection of pancreatic cysts no series to our knowledge exist that report these long term patient reported outcomes. We evaluated long-term general and disease-specific QoL, prevalence of pancreatic insufficiency and survival. In addition we analyzed potential predictors of outcome after (partial) resection.

GIQLI, Gastrointestinal Quality of Life Index
IPMN, intraductal papillary mucinous neoplasm
SF-36, Short Form-36
QoL, quality of life
QLQ-C30, Quality of Life Questionnaire C30
QLQ-PAN26, Quality of Life Questionnaire Pancreas 26
METHODS

Patient Population
A consecutive series of 108 patients who had undergone a surgical procedure for a pathologically proven primary cystic neoplasm in the period January 1992-June 2007 were selected for the present study. Procedures included (pylorus-preserving) pancreatoduodenectomy, left-sided, central or total pancreatectomy, depending on localization and extent of the lesion. Clinicopathological data of patients undergoing pancreatic surgery at the Academic Medical Center are permanently collected in a prospective database.

Clinical Data
We assessed postoperative surgical complications according to definitions published previously and the generally accepted international study group criteria.14-17 In-hospital mortality was defined as death during hospital stay, including death during readmission within 30 days after discharge. For follow-up investigation general practitioners were contacted for patient’s present health status. Alive patients were contacted for participation and asked to complete various questionnaires prior to a single prospective visit to the outpatient clinic. Patients not able to visit the outpatient clinic were offered to be visited at home by one of the investigators. The questionnaires were mailed to patients’ homes to avoid observer bias.

To evaluate medical consequences of surgery fasting blood glucose (FBG) was determined at the time of the outpatient clinic visit. Endocrine insufficiency was defined as a FBG level >6.7 mmol per liter (121 mg per deciliter) or when receiving prescription antidiabetic medication (insulin, oral medication) for previously diagnosed diabetes mellitus, regardless of FBG level. Glycemic control by antidiabetic medication was considered adequate when the glycated hemoglobin level was <7%. Exocrine insufficiency was defined as a feces elastase level of less than 200 μg per gram of feces (100-200: moderate; <100 severe), as described by the manufacturer of the test. Use of pancreatic enzyme replacement therapy was recorded.

Health-Related Quality of Life
We included the Short Form-36 (SF-36) to evaluate generic QoL, whose 36 items are combined to form 8 domains: physical functioning, role-physical, bodily pain, general health perception, vitality, social functioning, role-emotional, and mental health.18 The domains can be summarized into two core dimensions, a composite physical and mental score. The European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire C30 (QLQ-C30) and its pancreas module (QLQ-PAN26) were used as generic and disease-specific QoL instruments.19,20 The QLQ-C30 and of the QLQ-PAN26 comprise an overall global health score, and several function and symptom scores, linearly transformed to a scale of 0–100. For disease-specific QoL we also used the Gastrointestinal Quality of Life Index (GIQLI), which was developed as an instrument to be specifically used for gastrointestinal dis-
orders. The GIQLI comprises 5 domains with the total GIQLI score being the sum score of the domains (range 0-144). Generally, a higher score QoL score represents a better QoL with the exception of symptom scores (higher is more symptoms, i.e. worse QoL). Results of the SF-36 and QLQ-C30 could be compared with a reference population, matched for age and gender.

**Statistical Analysis**

For clinical-pathological characteristics we performed an explorative analysis for which summary statistics are presented either as mean with standard deviation (SD) or with standard error (SEM) or median with (interquartile) range, depending on normal or non-normal distribution. Overall survival rates were calculated on an actuarial basis with the Kaplan-Meier method and comparisons between groups were analyzed using the log-rank test.

For (continuous) QoL outcome comparisons between patients and reference population, when available, were made using Student’s t-tests, irrespective of type of distribution due to the large sample normal distribution approximation rule. To determine the magnitude of the differences in means, effect sizes were calculated. The effect size is equal to the difference in mean scores of the two groups, divided by the standard deviation of the reference population. Cohen interpreted ESSs as trivial (<.2), small (.2-.49), moderate (.5-.79) or large (.8). Univariable linear regression analyses are performed for risk factors for global health status (QLQ-C30) and total GIQLI score. Continuous variables were examined for linearity with the outcome measure and appropriately transformed using restricted cubic splines (3 knots) if the relationship was clearly non-linear. Multivariable regression analysis for association models was performed using both backward selection procedure of significant variables with significance defined as P<.1. For other analyses a P-value of <.05 was considered statistically significant. Statistical analysis was performed with the use of SPSS statistical software version 17.0.1 (SPSS Inc, Chicago, Ill, USA) and the R 2.9.0 table Project for Statistical Computing (Harrell’s Design, Hmisc and Foreign libraries).

