Cystic Lesions of the Pancreas

Serge Sorser, MD
Outline

• Overview/Introduction
• What is EUS?
• Serous Cystadenoma (SCA)
• Pseudocyst
• Walled-off Pancreatic Necrosis (WOPN)
• Mucinous Cystic Neoplasm
• Intraductal Papillary Mucinous Neoplasm
• Rare Lesions
• Summary
Overview

• Use of cross-sectional imaging

• Cysts elsewhere
  • Renal 41%
  • Hepatic 18%
  • Pancreatic? 13.5%

• Role of EUS

What is EUS?

Combination of Endoscopy and Ultrasound

https://gi.jhsps.org/GDL_Disease.aspx?CurrentUDV=31&GDL_Cat_ID=551CDCA7-A3C1-49E5-B6A0-C19DE1F94871&GDL_Disease_ID=0ADCFDB3-7DE7-4D53-82F5-6F0C9BFB7F14

January 19, 2015

Kulkarni K. Endoscopic Ultrasound of the Gastrointestinal Tract. JLGH. 2010. 5(2);50-3
SCA

• Previously known as a microcystic adenomas and are benign\(^1\)

• Second most common cystic tumor of the pancreas, accounting for up to 30% of pancreatic cysts\(^2\)

• Occur most commonly in the body and tail of the pancreas\(^3\)

• Often seen in middle aged-women, but can occur in both sexes and at any age\(^4\)

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Patients are commonly asymptomatic\(^1\)

- may present with abdominal pain and a palpable mass

Cross sectional imaging may help make the diagnosis\(^2\)

- multi-septated cyst with so-called “honeycombing”

- A typical central, often spiculated (“sunburst”) calcification may be seen\(^3\)

Fluid\(^4\)

- clear with cuboidal cells lining the cyst cavity

- low cyst fluid CEA and bland cytology are noted

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2 Kim HJ, Lee DH, Ko YT, et al. CT of Serous Cystadenoma of the Pancreas and Mimicking Masses. AJR. 2008;190:406-12


Kim HJ, Lee DH, Ko YT, et al. CT of serous cystadenoma of the pancreas and mimicking masses. AJR. 2008;190:406-12
SCA
• Benign nature of SCA - no surveillance
• Low rate of malignant transformation (< 3%)\(^1\)
• Surgical intervention is not indicated unless symptoms
  • consideration of surgical intervention in the appropriate patient if
    • symptoms that can be attributed to the lesion
    • the cyst in aggregate is greater than 4 cm

Pseudocyst

- Most commonly a complication of acute or chronic pancreatitis
- can occur following trauma to the pancreas
- Rich in amylase and other pancreatic enzymes
- not lined by an epithelium
- Underlying etiology is multifactorial and leads to ductal disruption
- increase in pancreatic ductal pressure
- Present with ongoing abdominal pain and anorexia weeks after their initial presentation
- jaundice or sepsis also noted
- Large cysts frequently compress the stomach and/or duodenum
- can cause gastric outlet obstruction

Pseudocyst

- Pseudocysts are usually distinguished by lack of significant solid debris (as is more commonly seen in walled of pancreatic necrosis (WOPN))
- Diagnosis is made by cross-sectional imaging
  - CT of the abdomen/pelvis\(^1\)
  - MRI, EUS or ERCP may also be considered\(^2\)
  - MRI and EUS give more accurate assessment of the amount of solid debris with in a pancreatic fluid collection


Pseudocyst

- High cyst fluid amylase with a low cyst fluid CEA\(^1,2,3\)
- Treatment modalities
  - endoscopic
  - surgical
  - interventional radiology

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Pseudocyst

- Endoscopy
  - transampullary drainage via pancreatic duct stent placement
    - through the pancreatic duct and the stent
    - the pancreatic stent may simply relieve pressure on the pancreatic duct and stops backfilling of the cyst, allowing it to resolve over time
  - transpapillary drainage may be an adequate approach in up to 79.5% of patients

Pseudocyst

- Endoscopy

- transmural drainage\(^1,2,3,4\)
  - puncturing the cyst via EUS with fluoroscopic guidance
  - delineating the cyst cavity
  - dilating the tract
  - placing multiple plastic double pigtail stents or single metal stents

- some patients warrant both transmural and transampullary drainage simultaneously\(^5\)

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Pseudocyst
Pseudocyst - Xlumena™
Pseudocyst

