Intraductal papillary mucinous neoplasm (IPMN) of the pancreas is characterized by intraductal proliferation of mucin-producing epithelial cells that exhibit various degrees of dysplasia. IPMN is classified into four histological subtypes (gastric, intestinal, pancreatobiliary, and oncocytic) according to its histomorphological and immunohistochemical characteristics. Endoscopic retrograde cholangiopancreatography plays a crucial role in the evaluation of these features of IPMN. Endoscopic ultrasonography (EUS) has proven to be more sensitive than computed tomography or magnetic resonance imaging for early detection of malignancy. The present review addresses the current roles of endoscopy and related techniques in the management of IPMN. The particular focus is on diagnosing IPMN and malignancy within IPMN, detecting pancreatic cancer concomitant with IPMN, differentiating the epithelial subtypes of IPMN, determining the optimal strategy for the management of branch duct IPMN, and discussing innovative endoscopic technology related to IPMN. The disadvantages of endoscopic examinations of IPMN and different attitudes toward EUS-guided fine-needle aspiration for IPMN between Japan (negative) and other countries (active) are also discussed.

Key words: endoscopic retrograde cholangiopancreatography, endoscopic ultrasonography, epithelial subtype, intraductal papillary mucinous neoplasm, pancreatic cancer

INTRODUCTION

Intraductal papillary mucinous neoplasm (IPMN) of the pancreas is a unique entity characterized by intraductal proliferation of mucinous epithelium that produces excessive mucin. The macroscopic morphology is divided into three types: main duct type (MD-IPMN), branch duct type (BD-IPMN), and mixed type. Endoscopy has played an important role in the diagnosis of IPMN since the discovery of this neoplasm. Ohashi et al. first observed a patulous duodenal papilla that was markedly dilated by protruding mucin and reported it as the first case in 1980; they then reported a series of IPMN in 1981. This phenomenon was caused by MD-IPMN and was considered to be a unique feature of ‘mucin-hypersecreting pancreatic cancer’, which was considered a special type of pancreatic cancer associated with a better prognosis than that of ordinary pancreatic cancer.

The international consensus guidelines for the management of IPMN, as revised by the International Association of Pancreatology in 2012, do not recommend endoscopic retrograde cholangiopancreatography (ERCP) as a routine examination for sampling of fluid or brushings in IPMN. Thus, it is considered a special examination to be carried out only in the context of research. However, ERCP still has distinct roles in the investigation of IPMN. Moreover, endoscopic ultrasonography (EUS) has now become an indispensable modality with which to examine the pancreas harboring IPMN. This review describes the current roles of endoscopy, including ERCP and EUS, in the exploration of this unique and fascinating entity. Readers may refer to a recent publication for more details.
MD-IPMN from chronic pancreatitis is very difficult, even by ERCP or EUS, and especially in patients with diffuse MPD dilation. In such cases, instead of carrying out immediate resection, it is necessary to observe the patient for a few months to determine whether the MPD dilation is progressive.

One of the specific features of BD-IPMN is the presence of communication with the MPD, which is not a common feature of mucinous cystic neoplasm. However, the accumulation of mucus within the BD-IPMN and its communicating branch frequently hampers the demonstration of the communication, even by ERCP. Instead, ERCP often reveals mucus moving within the MPD and changing its shape. The presence of mucus as shown by ERCP is regarded as a confirmatory finding of IPMN. EUS is often useful to demonstrate communication between the BD-IPMN and MPD, even when occluded by mucus.

**DIAGNOSIS OF MALIGNANCY IN IPMN**

Cytology is the gold standard examination technique for diagnosis of malignancy in IPMN. Cytological examination can be done using pancreatic juice obtained during ERCP or cyst fluid sampled by EUS-guided fine-needle aspiration (EUS-FNA). Both of these approaches have advantages and disadvantages (Table 1).

Cytology of the pancreatic juice is associated with relatively low sensitivity of 10–50% for diagnosing malignancy (Table 2). The sensitivity can be increased to 80% with the use of repeated sampling through a nasopancreatic catheter. Irrigation of the pancreatic duct also reportedly increases the diagnostic sensitivity of ERCP cytology to 78%. Both histological grades and subtypes can be diagnosed fairly well by cell block cytology of the pancreatic juice, but these parameters are consistent with the histo-