**RESULTS**

**Clinical Outcomes**

Table 1 shows clinical-pathological characteristics of patients. The majority of patients was female. Pancreatoduodenectomy and tail resection were the most commonly performed procedures. Classification of pathological findings was derived from the World Health Organization (WHO) international classification of tumors. Most patients had either an intraductal papillary mucinous neoplasm (IPMN) (n=32), mucinous cystic neoplasm (n=29), or serous cyst neoplasm (n=34). In total 29 (27%) patients had a (borderline) malignant cystic neoplasm according to WHO criteria. After a median follow-up of 59 (IQR 36-103) months 20 patients had died.
five-year survival rate for the entire cohort was 85%; rates for benign and malignant lesions were 94% and 62% respectively (P<.001) (Figure 1). Median survival rates for groups could not be calculated, since these were not reached during the observed follow-up period.

Table 1  Demographic, clinical, and pathological characteristics of entire cohort of 108 patients who underwent surgery for a primary pancreatic neoplasm.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>(N=108)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age – yr (SD)</td>
<td>55.5 (17)</td>
</tr>
<tr>
<td>Males – no. (%)</td>
<td>30 (28)</td>
</tr>
<tr>
<td>Index surgical procedure – no. (%)</td>
<td></td>
</tr>
<tr>
<td>(pylorus presevering) pancreatoduodenectomy</td>
<td>53 (49)</td>
</tr>
<tr>
<td>Tail resection</td>
<td>42 (39)</td>
</tr>
<tr>
<td>Total pancreatectomy</td>
<td>7 (6)</td>
</tr>
<tr>
<td>Central pancreatectomy</td>
<td>6 (6)</td>
</tr>
<tr>
<td>Median p.o. hospital stay, days (range)</td>
<td>13 (5-111)</td>
</tr>
<tr>
<td>Postoperative complications – no. (%)*</td>
<td>24 (22)</td>
</tr>
<tr>
<td>Postoperative mortality – no. (%)</td>
<td>2 (2)</td>
</tr>
<tr>
<td>Pathological diagnosis – no. (%)¶</td>
<td></td>
</tr>
<tr>
<td>Serous cystic neoplasm</td>
<td></td>
</tr>
<tr>
<td>Benign</td>
<td>34 (32)</td>
</tr>
<tr>
<td>Malignant</td>
<td></td>
</tr>
<tr>
<td>Intraductal papillary mucinous neoplasm</td>
<td></td>
</tr>
<tr>
<td>Benign</td>
<td>18 (17)</td>
</tr>
<tr>
<td>Moderate dysplasia</td>
<td>5 (5)</td>
</tr>
<tr>
<td>Malignant</td>
<td>9 (8)</td>
</tr>
<tr>
<td>Mucinous cystic neoplasm</td>
<td></td>
</tr>
<tr>
<td>Benign</td>
<td>14 (13)</td>
</tr>
<tr>
<td>Malignant</td>
<td>15 (14)</td>
</tr>
<tr>
<td>Solid pseudopapillary neoplasm</td>
<td></td>
</tr>
<tr>
<td>Benign</td>
<td>11 (10)</td>
</tr>
<tr>
<td>Malignant features</td>
<td>2 (2)</td>
</tr>
</tbody>
</table>

SD denotes standard deviation. P.O. denotes postoperative.

* number of patients with one or more of the following complications: pancreatic fistula, hepaticojejunostomy leakage, delayed gastric emptying, bleeding, intra-abdominal abscess requiring intervention, wound infection, chylous ascites.

¶ classification derived from WHO classification of tumours²⁵.

Of the 88 alive patients 65 (74%) agreed to participate to the follow-up study. There were no statistically significant differences in baseline characteristics between patients who participated in the present study and those who did not, except for presence of malignancy in the resected specimen, 15% (11 of 65) versus 39% (9 of 23) respectively (P=.03). Of 60 available patients 10 (17%) had endocrine insufficiency prior to surgery, while 14 (28%) of the remaining 50 patients developed insufficiency afterwards (new-onset diabetes). Exocrine insufficiency at follow-up had developed in 32 (59%) of 54 available patients, of whom 25 were using pancreatic replacement therapy.
Health-Related Quality of Life Outcomes

The health-related QoL scores are summarized in Table 2. Compared to an age and gender matched control population the global health status score was significantly higher for patients (‘large’ magnitude of difference in mean score according to Cohen, in favor of patients). Physical and mental component scores of SF-36 were not significantly different compared to the norms of the general Dutch population with only trivial effect sizes. Also, none of the individual SF-36 domains were significantly different (data not shown), except for a lower vitality score (61 versus 69, \( P<.05 \)). Component and domain scores of patients that had undergone resection of a (pre) malignant or a benign lesion were equal.