- Surgery\(^1,2\)
  - cystenterostomy in the most dependent part of the cyst cavity
  - remains patent for months
- IR\(^3,4\)
  - most appropriate window
    - transperitoneal
    - retroperitoneal
    - transgastric
    - transduodenal
    - transhepatic
  - placement of a percutaneous external drain
- least invasive and can be favored in patients who are poor candidates for other interventions

WOPN

- WOPN
- coined in 2007
- complication of necrotizing pancreatitis
- a collection of fluid and solid components that tends to develop 3 to 6 weeks after an episode of pancreatitis,
- some patients develop an immature form of this lesion in a shorter timeframe¹
- seen in 1 to 9% of cases of acute pancreatitis and occurs most commonly after biliary pancreatitis²

WOPN

- Ongoing abdominal pain, as well as fever and leukocytosis\(^1\)
  - can be present even in the absence of infection
- Diagnosis typically made on cross-sectional imaging\(^2\)
  - visualizing a non-enhancing pancreatic fluid collection, which may contain solid debris
- Indications for intervention include clinical suspicion of\(^3\)
  - infected necrotizing pancreatitis with clinical deterioration
  - gastric outlet obstruction
  - intestinal or biliary obstruction
  - due to mass effect of walled-off necrosis
  - persistent symptoms in patients with walled-off necrosis without signs of infection

\(^2\) Murphy KP, O’Connor OJ, Maher MM. Updated imaging nomenclature for acute pancreatitis *AJR.* 2014;203(5):464-9
Many therapeutic modalities for WOPN exist

- not all infected pancreatic necrosis requires intervention

- Good clinical outcome in patients treated conservatively with a prolonged course of antibiotics and supportive care\(^1,2\)

- supported by a meta-analysis of eight studies, including 324 patients\(^3\)

- conservative management without necrosectomy - successful in 64% of patients

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WOPN

- Endoscopic drainage methods
  - endoscopic transmural drainage
  - held open via plastic or metal stents
  - combined percutaneous/endoscopic techniques
  - dedicated, covered self-expanding metal stents
    - fully covered esophageal and biliary stents has also been noted for these purposes
  - procedure related complications have as high as 21-25%
    - bleeding
    - sepsis
    - perforation
  - overall success rate of 82-93%

• Radiologic approach
  • retroperitoneal approach to the necrotic cavity
  • minimally invasive and has an overall success rate of 33-56%\textsuperscript{1,2}
• complications
  • internal and external pancreatic fistulas\textsuperscript{3}
• overall mortality rate of 17.4%
• Surgical approaches
  • minimally invasive/laparoscopic techniques
    • transgastric endolumenal cystogastrostomy\textsuperscript{4}
  • common adverse events include\textsuperscript{5}
    • pancreatic fistulae 28.6%
    • debris recollection 10.7%
    • wound infection 10.7%

WOPN

- Combined/multidisciplinary approach
- reduced
  - length of stay
  - number of radiological procedures
  - number of ERCPs
- durable long-term outcome
  - 100/103 patients did not require surgery at two years\(^1,2\)
- modalities selected should rely on\(^3,4\)
  - individual center expertise
  - anatomic position
  - ratio of solid to fluid components within the collection
  - degree of systemic organ dysfunction

\(^1\) Gluck M, Ross A, Irani S, et al. Dual modality drainage for symptomatic walled-off pancreatic necrosis reduces length of hospitalization, radiological procedures, and number of endoscopies compared to standard percutaneous drainage. *J Gastrointest Surg.* 2012;16(2):248-56
MCN

- Most common types of pancreatic cysts
- constitute up to one half of all known cystic lesions of the pancreas.
- Range in size from 5 to 35 cm
- Predominantly found in females\(^1,2\)
- Fifth or sixth decade of life\(^3\)
- Tends to localize in the body or tail of the pancreas\(^4,5\)
- Defined strictly by the presence of ovarian type stroma within the tumor\(^6\)

MCN

- No communication with the main pancreatic duct is noted
- Fluid analysis
  - thick and mucoid material
  - low amylase
  - high CEA
- Histology
  - mostly benign
  - Adenoma 72%
  - Borderline neoplasm 10.5%
  - Carcinoma in situ 5.5%
  - Invasive cancer 12%
- Malignant transformation may occur via K-ras and p53 mutations
- Surgical resection is recommended for all MCNs
- Cysts are typically unifocal and when the resected tumor is non-invasive, no surveillance is required

