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Current Guidelines for the Management of Branch Duct Intraductal Papillary Mucinous Neoplasms

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The management of pancreatic cystic neoplasms has been constantly evolving and changing over the past 2 decades [1-3]. This is mainly due to the rapid advancement of knowledge in this field resulting in particular: 1) the improved understanding of the natural history and biological behavior of the different pathological entities which comprise pancreatic cystic neoplasms and 2) more accurate preoperative diagnosis of these neoplasms as a result of a better understanding of their individual morphological characteristics on imaging and the introduction of newer diagnostic modalities such as endoscopic ultrasonography with fine needle aspirate (EUS-FNA) [2-4]. In general, the management approach has trended from that of aggressive surgical resection [5] to a more selective approach whereby most cystic neoplasms are now managed via surveillance [1,6-8]. Since the landmark paper by Compagno and Oertel [9]; the general consensus was that all mucinous neoplasms were potentially malignant or malignant and should be surgically resected whereas serous cystic neoplasms were benign and could be managed conservatively [2,10,11]. Subsequently, investigators recognized that mucinous neoplasms were actually composed of 2 distinct pathological entities i.e. mucinous cystic neoplasms (MCNs) and intraductal papillary mucinous neoplasms (IPMNs) [10,12,13]. More recently, it was recognized that IPMNs could be classified into branch-duct (BD), main-duct (MD) and mixed-duct types (MT) [14,15]. BD-IPMNs were found to be associated with a less aggressive biological behavior when compared to MD/MT-IPMN and many investigators have since demonstrated that selected BD-IPMNs could be managed conservatively [1,6,8,14-16].

In 2006, an international panel of experts formulated the Sendai Consensus Guidelines (SCG) to guide the management of IPMNs and MCNs [2,14]. According to these guidelines, all MD/MT-IPMNs and MCNs should be resected whereas selected BD-IPMNs without 'suspicious features' (SCG-ve) could be observed [2,14]. The suspicious features were cyst size >3 cm, presence of symptoms, dilated main pancreatic duct (>6 mm), presence of solid component and/or a positive cyst fluid cytology [2,14]. The SCG has since been validated by several studies [2,6,7]. It is widely recognized that the main limitation of the SCG is its low positive predictive value (PPV) resulting in resection of many benign BD-IPMNs [2,15,17]. However, the safety of the SCG has been confirmed by several large studies which have reported a high Negative Predictive Value (NPV) of 86% to 100% [2,17]. Even more importantly, all of the malignant lesions missed in most of these studies were IPMNs with high grade dysplasia and none had invasive carcinoma [2,17]. We recently performed a systematic review of studies validating the SCG for BD-IPMN which confirmed that the SCG was associated with a low PPV but high NPV (personal communication). Pooled analysis of 10 studies demonstrated that the PPV of SCG+ve BD-IPMNs was 34% and 26 of 242 (11%) resected SCG-ve BD-IPMNs were malignant (11 invasive). However, it was important to note that 17 of the 18 patients including all 11 invasive BD-IPMNs were from a single study from Germany [8,17]. More recent results from the Memorial Sloan-Kettering Cancer Center reported 5 (14%) HGD among 35 resected SCG -ve BD-IPMN [18] whereas the Massachusetts General Hospital reported a 6.5% risk of HGD among 46 SCG -ve BD-IPMN smaller than 3 cm based on the revised 2012 SCG [6,17]. Importantly, unlike the German study; no invasive cancers were detected in both these studies among the SCG -ve neoplasms [17]. There are several possible reasons why data from the German study was contrary to that from data available from most other studies in the literature [17-19]. The main reason was likely due to the fact that the investigators included lesions suspected but not pathologically confirmed as BD-IPMNs. Eight of the 17 malignant IPMNs in the study were by definition mixed type-IPMNs as there was focal tumor involvement of the main pancreatic duct [17].

As many investigators recognized the limitations of the original SCG, the SCG was revised in Fukouka in 2010 and published recently in 2012 [2,7,14,15]. These revisions to the SCG were made to overcome its main limitation of its low PPV which resulted in a large number of benign BD-IPMNs being resected. The revised 2012 SCG classified BD-IPMNs into 3 categories (high risk, worrisome risk and low risk) instead of 2. According to these revised guidelines, some BD-IPMNs which would be classified as SCG+ve were now classified in the worrisome risk group and could potentially be observed after further evaluation by EUS=FNA [15]. The utility of these revised guidelines were validated by 2 recent studies [6,7].

Finally, it is imperative to remember that although both the SCG and the revised SCG are useful in guiding the management of IPMNs, guidelines are merely guidelines [17]. The limitations of these guidelines are they do not take into account important factors which would influence management such as a patient's fitness for surgery, life expectancy, risk and type of surgery and even the cost of treatment or investigations [17]. The main consideration when deciding whether to surgically treat or observe a BD-IPMN should be to balance the risk of surgery versus the risk of the patient developing and dying from pancreatic malignancy [17]. For example, most would agree that the ideal treatment for an 85-year old with a 2 cm BD-IPMN in the head of pancreas with a normal sized main pancreatic duct would differ significantly from a 55-year old with a 2.8 cm BD-IPMN in the tail of pancreas associated with a 4 mm dilated main pancreatic duct although both would be considered low risk SCG lesions.

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