

RESEARCH ARTICLE

Management of pancreatic pseudocysts—A retrospective analysis

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Abstract

Background

Pancreatic pseudocysts arise mostly in patients with alcohol induced chronic pancreatitis causing various symptoms and complications. However, data on the optimal management are rare. To address this problem, we analysed patients with pancreatic pseudocysts treated at our clinic retrospectively.

Methods

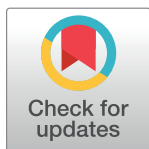
We searched our clinical database for the diagnosis pancreatitis from 2004 till 2014, selected patients with pseudocysts larger than 10 mm and entered all relevant information in a database for statistical analysis.

Results

In total, 129 patients with pancreatic pseudocysts were treated at our institution during the study period. Most patients suffered from alcohol induced chronic pancreatitis (43.4%; 56/129). Pseudocysts were more frequent in female than in male (2:1) and were mainly located in the pancreatic head (47.3%; 61/129). Local complications like obstructive jaundice were associated with the diameter of the cysts (AUC 0.697 in ROC-curve analysis). However, even cysts up to a diameter of 160 mm can regress spontaneously. Besides a lower re-intervention rate in surgically treated patients, endoscopic, percutaneous and surgical drainage are equally effective. Most treatment related complications occur in large pseudocysts located in the pancreatic head.

Conclusion

Conservative management of large pseudocysts is successful in many patients. Therefore, indication for treatment should be made carefully considering the presence and risk of local complications. Endoscopic and surgical drainage are equally effective.



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Introduction

Pancreatic pseudocysts belong to the diverse entity of pancreatic fluid collections and cystic pancreatic lesions. As features and complications of the different fluid collections and cystic lesions are variable, a classification system was established in 1992 by a consensus meeting in Atlanta and was revised in 2011.[1, 2] According to the revised Atlanta classification, pancreatic pseudocysts usually develop with a delay of at least 4 weeks to the initiating event and are characterized by a well defined inflammatory wall and a homogeneous fluid content without necrosis.[1] Particularly small pseudocysts are difficult to differentiate from cystic tumors of the pancreas.

About 70% of pancreatic pseudocysts arise in patients with alcohol induced chronic pancreatitis. In addition, pseudocysts can also evolve after acute pancreatitis, trauma, and surgery.[3–5] Although symptoms and complications are diverse and heavily depend on localisation and size of the pseudocyst, most frequently patients with pancreatic pseudocysts present with abdominal pain.[6] Accordingly, treatment is variable and apart from a few clear indications like infection of the cyst or biliary obstruction neither well defined nor standardized. As the few published studies on pancreatic pseudocysts rely on relatively few patients and do not use uniform definitions, meta-analysis with a sufficient cohort size are difficult so far.[5, 7] Additionally, endosonographic drainage techniques evolved in the last decade and more and more replace surgical drainage procedures like pseudocystojejunostomy—the former standard of therapy. (Fig 1) Although endosonographic drainage has been compared to conventional drainage techniques in randomized controlled trials, in particular the question which patient has to be treated when has hardly been addressed.[7, 8]

With this unicenter retrospective analysis we aimed to address this problem by evaluating treatment indication, analysing treatment options and assessing the course of the disease and the outcome.

Materials and methods

We performed a unicenter retrospective analysis of patients presenting with pancreatic pseudocysts between 2004 and 2014 at the tertiary referral center Klinikum rechts der Isar der Technischen Universität München. We screened our administrative diagnosis database for patients with pancreatitis (International Classification of Diseases (ICD)-10 code K85 and K86; n = 3281). Pancreatic pseudocysts were defined according to the revised Atlanta classification.[1] Patients with pancreatic pseudocysts larger than 10 mm who presented more than one time were eligible for this study. Patients with cysts suspicious of dysplasia or walled of necrosis were excluded. We reviewed the medical charts of all 3281 patients diagnosed with chronic and acute pancreatitis. Thus, we identified 129 patients with pancreatic pseudocysts that met the inclusion criteria. All patients were registered in a database containing 105 clinical parameters. The study was approved by the local ethics committee (Ethikkommission der Fakultät für Medizin der Technischen Universität München, project number 466/14). Written consent was specifically waived by the approving institutional review board.