For the disease-specific QoL the total GIQLI score is shown in Table 2. Only 3% of patients scored a total GIQLI score below 70, defined as poor gastrointestinal QoL. Selected QLQ-C30 and PAN-26 scores are displayed in Figure 2. For none of the individual QLQ-C30 and PAN-26 symptom scores were above mean 50, which equal none to mild symptoms. Flatulence, altered bowel habit, body image, and bloated abdomen were the most significant compromised symptom scores with around 22% of patients that scored >50 (moderate-severe symptoms).
Table 2  Significant selected quality of life scores for patients at follow-up with comparison to a healthy reference population (when available). Mean values with standard deviation are given including selected percentages of patients with compromised QoL.*

<table>
<thead>
<tr>
<th>Variables</th>
<th>All patients</th>
<th>General Population Norms</th>
<th>ES**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Generic quality of life scores, mean (SD) [%]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Global Health Status [QLQ-C30]</td>
<td>77 (20) [11]</td>
<td>66 (7)</td>
<td>-1,64b</td>
</tr>
<tr>
<td>Physical Component Score (SF-36)</td>
<td>46 (10)</td>
<td>47 (10)</td>
<td>0,09a</td>
</tr>
<tr>
<td>Mental Component Score (SF-36)</td>
<td>50 (9)</td>
<td>51 (10)</td>
<td>0,04a</td>
</tr>
<tr>
<td>GIQLI, Total Score</td>
<td>113 (20)</td>
<td>110 (10)</td>
<td></td>
</tr>
</tbody>
</table>

SD - Standard Deviation; GIQLI - Gastrointestinal Quality of Life Index.

* For Global Health Status (possible range 0-100, higher is better QoL) compromised quality of life defined as score <50; for GIQLY (possible range 0-144, higher is better QoL) compromised quality of life defined as score <70.

** ES - effect size between patients and General Population Norms according to Cohen: a-trivial effect; b-large effect. Minus sign indicates favorable outcome for patient cohort.

Figure 2  Bars represent mean scores (with standard error) of selected disease-specific symptom scales (EORTC QLQ-C30, PAN-26). The dotted line at score 50 indicates the threshold between moderate to severe (score >50), and none to mild symptoms (score <50).

Predictors of Quality of Life Outcome
Univariable analysis of potential predictors of global health status at follow-up revealed that older age and an extensive resection (compared to tail resection), defined as pancreatoduodenectomy, central or total pancreatectomy, were negatively
associated with QoL outcome. Current employment was positively associated with global health status. Multivariable analysis showed that older age was an independent negative predictor, whereas malignancy in the resected specimen was a positive predictor for global health status.

For the gastrointestinal QoL score univariable analysis revealed that an extensive resection was a predictor for a negative outcome, and current endocrine insufficiency and current employment were positive predictors. Independent negative prognosticators were female gender and extensive resection; positive predictors were endocrine insufficiency and employment.

Table 3  Uni- and multivariable analysis, following backward selection, of predictors associated with global health status, as measured by the EORTC QLQ-C30.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Univariable</th>
<th></th>
<th>Multivariable</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>B 95% CI</td>
<td>B 95% CI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age at follow-up, one year increment(^1)</td>
<td>-0.33 [-0.64 – -0.02](^1)</td>
<td>-0.75 [-1.51 – 0.01](^2)*†</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female gender</td>
<td>-1.04 [-11.5 – 9.46]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Extensive resection(^2)</td>
<td>-10.4 [-20.1 – -0.61](^1)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Postoperative surgical complications</td>
<td>1.43 [-9.58 – 12.6]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Borderline) malignancy in resected specimen 6,94</td>
<td>[-5.85 – 19.7]</td>
<td>13.0</td>
<td>[-1.08 – 27.1](^2)</td>
<td></td>
</tr>
<tr>
<td>Current endocrine insufficiency(^3)</td>
<td>3.63 [-7.30 – 14.6]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current exocrine insufficiency(^4)</td>
<td>-7.28 [-18.6 – 4.00]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Currently employed(^5)</td>
<td>12.5 [2.93 – 22.2](^2)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 4  Uni- and multivariable analysis, following backward selection, of predictors associated with total gastrointestinal QoL score, as measured by the GIQLI.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Univariable</th>
<th></th>
<th>Multivariable</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>B 95% CI</td>
<td>B 95% CI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age at follow-up, one year increment(^1)</td>
<td>-0.12 [-0.45 – 0.20]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female gender</td>
<td>-6.08 [-16.9 – 4.72]</td>
<td>-11.6</td>
<td>[-23.6 – 0.44](^3)</td>
<td></td>
</tr>
<tr>
<td>Extensive resection(^7)</td>
<td>-14.7 [-24.5 – -4.89](^1)</td>
<td>-12.7</td>
<td>[-23.9 – -1.48](^1)</td>
<td></td>
</tr>
<tr>
<td>Postoperative surgical complications</td>
<td>4.57 [-6.77 – 15.9]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Borderline) malignancy in resected specimen</td>
<td>6.51 [-6.53 – 19.6]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current endocrine insufficiency(^3)</td>
<td>10.3 [-0.20 – 20.9](^1)</td>
<td>13.1</td>
<td>[2.69 – 23.5](^1)</td>
<td></td>
</tr>
<tr>
<td>Current exocrine insufficiency(^4)</td>
<td>-3.02 [-14.4 – 8.35]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Currently employed(^5)</td>
<td>11.0 [0.92 – 21.1](^1)</td>
<td>14.5</td>
<td>[3.30 – 25.7](^1)</td>
<td></td>
</tr>
</tbody>
</table>

