Evolution of incidental branch-duct type intraductal papillary mucinous neoplasm (bd-IPMN) of the pancreas over a prolonged follow-up time: a study with magnetic resonance imaging cholangiopancreatography (MRCP)

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Aims and objectives

Background

1. Pancreatic cysts are a frequent incidental finding, with a prevalence up to about 45% in patients undergoing MRCP for symptoms unrelated to the pancreas [1-2]. Most incidental cysts show a bd-IPMN-like pattern [2].

2. Asymptomatic bd-IPMN with no suspicious signs at MRCP (e.g., wall thickening or mural nodules) are currently managed with imaging surveillance, since only a minority of cases (4-6%) have been shown to harbor high-grade dysplasia or malignancy, regardless of the size [3-4]. On the other hand, natural history of bd-IPMN remains largely undefined [3]. This reflects into uncertainty about the most cost-effective schedule of repeated MRPCs and the overall duration of the surveillance [3].

Purpose

To evaluate the evolution of incidental bd-IPMN over time.
Methods and materials

Study population

We retrospectively searched our institutional database (period June 2006- March 2014) to identify: i) patients showing incidental pancreatic cysts on a baseline MRCP performed to evaluate conditions clinically unrelated to the pancreas; ii) patients who underwent a baseline MRCP to better assess pancreatic cysts incidentally found with previous US and/or CT performed no more than 1 month before. A total of 153 subjects were found. Of them, 77 patients (56 female, 21 male, age range 32-83 years, mean age 63.5 years) with a presumptive diagnosis of bd-IPMN formed the study population after applying inclusion and exclusion criteria detailed in Fig. 1 on page 5.

MRCP protocol

Examinations were performed on two 1.5T systems (Avanto (1) and Aera (2), Siemens Medical Systems, Erlangen, Germany) and/or a 3.0T magnet (Achieva, Philips HealthCare, Best, Netherlands) using a surface body coil and 2D and/or 3D T2-weighted MRCP protocols illustrated in Table 1 on page 5. MRCP was performed after oral administration of 1 cc of a gadolinium contrast agent diluted with water (1:10) to reduce signal intensity from fluids in the stomach and/or small bowel.

During baseline and follow-up examinations, MRCP was always associated with axial and coronal T2-weighted HASTE/SS-FSE, axial Diffusion-weighted EPI and axial T1-weighted VIBE/THRIVE sequences. Optional sequences included axial T1-weighted GE in-phase/out-of-phase and axial T2-weighted STIR/SPAIR. Multiphasic contrast-enhanced study was performed during the baseline examination or in the case of suspicious findings, using 0.1 mL/Kg of Gd-BOPTA (Multihance, Bracco, Milan, Italy) at an injection rate of 2 mL/sec and the axial T1-weighted VIBE/THRIVE sequence.

Image analysis

Image analysis was performed in consensus by two readers (with 11 and 5 years of experience, respectively), who reviewed baseline and follow-up examinations, as well as medical history and patients’ workup. After assessing baseline features, they recorded any per-patient variation of the cysts pattern in terms of:

1. number of baseline cysts;

2. cysts’ size (increase or decrease of at least 50% of the baseline larger diameter);
3. occurrence of at least one suspicious MRCP finding, confirmed to be malignant at a subsequent EUS with fine needle aspiration (FNA) and/or histological examination after surgery. Suspicious findings included [3-4]: i) solid mural nodules; ii) thick septa; iii) wall thickening; iv) dilatation of the MPD; v) cyst size larger than 30 mm.

Time of occurrence (in months) from the baseline MRCP was also recorded. In the case of multilocular cysts, lesion size was measured as a whole.

Data analysis

1. We calculated the mean and median time of occurrence from the baseline MRCP of the above imaging outcomes, as well as the incidence rate according to the equation [5]:

   \[
   \text{number of new cases of disease/number of persons at risk per unit time (12 months).}
   \]

2. We also performed Cox proportional hazard analysis to assess for risk factors associated with the development of malignancy, including: sex, age > 60 yrs, baseline size 1-2 cm, baseline size >2 cm, baseline number of cysts >2, baseline number of cysts >5, increase in cysts number, increase in cysts size, history of cancer of any nature. Alfa level was set 0.01.
Fig. 1: Study population. We included patients showing a bd-IPMN-like pattern with at least one cyst larger than 5 mm in size, with clear communication with the main pancreatic duct (MPD), and at least two follow-up MRCPs performed over a minimum overall period of 24 months. Yellow line refers to inclusion criteria, whereas green line refers to exclusion criteria. MPD = main pancreatic duct.

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<table>
<thead>
<tr>
<th>Sequence</th>
<th>1.5T (1)</th>
<th>1.5T (2)</th>
<th>3.0T</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.5T (1)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Radial 2D</td>
<td>HASTE</td>
<td>TSE</td>
<td></td>
</tr>
<tr>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Type of</td>
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<td>Navigator-gated</td>
<td>Breath-hold</td>
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<td>cor</td>
<td>cor</td>
<td>cor</td>
</tr>
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<td>cor</td>
<td>cor</td>
<td>cor</td>
</tr>
<tr>
<td>TR (ms)</td>
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<td>2500</td>
<td>4500</td>
</tr>
<tr>
<td>TE (ms)</td>
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<td>725</td>
</tr>
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</tr>
<tr>
<td>Matrix</td>
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<td>357x384</td>
<td>269x384</td>
</tr>
<tr>
<td>Number of</td>
<td>1 x 8</td>
<td>72</td>
<td>1 x 8</td>
</tr>
<tr>
<td>slices</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Slice thickness (mm)</td>
<td>40</td>
<td>1</td>
<td>40</td>
</tr>
<tr>
<td>NEX</td>
<td>1</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Acquisition time</td>
<td>4.5 s x 8</td>
<td>3 min 4 s</td>
<td>36 s</td>
</tr>
</tbody>
</table>

