Editorial Commentary

Surveillance of non-resected branch-duct intraductal papillary mucinous neoplasms: is a simplified algorithm justified?

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We read with great interest the recent guideline by Ohtsuka *et al.* entitled "International evidence-based Kyoto guidelines for the management of intraductal papillary mucinous neoplasm of the pancreas" on behalf of the International Association of Pancreatology (IAP) (1). This most widely used guideline has been updated to incorporate the most recent evidence as well as expert consensus on the management of intraductal papillary mucinous neoplasm (IPMN). One major revision in this guideline is simplifying the surveillance protocol of non-resected IPMN and offering the possibility of stopping surveillance for small branch duct IPMN (BD-IPMN) that remains stable during a 5 years period (1). The changes in the surveillance protocol are particularly important as most people are diagnosed with asymptomatic small BD-IPMN that does not require surgery at the time of diagnosis.

The Kyoto guideline (1) recommends the surveillance protocol of non-resected BD-IPMN based on the cyst size: (I) for cyst diameter <20 mm, 6 months once, then every 18 months if stable, (II) for cyst diameter ≥20 and <30 mm, 6 months twice, then every 12 months if stable, and (III) every 6 months for cyst diameter ≥30 mm. In addition, the new guideline cautiously recommends the option of stopping surveillance for individuals with cyst diameter <20 mm which remains stable after 5 years of surveillance, with consideration of patient condition and life expectancy. Another change is the imaging modalities for surveillance. Magnetic resonance imaging (MRI) is recommended as the preferred modality for surveillance purposes. Multi-detector computed tomography (MDCT) and endoscopic ultrasound (EUS) are considered only when MRI detects changes. In summary, there are three major changes in the updated Kyoto guideline with regard to the surveillance for non-resected BD-IPMN, including a simplified protocol, the option of stopping surveillance, and the preferred imaging modality.

Although this new guideline has incorporated available evidence, high-level evidence is still scarce. Most of the studies on IPMN are retrospective and findings from different studies may vary or even conflict. That's the reason why recommendations from different guidelines vary considerably, especially in the surveillance protocol (*Table 1*). Nevertheless, most guidelines use cyst size as the stratification factor for surveillance of non-resected

Table 1 Recommendations on surveillance of non-resected BD-IPMN by current guidelines

Guidelines	Surveillance intervals and imaging modalities	Termination of surveillance
2024 Kyoto (1)	<2 cm, MRI 6 mo once, then every 18 mo if stable 2–3 cm, MRI 6 mo twice, then every 12 mo if stable ≥3 cm, MRI every 6 mo	Optional, stop after 5 y if stable or no longer fit for surgery or have a life expectancy of <10 y
2018 ACG (2)	<1 cm, MRI every 2 y for 4 y, then consider lengthening if stable 1–2 cm, MRI yearly for 3 y followed by every 2 y for 4 y, then consider lengthening if stable 2–3 cm, MRI or EUS every 6 mo to 1 y for 3 y followed by MRI yearly for 4 y, then consider lengthening if stable >3 cm, MRI alternating with EUS every 6 mo for 3 y followed by MRI alternating with EUS yearly for 4 y, then consider lengthening if stable	Lifelong until no longer fit for surgery
2018 European (3)	MRI, every 6 mo for 1 y, then yearly	Lifelong until no longer fit for surgery
2015 AGA (4)	MRI at 1 y, then every 2 y	Stop after 5 y if stable or no longer fit for surgery

BD-IPMN, branch duct intraductal papillary mucinous neoplasm; mo, months; y, years; MRI, magnetic resonance imaging; ACG, American College of Gastroenterology; EUS, endoscopic ultrasound; AGA, American Gastrointestinal Association.

BD-IPMN after careful risk assessment ruling out high-risk stigmata (HRS) and worrisome features (WFs). The American Gastrointestinal Association (AGA) (2) and the Kyoto (1) guidelines presented an option for stopping surveillance after 5 years, while others recommend lifelong surveillance (3,4). MRI is the most favorable imaging modality across guidelines, with EUS and CT as alternatives in some guidelines. In the following section, we provide a step-by-step review of the key elements in establishing a practical surveillance algorithm for non-resected BD-IPMN.

Surveillance intervals

The surveillance protocol in the Kyoto guideline has been generally simplified in comparison to the previous Fukuoka guideline (5). Like the Fukuoka guideline, it stratifies non-resected BD-IPMN in terms of cyst diameter for determining the surveillance intervals. However, the Kyoto guideline lengthens the interval for BD-IPMN <2 cm and those ≥3 cm. Several recent studies have shown that malignant transformation in small BD-IPMN without HRS or WFs is very low thus, a longer surveillance interval is safe for this population (6-8). Especially a recent large retrospective study including 3,656 BD-IPMN patients reported for cysts smaller than 20 mm, the time to 50% increase and the doubling time of 95% of the cysts were 1.1 and 2.2 years, respectively, for cyst sizes of 20 to 30 mm, most of the cyst morphologic changes including size increment to 30 mm may be detected with 1-year of follow-up, and for cysts over 30 mm, the median time to progression of WFs is 7 months (6). Thus, they conclude a 1.5-, 1-, and 0.5-year surveillance interval could be optimal for cysts smaller than 20 mm, 20 to 30 mm, and over 30 mm, respectively. Less frequent surveillance may increase patient adherence and reduce healthcare expenditure without endangering the patient by current available evidence. Overall, emerging new evidence has enabled the Kyoto guideline to recommend a higher level of evidence-based surveillance protocol, compared with other guidelines which were all published more than 6 years ago.

Termination of surveillance

The AGA guideline is the first guideline to recommend termination of surveillance for pancreatic cystic neoplasms that are stable or no longer fit for surgery after 5 years of surveillance (2). This recommendation has been causing significant controversy for years. Nevertheless, more and more evidence has supported that cessation of surveillance after several years would be a rational choice for patients with a stable small BD-IPMN. Several large retrospective studies demonstrated the long-term risk of malignancy in BD-IPMN to be around 3.7–5.5% in more than 5 years of follow-up (6,9-11). Han *et al.* (6) found that no malignant conversion

was observed in stable cysts after 5 years of surveillance, and the conversion rate was only 1.7% in changing cysts. Thus, they suggested that surveillance may be discontinued in older patients (those unfit for surgery, or those with a life expectancy of 10 years or less) with cysts smaller than 20 mm, no WFs, and no morphologic changes during the first 5 years of surveillance. The Kyoto guideline has embraced the above evidence and proposes one option of "stop surveillance" for individuals with small stable cysts, no longer fit for surgery, or have a life expectancy of less than 10 years. Of note, "continue surveillance" remains an alternative option in this new guideline, considering that the cumulative risk of malignant transformation in BD-IPMN grows continually as reflected in a large retrospective study (12).

Conclusions

The Kyoto guideline has established a simplified and evidence-based algorithm for the surveillance of non-resected BD-IPMN. Its cost-effectiveness needs to be validated in further studies. Although surveillance termination is recommended as an option for stable small BD-IPMN in this guideline, it emphasizes a tailor's approach based on patients' general condition, comorbidity, life expectancy, and preference. Finally, it is imperative to acknowledge that the quality of evidence of all available guidelines is low given they are generally based on retrospective studies. Several large prospective clinical trials have been evaluating different surveillance protocols for BD-IPMN. Future high-level evidence will undoubtedly strengthen the guidelines and alter the clinical practice.

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