Statistical analysis was performed using IBM SPSS Statistics 22 (SPSS Inc, Chicago, Illinois, USA). To compare qualitative parameters, chi-square test was used and in small samples (expected frequency of test variable less than 5), Fisher's exact test was used. For the analysis of quantitative parameters, Mann-Whitney-U test was employed. All statistical tests were two sided with a level of significance (p-value) of 5%. A binary logistic regression model was used to analyse the effect of patient characteristics on the development of symptomatic cysts or local complications. Factors with a p-value below 0.1 in univariate analysis or a high probability according to our data or the literature were included in regression analysis. The p-value

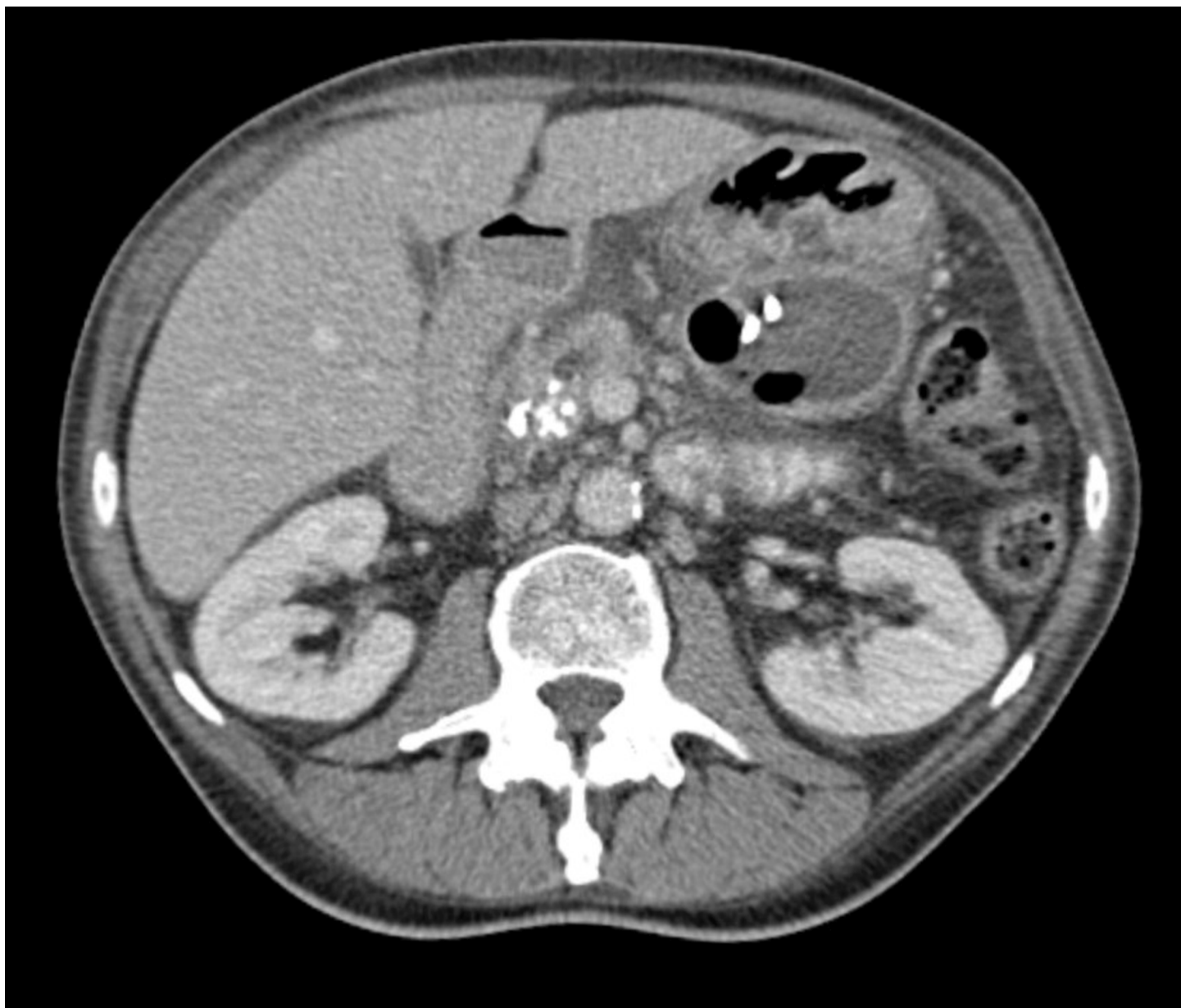


Fig 1. Abdominal CT-scan with venous contrast: Pancreatic pseudocyst with transgastric drainage.

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remained 0.05 after a Benjamini-Hochberg correction to control the false discovery rate, as several regression analyses were performed.[9] Descriptive data are presented as mean \pm standard deviation (SD) for normally distributed parameters and median, range and interquartile range (IQR) for not normally distributed parameters. Risk ratios were displayed as odds ratio (OR) with 95% confidence interval (CI).

Drainage techniques

All endoscopic drainage procedures were performed under endosonographic guidance by a linear scanner. A gastro- or duodenocystostomy was carried out with a cystostome, fluid specimen were obtained by aspiration and 1–3 double pig tails were placed via a guide wire. For

percutaneous drainage pig tail catheters were placed by Seldinger’s technique under sonographic or computertomographic guidance. All surgical drainage procedures were cystojejunostomies with a Roux-en-Y reconstruction.