**Table 1:** Acquisition parameters of the MRCP sequences used to evaluate bd-IPMNs over time.

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Results

Cysts characteristics; number and timing of follow-up examinations

Patients showed a total of 406 cysts on baseline MRCP (per patient range 1-10, average 5.2). Cysts size spanned from 5 to 22 mm (mean size 8.52 mm). Larger lesions' size was: i) lower than 10 mm in 331 cases (81.5%); ii) between 10 and 19 mm in 64 cases (15.7%); iii) between 20 and 29 mm in 11 cases (2.7%).

After baseline MRCP, patients underwent a total of 281 follow-up examinations, corresponding to a mean of 3.6 examinations per-patient (range 2-8). Median follow-up duration was 37 months (range 12-81 months). Median interval of time between repeated follow-up examinations was 17 months (range 2-58 months).

Cysts variation over the follow-up

Table 2 on page 8 shows changes occurred during the follow-up in the number (Fig. 2 on page 8) and size (Fig. 3 on page 9) of cysts, as well as suspicious findings associated with malignancy (Fig. 4 on page 10). There was overlap between: i) increase in cysts number and size in 3/77 subjects (3.9%); ii) increase in cysts size and development of malignancy in 2/77 subjects (2.6%).

Table 3 on page 11 provides an overview of changes occurred in 3/77 patients with proven malignancy. Of them, one showed involvement of the MPD, with final diagnosis of mixed-type IPMN.

Risk factors for cysts evolution

No significant clinical or imaging predictive factors were found for the above MRCP outcomes (p>0.01).
<table>
<thead>
<tr>
<th>MRI outcome</th>
<th>Number of pts.</th>
<th>Number of cysts involved</th>
<th>Per-pt. number of cysts involved</th>
<th>Mean/median time of occurrence from baseline MRCP (months)</th>
<th>Incidence rate per 12 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increase in cysts number</td>
<td>4/77 (5.1%)</td>
<td>14/402 (3.4%)</td>
<td>3.5</td>
<td>33.5/30 (range 16-58)</td>
<td>0.02%</td>
</tr>
<tr>
<td>Increase in cysts size</td>
<td>18/77 (23.3%)</td>
<td>22/402 (5.4%)</td>
<td>1.22 (mean increase 5.18 mm)</td>
<td>18.7/16.5 (range 4-58)</td>
<td>0.03%</td>
</tr>
<tr>
<td>Occurrence of suspicious findings confirmed to be malignant</td>
<td>3/77 (3.8%)</td>
<td>2 + 1 MPD</td>
<td>-</td>
<td>25.3/13 (range 6-57)</td>
<td>0.02%</td>
</tr>
</tbody>
</table>

**Table 2:** Characteristics of the MRCP outcomes observed during the follow-up.

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Fig. 2: MIP reconstruction from 3D MRCP in a 64 years-old male patient who underwent baseline examination because of an increase in liver function tests. After 24 months, cysts increased in number in the head and tail.

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Fig. 3: 2D MRCPs in a 72-years-old female subject who performed baseline MRCP to assess a pancreatic cyst incidentally found on US. Larger cyst increased from 20 to 29 mm over three years. Communication with the MPD was confirmed at EUS.

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Fig. 4: Mixed type-IPMN in a 65 male years-old patient in which the slight MPD dilatation was not evident in a MRCP performed 6 months earlier. Histological examination after resection showed malignancy.

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Table 3: Changes occurred in patients with proven malignancy.

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<table>
<thead>
<tr>
<th>Pt./Sex/Age</th>
<th>Number of cysts/larger cyst at baseline MRCP</th>
<th>Increase in number</th>
<th>Increase in size</th>
<th>Finding</th>
<th>Involvement of the MPD</th>
<th>Time of occurrence from baseline MRCP (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (F, 55 years)</td>
<td>7/10 mm</td>
<td>No</td>
<td>1 (5 → 15 mm)</td>
<td>1 mural nodule in the larger cyst</td>
<td>No</td>
<td>57</td>
</tr>
<tr>
<td>2 (M, 65 years)</td>
<td>10/22 mm</td>
<td>No</td>
<td>No</td>
<td>dilation of the MPD</td>
<td></td>
<td>6</td>
</tr>
<tr>
<td>3 (F, 72 years)</td>
<td>3/16 mm</td>
<td>No</td>
<td>1 (16 → 27 mm)</td>
<td>1 mural nodule in the larger cyst</td>
<td>No</td>
<td>13</td>
</tr>
</tbody>
</table>
Conclusion

1. The incidence rate of (i) cysts changes (increase in number and size) and (ii) occurrence of suspicious findings proven to be malignant was low during the MRCP follow-up of bd-IPMN (incidence rates 0.02-0.03%).

2. Time of occurrence of malignancy during the follow-up spanned over a wide range (from 6 months to 57 months). Moreover, no definite imaging or clinical features are predictors of cysts evolution, suggesting that - regardless of the number and size of initial cysts - the follow-up should be prolonged over time.
Personal information

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