IPMN Management – Fukuoka Consensus vs. European Evidence-Based Guidelines

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Slovenian Journal of Gastroenterology / Gastroenterolog 2025; supplement 1: 112–115

***Keywords**: IPMN, pancreatic cyst, endoscopic ultrasound, MRCP*

INTRODUCTION

Intraductal papillary mucinous neoplasms (IPMNs) of the pancreas are increasingly recognized cystic lesions with variable malignant potential, ranging from benign adenomas to invasive carcinomas. They are classified into main duct (MD), branch duct (BD), and mixed types, with MD-IPMNs carrying a significantly higher risk of malignancy. Mean rates of high-grade dysplasia (HGD)/invasive carcinoma (IC) in MD-IPMN are 62% (36%-100%) compared to 31% (15-48%) in BD-IPMN.(1–5) MD-IPMN is defined by segmental or diffuse dilation of the main pancreatic duct (MPD) >5 mm without another cause of obstruction. In contrast, BD-IPMN is characterized by pancreatic cysts >5 mm that communicate with the MPD. Mixed-type IPMN fulfills criteria for both.(6)

With the rise in incidental detection due to widespread use of high-resolution cross-sectional imaging, the need for standardized diagnostic and management strategies has become critical (6,7). In response, several international guidelines have emerged, most notably the International Consensus Guidelines, initially published in 2006 (Sendai Guidelines) and revised in 2012 and 2017 (Fukuoka Guidelines) (1,6,8). These were further refined in the recent International Evidence-Based Kyoto Guidelines (9). In parallel, the European Evidence-Based Guidelines, first introduced in 2013 and revised in 2018, offer an alternative, evidence-oriented framework for clinical decision-making

This article compares the management strategies of the Fukuoka and European guidelines and evaluates the emerging role of the Kyoto Guidelines in modern clinical practice.

INDICATIONS FOR SURGERY

The European Guidelines categorize indications for surgery as absolute and relative:

- **Absolute indications**: jaundice, enhancing mural nodule ≥5 mm, positive cytology, MPD ≥10 mm –all strongly predictive of malignancy.
- **Relative indications**: MPD 5–9.9 mm, cyst growth ≥5 mm/year, CA 19-9 >37 U/mL, symptoms, enhancing mural nodule <5 mm, and cyst ≥40 mm.

Surgery is advised for patients with multiple relative indications and for those with one and without significant co-morbidities. Intensive surveillance is advised for those with one relative feature and significant comorbidity or short life expectancy.

The Fukuoka Guidelines divide risk features into high-risk stigmata (HRS) and worrisome features (WF):

- HRS (surgery recommended): obstructive jaundice in a patient with cystic lesion of the head of the pancreas, enhancing mural nodule ≥5 mm, MPD ≥10 mm.

- WF (EUS recommended): acute pancreatitis, cyst ≥3 cm, mural nodule <5 mm, thickened cyst walls, MPD 5–9 mm, abrupt MPD change with distal atrophy, lymphadenopathy, elevated CA 19-9, and cyst growth >5 mm/2 years. In Kyoto update recent-onset diabetes is included and cyst growth is downgraded to >2.5 mm/year.

  If EUS identifies definitive high-risk features (e.g., mural nodule ≥5 mm, main duct features suspicious for involvement or suspicious cytology), resection is recommended. Otherwise, surveillance is advised.

The Kyoto Guidelines add suspicious or positive results of cytology (if performed) to WF and endorse surgery in cases of multiple WF, repeated pancreatitis affecting quality of life, or in young, fit patients. They also uniquely emphasize quality-of-life impact, general condition, comorbidity, life expectancy, and preference, and propose more individualized approach to decision making [5].

All three guidelines recommend oncologic resection with lymphadenectomy when invasive carcinoma is suspected. Parenchyma-sparing procedures can be done in low-risk cases (non-invasive lesion suspected).

POSTOPERATIVE SURVEILLANCE

Both Fukuoka and European guidelines recommend lifelong surveillance for resected IPMN patients who are fit for surgery. For those with associated invasive carcinoma, surveillance mimics protocols for resected pancreatic adenocarcinoma.