Results

Patients’ characteristics

Overall, 161 pancreatic pseudocysts in 129 patients were identified. Accordingly, pseudocysts occurred in 3.93% (129/3281) of the patients. Most of the patients’ characteristics are summed up in Table 1. The median follow up time was 4.7 months (IQR 1.6–15.1, range 0.2–102). In 6.2% (8/129) of the patients the pseudocyst was an incidental finding, 28.7% (37/129) of the

Table 1. Patient characteristics.

Patient characteristics, n = 129	
Gender (♂: ♀)	1:2
Mean age (years)	52 (±14.9)
median follow up in days	141 (IQR 48–452; range 3–3056)
Cyst	
Etiology	
acute pancreatitis	14.7% (19/129)
- alcoholic	42.1% (8/19)
- biliary	57.9% (11/19)
chronic pancreatitis	65.1% (84/129)
- alcoholic	66.7% (56/84)
- hereditary	3.6% (3/84)
- other/idiopathic	29.8% (25/84)
iatrogen and trauma	3.9% (5/129)
Idiopathic pseudocysts	16.3% (21/129)
median number per patient	1 (IQR 1–2; range 1–5)
median diameter (mm)	60 (IQR 32–88; range 10–180)
Location	
Head	47.3% (61/129)
Body	27.1% (35/129)
Tail	24.8% (32/129)
Extrapancreatic	25.6% (33/129)
Symptoms	
abdominal pain	63.6% (82/129)
nausea/vomitting	19.4% (25/129)
weight loss	18.6% (24/129)
Indigestion	6.2% (6/129)
Bloating	6.2% (6/129)
Jaundice	3.9% (5/129)
Local complications	
pancreatic duct obstruction	17.8% (23/129)
blood vessel obstruction	15.5% (20/129)
intestinal obstruction	15.5% (20/129)
bile duct obstruction	13.2% (17/129)
venous thrombosis	8.5% (11/129)
Cholangitis	1.6% (2/129)

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patients were active smokers. Concomitant liver cirrhosis was present in 7.0% (9/129) of the patients, 11.6% (15/129) were suffering from diabetes mellitus type 2 and 5.4% (7/129) of diabetes mellitus type 3c. No pancreatic pseudocyst due to acute pancreatitis was diagnosed after publication of the revised Atlanta classification in 2012.