IPMN

- Mucin producing lesions of the exocrine pancreas
- Account for up to one third of pancreatic cysts
- responsible for only one percent of pancreatic cancers
- May be subcategorized in terms of their ductal involvement
  - main duct 16-30%
  - side branch 40-65%
  - mixed type 15-23%
- Most are solitary and are located in the pancreatic head
- 20-40% may be multifocal

IPMN

- Histologically graded as:
  - low grade dysplasia
  - intermediate grade dysplasia
  - high grade dysplasia
- Also sub-classified into four different types:
  - gastric
  - intestinal
  - pancreaticobiliary
  - oncocytic
- Classification is descriptive and indicative of different pathways of differentiation and progression to carcinoma

IPMN

- Cyst content may be analyzed in a number of ways:
  - mucin stain
  - viscosity
  - CEA count > 192 used as the most reliable test.
    - CEA is the most diagnostic marker for IPMN in fluid analysis based on receiver operator curve extrapolation.
- IPMN may be malignant at presentation
  - carry a better prognosis than pancreatic adenocarcinoma in this setting
- Worrisome features of IPMN lesions:
  - size greater than 3 cm
  - presence of mural nodules
  - dilation and/or involvement of the main pancreatic duct and cyst location (main duct versus side branch)

IPMN

IPMN


### Table 1: Meta-analysis of PD size

<table>
<thead>
<tr>
<th>Study name</th>
<th>Statistics for each study</th>
<th>Odds ratio and 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nepal</td>
<td>2.494 (0.910 - 6.660)</td>
<td>1.960 (.159)</td>
</tr>
<tr>
<td>Caboggin</td>
<td>189.809</td>
<td></td>
</tr>
<tr>
<td>Sai</td>
<td>33.571 (1.318 - 854.947)</td>
<td>2.127 (.033)</td>
</tr>
<tr>
<td>Wakabayashi</td>
<td>4.949 (0.226 - 193.825)</td>
<td>1.000 (.313)</td>
</tr>
<tr>
<td>Maguchi</td>
<td>2.917 (0.514 - 16.804)</td>
<td>1.902 (.106)</td>
</tr>
<tr>
<td>Sakai</td>
<td>8.054 (0.698 - 81.201)</td>
<td>1.000 (.354)</td>
</tr>
<tr>
<td>Akita</td>
<td>7.933 (1.470 - 42.561)</td>
<td>2.410 (.313)</td>
</tr>
<tr>
<td>Takekita</td>
<td>18.000 (2.468 - 131.285)</td>
<td>2.661 (.036)</td>
</tr>
<tr>
<td>H</td>
<td>7.27 (3.022 - 17.380)</td>
<td>4.462 (.000)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Meta-analysis</th>
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<tbody>
<tr>
<td>Benign</td>
</tr>
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<td>0.01 1 0.1 1 0.01</td>
</tr>
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### Table 2: Mural nodules meta-analysis

<table>
<thead>
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<th>Study name</th>
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<tr>
<td>Nepal</td>
<td>3.828 (1.539 - 9.640)</td>
<td>2.849 (.004)</td>
</tr>
<tr>
<td>Jang</td>
<td>2.576 (0.919 - 7.357)</td>
<td>1.800 (.072)</td>
</tr>
<tr>
<td>Schultz</td>
<td>5.500 (1.559 - 19.522)</td>
<td>2.638 (.006)</td>
</tr>
<tr>
<td>Rodriguez</td>
<td>39.827 (11.735 - 135.171)</td>
<td>5.950 (.000)</td>
</tr>
<tr>
<td>Han</td>
<td>61.322 (10.824 - 347.529)</td>
<td>4.850 (.000)</td>
</tr>
<tr>
<td>Serikawa</td>
<td>2.806 (0.723 - 10.771)</td>
<td>1.486 (.134)</td>
</tr>
<tr>
<td>Chtuka</td>
<td>15.167 (2.733 - 84.162)</td>
<td>3.110 (.002)</td>
</tr>
<tr>
<td>Nakajima</td>
<td>93.006 (1.039 - 9692.657)</td>
<td>2.804 (.007)</td>
</tr>
<tr>
<td>Caboggin</td>
<td>657.006 (11.567 - 3175.410)</td>
<td>2.347 (.002)</td>
</tr>
<tr>
<td>Sai</td>
<td>15.867 (5.647 - 449.115)</td>
<td>1.607 (.108)</td>
</tr>
<tr>
<td>Sugihara</td>
<td>5.026 (0.419 - 63.657)</td>
<td>1.372 (.003)</td>
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<tr>
<td>Wakabayashi</td>
<td>42.778 (1.976 - 925.070)</td>
<td>2.534 (.017)</td>
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<tr>
<td>Nakajima</td>
<td>5.206 (0.981 - 27.524)</td>
<td>1.787 (.073)</td>
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<tr>
<td>Chtuka</td>
<td>5.547 (1.938 - 15.891)</td>
<td>3.190 (.001)</td>
</tr>
<tr>
<td>Arimoto</td>
<td>32.069 (0.223 - 3.600)</td>
<td>0.823 (.386)</td>
</tr>
<tr>
<td>Hwang</td>
<td>14.131 (5.692 - 35.334)</td>
<td>5.867 (.000)</td>
</tr>
<tr>
<td>Akita</td>
<td>32.832 (4.822 - 119.597)</td>
<td>3.357 (.001)</td>
</tr>
<tr>
<td>Vo</td>
<td>12.429 (2.327 - 62.243)</td>
<td>2.946 (.000)</td>
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<tr>
<td>Takekita</td>
<td>11.006 (1.764 - 69.085)</td>
<td>2.744 (.006)</td>
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<td>9.274 (0.931 - 16.140)</td>
<td>7.482 (.002)</td>
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### Table 3: Size x 3mm meta-analysis