\(B\) - regression coefficient; 95% CI - 95 percent confidence interval.

1 Analyzed with restricted cubic splines technique (three knots).
2 Head, total or central pancreatectomy, compared to tail resection (reference treatment).
3 Defined as: using prescribed anti-diabetic medication or fasting glucose >6.7 mmol/L.
4 Defined as elastase level of <200 ug/gFaeces.
5 Paid parttime or fulltime employment.
† Significant at P<.05 level; ‡ Significant at P<.1 level.
* Coefficient of third knot (oldest patient category) displayed.
DISCUSSION

In the present study 27% of the patients, who were operated for suspicion of a (pre) malignant lesion, appeared to have of a (borderline) malignancy. Five year overall survival was 94% for benign and 62% for malignant neoplasia. Long term generic physical and mental QoL was equal or better compared to a healthy reference population. None of the disease-specific symptom scales were above mean 50, implicating none to mild complaints. Independent predictors for good global health status at follow-up were young age, and resected (pre)malignancy, while for good gastrointestinal QoL male gender, limited resection, endocrine insufficiency, and employment were significant predictors. Despite the occurrence of iatrogenic exocrine and endocrine pancreatic insufficiency due to resection in 59% and 40% respectively, QoL at follow-up was not impaired.

The overall survival figures of patients that underwent resection of a (pre)malignant lesion in the present study were comparable to other series, and relate excellent compared to pancreatic adenocarcinoma. Although we are aware of the fact that for optimal prognostication differentiation between the different subtypes (e.g. mucinous cystic neoplasia versus IPMN) is important we choose not to report these in detail for the small numbers of the individual groups. Moreover, the primary aim of our study was to investigate the long-term patient reported outcomes of patients, who were diagnosed with a cystic neoplasm of the pancreas and operated under the assumption of having a primary cyst with malignant potential. This scenario resembles daily clinical practice.

The optimal diagnostic and management strategy of primary pancreatic cysts, and in particular the differentiation between lesions with or without malignant potential, is still subject of discussion. The high rate of resected benign lesions in our series is characteristic for the patient population with primary cystic lesions of the pancreas and is in line with reports from others. It has been suggested that a cyst diameter of more than 3 centimeter is a potential threshold for operation. For the current study we did not incorporate cyst size as prognosticator, but the treatment philosophy in our center follows these guidelines. A recent study on clinical decision making for patients with pancreatic cysts, specifically asymptomatic suspected IPMN, confirms that this generally accepted threshold for operation of asymptomatic cysts achieves the most optimal quality-adjusted survival. In addition, combining clinical features (e.g. age, gender) and selective use of radiological modalities (computed tomography, magnetic resonance imaging), and invasive diagnostics (endoscopic ultrasound with fine-needle aspiration, endoscopic retrograde cholangiopancreatography) can increase the preoperative likelihood for malignancy. Several guidelines and studies have employed these features to set up treatment algorithms for different cyst types to aid the clinician in deciding which cyst to remove, discard, or follow-up. Still, a decisive gold standard with 100% sensitivity to detect and select malignant cysts or cysts with malignant potential for operation does not yet exist. Moreover, some patients themselves prefer operation over continued observation once the inci-
dental radiological diagnosis of a cystic pancreatic neoplasm has been established. Therefore, our finding that patients with a primary cystic neoplasm of the pancreas, benign and malignant, report excellent long-term QoL following resection, underlines the justification of a treatment strategy with a limited threshold to surgery. This evidently implies a high rate of resected benign lesions, albeit with a malignant potential, as was observed in the present study.