In multiple logistic regression analysis only cyst number and diameter was associated with a higher rate of local complications like stenosis of the pancreatic or biliary duct, of the intestine or vessels as well as thrombosis or ruptured cyst (number: OR 2.03, CI 1.10–3.76, $p = 0.024$; diameter: OR 1.30/cm, CI 1.14–1.49, $p < 0.001$). Neither location or the number nor the etiology of the pseudocyst or the gender had an impact on the development of a symptomatic disease or the occurrence of local complications (S1 and S2 Tables). Using receiver operating characteristic (ROC) -curve analysis, cyst diameter is only a fair predictor for the development of local complications. (Fig 2)

Therapy

An endoscopic or percutaneous puncture of the cyst was performed 54 times. The most frequent indication for puncture was for diagnostic purposes (72.2%, 39/54) to rule out malignancy or if an infection of the cyst was suspected. One puncture was technically unsuccessful, and in one case bleeding occurred after intervention. There was a complete resolution of the cyst after diagnostic puncture in 6 patients. However, repeated intervention was necessary in 50% (27/54) of the cases.

In total, 34.1% (44/129) of the patients were managed conservatively and 65.9% (85/129) required an intervention, respectively. In 40.0% (22/55) the indication for drainage was suspected infection. There was no significant difference in the complication rate after drainage between infected and not infected cysts (9.1% (2/22) versus 24.2% (8/33), $P = 0.284$). Details

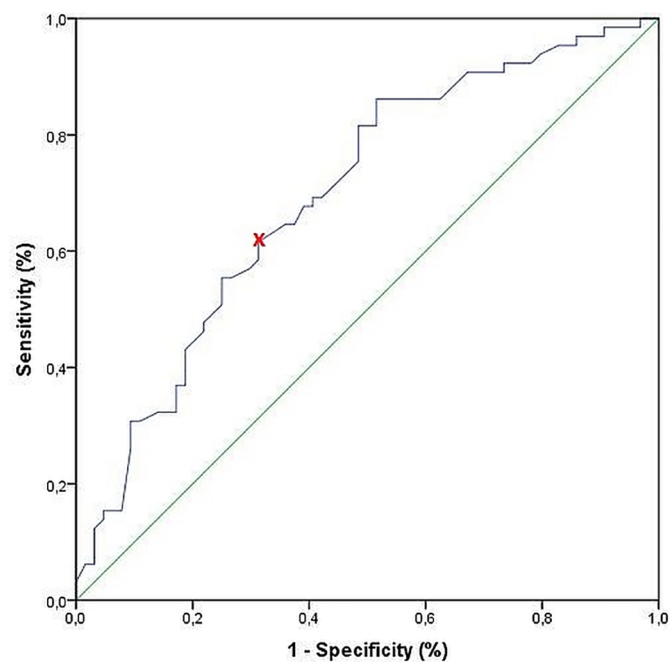


Fig 2. ROC-Curve for cyst diameter as predictor of local complications. Area under the curve (AUC): 0.697. x = cut-off with most equally high sensitivity and specificity: 61,0 mm (sensitivity: 61.5%, specificity: 68.7%).

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on the different treatment options are displayed in Table 2. Patients without an intervention on the cyst had a statistically significant shorter length of hospital stay compared to patients in whom a puncture of the cyst was performed (in days: median 3, IQR 0–13, range 0–30 versus median 14, IQR 9–24, range 0–52, $p < 0.001$). Surgically treated patients had a significantly lower re-intervention rate than patients with percutaneous or endoscopic drainage (0% (0/21) versus 26.5% (13/49), $p = 0.007$). Apart from that, there were no statistically significant differences considering length of hospital stay, complication rate, and re-intervention rate between the different treatment modalities.