- **European Guidelines**: For high-grade dysplasia or MD-IPMN, follow-up every 6 months for 2 years, then annually. others follow non-resected IPMN protocols

- **Fukuoka Guidelines**: Biannual follow-up in patients with risk factors (e.g., family history, positive margin for high-grade dysplasia, non-intestinal subtype). Others follow non-resected IPMN protocols.

Guidelines recommend MRI with MRCP as the preferred imaging modality for routine surveillance of IPMNs, due to its non-invasive nature and detailed ductal visualization. EUS is used when there are worrisome features (e.g., mural nodules or duct dilation) or when further assessment is needed, often alternating with MRI. CT is reserved for cases where MRI is contraindicated or for preoperative planning, but it is not recommended for regular follow-up due to radiation exposure and lower sensitivity for cyst characteristics.

SURVEILLANCE OF NON-RESECTED IPMN

In the literature, contrast-enhanced multi-detector computed tomography (MDCT), contrast-enhanced magnetic resonance imaging/cholangiopancreatography (MRI/MRCP) and EUS are equivalent in diagnosing IPMN with HGD/IC.(11) However both guidelines suggest MRI as the method of choice for follow-up. EUS can be used in selected cases, noting it is operator dependent.

- **European Guidelines**:
  - Cyst <15 mm without risk: MRI at 6 months, then annually.
  - Relative indications present or elderly/comorbid: 6-month intervals. Changes in symptoms prompt re-evaluation.

- **Fukuoka Guidelines**:
  - Cyst >3 cm: 3–6 months.

- Cyst 2–3 cm: EUS in 3–6 months, then annual imaging.
- Cyst 1–2 cm: Biannual imaging in year one, then annually for 2 years, then biennially.
- Cyst <1 cm: MRI every 6 months, then every 2 years.

Kyoto Guidelines simplify this by grouping all cysts <2 cm for follow-up at 6 months, then every 18 months.

DISCONTINUATION OF SURVEILLANCE

The European and Fukuoka guidelines advise continued follow-up as long as patients remain surgical candidates, recognizing the lifelong risk of progression.

In contrast, the Kyoto Guidelines suggest surveillance may be discontinued in small, stable cysts after 5 years without change, offering a more individualized and less burdensome approach for select patients [5,6].

DISSCUSSION

A study from Heidelberg assessing the timing of surgical intervention categorized resections as too early (adenoma/low-grade dysplasia), timely (intermediate-grade dysplasia/in situ carcinoma), or too late (invasive cancer). Out of 1,439 patients: 30.4% underwent resection too early, 35.1% had timely resections, and 34.5% had resections deemed too late. Notably, 24.9% of patients in the "too late" group had previously been under surveillance, highlighting the challenges in optimal timing for surgery.(12)

The Fukuoka Guidelines demonstrate moderate diagnostic performance, with studies reporting a positive predictive value (PPV) of around 33% for high-risk stigmata and 23.5% for worrisome features in predicting malignancy.(13) In other analyses, the PPV for high-risk stigmata rose to 81%, with a sensitivity of 68%, suggesting better performance in select cohorts.(14) In contrast, the European Guidelines show slightly higher diagnostic accuracy, with a sensitivity of 82% and a PPV of 78.8% when considering absolute indications for surgery. When both absolute and relative indications were included, the sensitivity and PPV remained high at 80%, indicating that these guidelines may more effectively identify patients who truly need timely resection.(14)

Both guidelines are instrumental in stratifying patients for surgical intervention. The Fukuoka guidelines, with their detailed criteria, may lead to more surgeries, potentially capturing malignancies earlier but also increasing the risk of overtreatment. The European guidelines aim for a balance, emphasizing both absolute and relative indications to guide decision-making. However, the risk of delayed surgery and progression to invasive cancer remains a concern, underscoring the need for individualized patient assessment and ongoing research to refine these guidelines.

CONCLUSION

Management of IPMNs remains a dynamic field. While the Fukuoka and European Guidelines offer structured, risk-stratified approaches, they diverge in thresholds and surveillance schemes. The Kyoto Guidelines provide a more flexible, quality-of-life-oriented model incorporating emerging evidence and patient-centered variables. Moving forward, integration of molecular markers, radiomics, and personalized risk assessments will likely enhance the precision of IPMN management strategies worldwide.

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