<table>
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<th>Statistics for each study</th>
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<tr>
<td>Nepal</td>
<td>27.413 (10.404 - 75.669)</td>
<td>6.859 (.000)</td>
</tr>
<tr>
<td>Jang</td>
<td>412.713 (142.389 - 1306.791)</td>
<td>10.899 (.000)</td>
</tr>
<tr>
<td>Schultz</td>
<td>44.956 (19.637 - 105.274)</td>
<td>8.187 (.004)</td>
</tr>
<tr>
<td>Rodriguez</td>
<td>668.333 (215.177 - 2068.124)</td>
<td>9.523 (.000)</td>
</tr>
<tr>
<td>Han</td>
<td>25.344 (5.557 - 55.892)</td>
<td>4.188 (.001)</td>
</tr>
<tr>
<td>Nakajima</td>
<td>40.218 (19.568 - 80.430)</td>
<td>14.811 (.000)</td>
</tr>
<tr>
<td>Chtuka</td>
<td>5.547 (1.938 - 15.891)</td>
<td>3.190 (.001)</td>
</tr>
<tr>
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<td>32.069 (0.223 - 3.600)</td>
<td>0.823 (.386)</td>
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Surgical intervention include\textsuperscript{1,2,3}
- pancreaticoduodenectomy
- distal pancreatectomy
- total pancreatectomy
- segmental resection
- enucleations
- duodenum preserving resections

For patients who are not surgical candidates, endoscopic ablation with ethanol has been described\textsuperscript{4,5,6} only considered experimental at this time

Surveillance strategies after definitive therapy are guided by the Sendai Criteria\textsuperscript{7}
- based on clean surgical margins
- extent of dysplasia
- whether known cystic lesions remain the pancreas

IPMN


<table>
<thead>
<tr>
<th>TABLE 3. Stratification of patients and outcome by ethanol concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
<tr>
<td>No. patients</td>
</tr>
<tr>
<td>Resolved</td>
</tr>
<tr>
<td>Persistent</td>
</tr>
<tr>
<td>Decreased</td>
</tr>
<tr>
<td>Similar size</td>
</tr>
<tr>
<td>Resected</td>
</tr>
<tr>
<td>Decreased/unknown</td>
</tr>
</tbody>
</table>

EtOH, Ethanol; NS, not significant.
IPMN

Rare Lesions

- Cystic lymphangioma
  - arise from lymphatic vessels
  - thought to be developmental aberrancies
  - account for 0.2% of all pancreatic cysts
  - benign, but may be locally invasive, and are more commonly found in women
  - symptomatic patients usually present with epigastric pain and a palpable mass
  - histology
    - interconnecting cysts separated by septa, lined by epithelial cells, and contain serous, serosanguineous, or chylous fluid (elevated triglyceride level)
  - benign nature
    - no further work-up is needed and lesions can be resected based on symptoms as needed

Rare Lesions

- Lymphoepithelial cysts
  - benign cystic entities, most commonly seen in men
  - abundant anucleated squamous cells, multinucleated giant cells, mature lymphocytes in a background of keratinaceous debris and a lack of neoplastic cells
  - surgery is not recommended in most patients unless they are symptomatic
- Other rare cystic tumors include
  - cystic degeneration of ductal adenocarcinoma
  - solid pseudo-pappillary tumors of the pancreas
  - other mesenchymal origin cysts