The localisation of the pseudocyst had no impact on whether patients were managed conservatively or invasively. Pseudocysts of patients who received an intervention had a significantly higher diameter than those of conservatively managed patients (median 67 mm, IQR 30.75 mm, range 15–180 mm versus median 36.5 mm, IQR 48.5 mm, range 10–160 mm, $p < 0.001$).

Neither cyst diameter, cyst location nor laboratory signs of infection prior to intervention (C-reactive protein > 0.5 mg/dl or white blood cell count > 9 G/l) were associated with complications due to intervention in multivariate logistic regression analysis (S3 and S4 Tables). However, with increasing age, cyst diameter and a location of the cyst in the pancreatic head, there was a higher rate of repeated interventions (age: OR 0.97, CI 0.93–1.00, $p = 0.045$; cyst diameter: OR 1.22/cm, CI 1.04–1.43, $p = 0.012$; cyst in pancreatic head: OR 12.81, CI 1.35–121.2., $p = 0.026$). In total, 16.3% (21/129) of the patients had to be admitted to an intensive care unit including 81% (17/21) of the surgical treated patients in part as routine surveillance after surgery. No patient died as a consequence of treatment for pancreatic pseudocysts.

The occurrence of symptomatic cysts, local complications of the cysts or the cyst diameter did not differ significantly between patients who initially presented to the medical or surgical department. When patients initially presented to the surgical department, significantly more received a surgical drainage or a resection compared to patients who presented to the medical department (42.1% (8/19) versus 4.1% (4/98), $p < 0.001$).

Discussion

The incidence of pseudocysts after acute pancreatitis is reported to be between 5–16% and after chronic pancreatitis 20–40%, respectively. [10–13] In our patient population pancreatic pseudocysts occurred less frequently in 3.9% after acute and chronic pancreatitis. In 2012

Table 2. Comparison of treatment options.

	Conservative Management	Endoscopic Drainage	Percutaneous Drainage	Surgical Drainage	Resection
N	44	41	8	6	15
as first intervention	44	68.3% (28/41)	50% (4/8)	83.3% (5/6)	46.7% (7/15)
Median cyst diameter in mm (IQR / range)	36,5 (28.5–59.25 / 10–160)	84 (66.5–100 / 50–180)	75 (63.5–96.75 / 38–117)	64,5 (53.75–109 / 35–160)	68 (50–100 / 25–154)
Improvement of symptoms	56.8% (25/44)	78% (32/41)	87.5% (7/8)	83.3% (5/6)	80% (12/15)
Decrease of cyst size	66% (29/44)	95.1% (39/44)	87.5% (7/8)	100% (6/6)	100% (15/15)
Complication rate		22% (9/41)	12.5% (1/8)	0% (0/6)	40% (6/15)
most frequent complications		stent occlusion, haemorrhage	haemorrhage		Infection
Reintervention		22% (9/41)	50% (4/8)	0% (0/6)	0% (0/15)
Median hospitalisation in days	3	16	21	19,5	27

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pancreatic pseudocysts were defined in the revised Atlanta classification as 'an encapsulated collection of fluid with a well defined inflammatory wall with minimal or no necrosis' and can since then be clearly distinguished from pancreatic fluid collections and walled of necrosis. According to the revised Atlanta classification, pseudocysts after acute pancreatitis are rare.[1] After the publication of the revised Atlanta classification in 2012 till 2014, no pseudocyst resulting from acute pancreatitis was diagnosed. So the real incidence of pseudocysts after acute pancreatitis is probably at the lower limit of the reported range. Consistent with the literature pancreatic pseudocysts most frequently developed in patients with chronic, alcohol induced pancreatitis.

While the median age of our patients is within the reported range for this patient population, the gender distribution is imbalanced.[14] Over 80% of the patients with chronic pancreatitis are male as the most frequent cause of chronic pancreatitis—alcoholism—is still a predominantly male problem. [15, 16] However, some studies from the USA and the Netherlands describe a tendency towards a more equal gender distribution.[17, 18] Nevertheless, as two thirds of the pancreatic pseudocysts in our patient population arose in female patients, other factors than alcoholism seem to be decisive for pseudocyst development.