The reported long-term QoL outcomes following resection in this study are excellent, both on general as well as disease-specific QoL domains. Compared to an age-matched reference population no significant differences were observed, while on some domains the mean scores of patients were even better. To our knowledge no studies exist that report long-term patient reported outcomes such as QoL following resection of a primary cystic pancreatic neoplasm. In the lack of objective QoL data following cyst resection derived knowledge comes from studies that concern various operative procedures for mainly pancreatic adenocarcinoma. Despite iatrogenic endocrine insufficiency it is generally assumed that QoL is not significantly affected by distal pancreatectomy. On the contrary, pancreatoduodenectomy for pancreatic and periampullary adenocarcinoma can significantly impair quality of life. However, in patients that remain disease-free after one year QoL seems to recover, sometimes to normal values. Long-term QoL after total pancreatectomy for various malignant and benign disorders does seem to remain severely impaired. In line with these findings we also found that global QoL was influenced by a more extensive resection, which we defined as pancreatoduodenectomy or total pancreatectomy versus distal pancreatectomy.

Another possible explanation for our excellent outcomes might be that patients who are operated for a suspected malignancy are overwhelmingly relieved when they learn that the final pathological diagnosis turns out to be benign. Furthermore, patients confronted with malignant disease are faced with the necessity to accommodate to the disease. As a result patients might lower internal standards (‘response shift’) and rate the same condition better than they would have if they had not experienced a serious illness. This could also explain the fact that patients who had undergone resection of a malignant lesion in the present series invariably had good to excellent scores. Moreover, the presence of malignancy in the resected specimen was an independent prognosticator of better outcome.

Exocrine or endocrine insufficiency in patients treated surgically for pancreatic cysts is primarily due to the surgical intervention, and the more extended the resection of the pancreas, the greater the risk of insufficiency. The incidence of endocrine insufficiency we observed, so-called pancreateogenic diabetes, and the incidence of exocrine insufficiency are in line with reports in literature for various resectional procedures. It is well conceivable that the functional consequences associated with insufficiency can have a profound impact on patient’s lives, especially in case of insulin-dependent diabetes. Interestingly we could not retrieve reports with sound data that address the influence of endocrine- and exocrine insufficiency due to pancreatic resection on long-term QoL. Although the fact that endocrine insufficiency
after operation being a prognosticator for a good gastrointestinal QoL, not overall QoL, in the present series is somewhat difficult to understand, the most important conclusion might be that it does not impair long-term QoL. Also the presence of exocrine insufficiency, which is generally easy to manage, did not adversely influence QoL. Thus, the potential risk to induce insufficiency with operation should not influence the decision to proceed with resection, once an indication for surgical resection has been established.

Our study has some limitations. We performed a retrospective analysis of a series of patients with only a single QoL measurement in time, precluding a longitudinal analysis. However, we observed scores at follow-up that were equal or better compared to healthy individuals, and although we cannot rule out the possibility, it seems unlikely that patients would report even higher scores prior to operation. Among the number of patients that responded to participate in the QoL the rate of benign lesions was slightly higher compared to non-responders, which possibly could have influenced the overall outcome. A relative limitation comprises the fact that we only investigated patients that underwent resection of a primary pancreatic cystic neoplasm. We did not include patients with unresectable disease. However, besides the fact that long-term QoL outcomes might be difficult to obtain for this group the potential influence of their outcome will be limited, considering the low preoperative likelihood for malignancy and the fact that primary cystic neoplasia of the pancreas follow a more indolent course compared to pancreatic adenocarcinoma with a low subsequent risk for unresectability at time of exploration.

In conclusion, we have demonstrated that patients who have undergone a pancreatic resection under the assumption of having a primary malignant cyst, or cyst with malignant potential, report an excellent long-term health-related QoL. Pancreatic insufficiency, partially iatrogenic due to resection, is prevalent, but does not impair QoL. Overall long term survival following resection of primary cystic neoplasia, but also malignant lesions in particular, relates positive compared to solid adenocarcinoma of the pancreas. Although a treatment strategy with low threshold to surgery results for primary cystic neoplasia of the pancreas in an anticipated high rate of resected benign lesions, potential concerns about a major negative impact on either of these items are therefore not justified. The decision to proceed with treatment, once an indication for surgical resection of a pancreatic cyst has been established, is valid.

REFERENCE LIST


(3) Compagno J, Oertel JE. Mucinous cystic neoplasms of the pancreas with overt and