## Risks - EUS/FNA


<table>
<thead>
<tr>
<th>Complication</th>
<th>%</th>
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<tbody>
<tr>
<td>Overall</td>
<td>2.75</td>
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<tr>
<td>Pancreatitis</td>
<td>1.1</td>
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<tr>
<td>Chest or abdominal pain</td>
<td>0.77</td>
</tr>
<tr>
<td>Fever</td>
<td>0.33</td>
</tr>
<tr>
<td>Bleeding</td>
<td>0.33</td>
</tr>
<tr>
<td>Infection</td>
<td>0.22</td>
</tr>
</tbody>
</table>

Summary


<table>
<thead>
<tr>
<th>Table 1. Characteristics of Common Pancreatic Cystic Lesions</th>
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<tbody>
<tr>
<td><strong>Inflammatory Lesions</strong></td>
</tr>
<tr>
<td>Pseudocysts Male</td>
</tr>
<tr>
<td>Gender Female</td>
</tr>
<tr>
<td>Age (decade) Variable</td>
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<tr>
<td>% of cystic neoplasms 75–80% of all cystic lesions</td>
</tr>
<tr>
<td>Epithelial lining None</td>
</tr>
<tr>
<td>Malignant potential None</td>
</tr>
<tr>
<td>Cytology Neutrophils and macrophages PAS-staining cuboidal epithelium</td>
</tr>
<tr>
<td>Prognosis Excellent</td>
</tr>
<tr>
<td><strong>Serous Cystadenoma</strong></td>
</tr>
<tr>
<td>Gender Female</td>
</tr>
<tr>
<td>Age (decade) 7th</td>
</tr>
<tr>
<td>% of cystic neoplasms 32–39% of all cystic lesions</td>
</tr>
<tr>
<td>Epithelial lining Glycogen-rich cuboidal epithelium without mucin</td>
</tr>
<tr>
<td>Malignant potential None</td>
</tr>
<tr>
<td>Cytology Very low; very few reports of serous cystadenocarcinoma</td>
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<tr>
<td>Prognosis Resection curative</td>
</tr>
<tr>
<td><strong>Mucinous Cystadenoma</strong></td>
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<tr>
<td>Gender Female</td>
</tr>
<tr>
<td>Age (decade) 5th–6th</td>
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<tr>
<td>% of cystic neoplasms 10–45% of all cystic lesions</td>
</tr>
<tr>
<td>Epithelial lining Columnar mucin-producing</td>
</tr>
<tr>
<td>Malignant potential High</td>
</tr>
<tr>
<td>Cytology High</td>
</tr>
<tr>
<td>Prognosis Excellent if resection before invasive carcinoma</td>
</tr>
<tr>
<td><strong>IPMN</strong></td>
</tr>
<tr>
<td>Gender Male</td>
</tr>
<tr>
<td>Age (decade) 6th–7th</td>
</tr>
<tr>
<td>% of cystic neoplasms 21–33% of all cystic lesions</td>
</tr>
<tr>
<td>Epithelial lining Papillary mucin-producing</td>
</tr>
<tr>
<td>Malignant potential Moderate</td>
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<tr>
<td>Cytology Moderate</td>
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<tr>
<td>Prognosis Excellent if resection before invasive carcinoma</td>
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<tr>
<td><strong>Mucinous Cystadenocarcinoma</strong></td>
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<tr>
<td>Gender Male</td>
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<td>Age (decade) 6th–7th</td>
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<tr>
<td>% of cystic neoplasms &lt;1% of all cystic lesions</td>
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<tr>
<td>Epithelial lining Dysplastic mucin-producing</td>
</tr>
<tr>
<td>Malignant potential —</td>
</tr>
<tr>
<td>Cytology —</td>
</tr>
<tr>
<td>Prognosis Poor, but better than ductal adenocarcinoma</td>
</tr>
</tbody>
</table>
Summary

- Cystic lesions of the pancreas are more commonly encountered
- Wide range of presenting symptoms
  - most patients are asymptomatic
- EUS/FNA plays a key role in the diagnostic work-up
  - offers prognostic value
  - surveillance recommendations made based on the cyst size and fluid characteristics
- Therapeutic modalities
  - endoscopic
  - radiologic
  - and/or surgical
- No definitive guidelines exist for surveillance of all the known cyst types
  - tailored approach is recommended in many cases
- Genetic profiles and tumor markers may play a role in improving treatment strategies
The End

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248 662 4110