The most challenging issue is to find the right patient and the right timepoint for invasive treatment of pancreatic pseudocysts. The indication in patients with local complications like obstructive jaundice is undoubted (Table 3). The rate of local complications correlates with the size of the cysts but not with symptoms like pain, malabsorption or weight loss. In addition, even large cysts can resolve spontaneously. According to the literature, only pseudocysts larger than 50 mm that do not regress within 6 weeks should be treated unless local complications arise. However, this recommendation relies on the first Atlanta consensus conference on acute pancreatitis in 1992.[2, 19, 20]

According to our data pancreatic pseudocysts with a size above 60 mm should be treated in case they do not resolve within 6 weeks to avoid the development of local complications. But considering the low sensitivity and specificity of this parameter other aspects like comorbidities and patients' symptoms should be taken into account as well.

According to Ardengh et al. puncture with aspiration and stent placement for endoscopic drainage are equally effective.[21] In contrast our patients frequently required a re-intervention after simple puncture. Consequently simply endoscopic or percutaneous puncture of pancreatic pseudocysts is predominantly a diagnostic procedure and usually drainage placement is required to control symptoms. Endoscopic, percutaneous or surgical drainage as well as resection are effective to improve symptoms and reduce the cyst size. As endosonographic guided punctures are superior to mere gastroscopic punctures all our endoscopic drainages were performed with endosonographic guidance.[22] Recent literature reported similar success and complication rates for surgical and endoscopic interventions, while the length of hospital stay was significantly shorter in endoscopically treated patients.[23–26] Our data are in line with these findings. And yet, surgical therapy seems to be associated with the lowest re-intervention rate. Although in our analysis the sample size is too small to identify significant differences

Table 3. Indication for treatment in pseudocysts with local complications.

Immediate treatment is indicated in case of local complications of pancreatic pseudocysts:

- Obstructive Jaundice
- Infection of the pseudocyst
- Obstruction of gastrointestinal tract
- Compression of intestinal vessels
- Hemorrhage

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between each intervention, endoscopic drainages tend to result in a shorter hospitalisation and fewer re-interventions than percutaneous drainages which is in line with the literature.[27, 28] So endosonographic drainage should be preferred to percutaneous drainage techniques in pancreatic pseudocysts.

There are conflicting results concerning the outcome of drainage of infected pseudocysts. Sadik et al. reported high complication rates after drainage of infected pseudocysts.[29, 30] Our results support the finding of Varandajuru et al. with low complication rates after drainage of infected pseudocysts.[25] In general, elevated infection parameters, such as C-reactive protein and white blood cell count, were not associated with more complications potentially indicating chronic systemic inflammation with accelerated biological ageing in patients with chronic pancreatitis.[31] Only large pseudocysts located in the pancreatic head are more prone to treatment associated complications like hemorrhage, perforation and formation of fistulae. The complication rate in these large cysts can possibly be further reduced by irrigation via a nasocystic drainage.[32]

Conclusion

Endoscopic and surgical drainage of pancreatic pseudocysts are equally safe and effective treatment options. Most interestingly, even large pseudocysts can regress spontaneously. Accordingly, many patients can successfully be managed conservatively and pseudocysts should only be treated in the presence of local complications like obstructive jaundice or infection. Large prospective studies are needed to identify clear treatment indications for uncomplicated pseudocysts and define the timepoint of intervention.

Supporting information

S1 Table. Variables included in regression model 1 about 'local complications'.
(XLSX)

S2 Table. Variables included in regression model 2 about 'symptomatic cysts'.
(XLSX)

S3 Table. Variables included in regression model 3 about 'complications of interventions'.
(XLSX)

S4 Table. Variables included in regression model 4 about 're-intervention rate'.
(XLSX)

Author Contributions

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