---

**Table 1** Advantages and disadvantages of endoscopy in the management of IPMN

| Advantage                                      | EUS                                      | ERCP                                      |
|-----------------------------------------------|------------------------------------------|-------------------------------------------|
| Delineation of mural nodules                  | Clear                                    | Not always possible                       |
| Demonstration of thickened septa              | Clear                                    | Seldom possible                           |
| Distinction of mural nodules from mucin       | Possible by Doppler and/or contrast enhancement | Not clear                               |
| Diagnosis of malignancy                       | Possible by FNA cytology                 | Possible by pancreatic juice cytology     |
| Detection of concomitant cancer               | Possible when a mass is detectable        | Possible by pancreatic juice cytology     |
| Differentiation of epithelial subtype         | Possible by FNA cytology                 | Possible by pancreatic juice cytology     |
| Disadvantages                                 |                                          |                                           |
| Observer dependency                           | High                                     | Minimal                                   |
| Expertise required                            | Great                                    | Great                                     |
| Bleeding                                      | Rare but possible                        | Extremely rare                            |
| Acute pancreatitis                            | Extremely rare                            | Rare but hampering its use in Western countries |
| Spillage and needle track seeding             | Possible during FNA, hampering its use in Japan | No                                      |

ERCP, endoscopic retrograde cholangiopancreatography; EUS, endoscopic ultrasonography; FNA, fine-needle aspiration; IPMN, intraductal papillary mucinous neoplasm.
logical findings of resected specimens in only 55.6% of BD-IPMN. However, 100% accuracy can be obtained for MD-IPMN and mixed-type IPMN.8,11,12

Cyst fluid obtained by EUS-FNA can also be used to diagnose malignant BD-IPMN with a reported sensitivity and specificity of 67% and 88%, respectively, at a special institution with expertise in FNA and sophisticated cytodiagnostic interpretation.13 A higher sensitivity of 80% and a similar specificity of 85% were also reported from the same institution.14 Pitman et al.15 claimed the significance of ‘atypical epithelial cells’, not malignant cells, alone or in combination with a carcinoembryonic antigen (CEA) level of >2500 ng/mL as more accurate indicators of malignancy than are the Sendai criteria.

EUS provides several useful findings for the diagnosis of malignancy in IPMN. Mural nodules as the most significant sign of a high risk of malignancy can be clearly demonstrated by EUS. Hirono et al.16 analyzed 134 patients with resected BD-IPMN and showed that a mural nodule size of >5 mm and a CEA level in the pancreatic juice of >30 ng/mL were independent predictors of malignancy. Ohno et al.17 reported contrast-enhanced EUS findings in 87 patients with resected IPMN. Mural nodules, defined as blood flow-supplied protrusions, were classified into four types: low papillary, polypoid, papillary, and invasive. The latter two types were diagnostic of malignancy with a sensitivity of 60.0%, specificity of 92.9%, and accuracy of 75.9%. The same group later reported the results of a long-term retrospective study of 142 patients with BD-IPMN.18 Malignant transformation occurred in nine patients (6.3%), with a 5-year transformation rate of 10.7%. The existence of mural nodules at initial diagnosis and involvement of the MPD were significant predictors of malignant change of BD-IPMN.

Although contrast-enhanced power Doppler ultrasonography is associated with blooming artifacts, poor spatial resolution, low sensitivity to slow flow, and high sensitivity to motion artifacts, this new EUS system has further allowed for the observation of images of the pancreatic microcirculation and parenchymal perfusion without Doppler-related artifacts.19 Contrast enhancement of mural nodules by computed tomography (CT) is described in the Fukuoka guidelines as a crucial finding suggestive of malignancy, but the same phenomenon by EUS should also be added. Thickening and irregularity of septa within BD-IPMN can also be clearly visualized by EUS.

**DETECTION OF PANCREATIC CANCER CONCOMITANT WITH IPMN**

The development of ordinary pancreatic cancer in patients with IPMN has been drawing attention during the past two decades (Fig. 2). The first case of non-invasive pancreatic cancer in a patient with BD-IPMN was reported in 1997.20 The location of non-invasive cancer was determined by endoscopic segmental cytology of the MPD with a balloon catheter. Since then, many series of patients have

---

**Table 2** Reported data of pancreatic juice cytology in IPMN and pancreatic cancer

| Author/Year | No. patients | Description |
|-------------|--------------|-------------|
| Yamaguchi et al., 2005 | 71 | Sensitivity for malignant IPMN of 14.1%, higher in main duct type |
| Yamaguchi et al., 2005 | 103 | Diagnostic in all but one patient with IPMN and in 82.7% of patients with PDAC |
| Catheter | 71 | Sensitivity of 38.2% for IPMN |
| Pancreatoscropy | 32 | Sensitivity of 62.2% for IPMN, 25.4% for PDAC |
| Hibi et al., 2007 | 19 | 79% consistent cytological and histological subclassifications |
| Mikata et al., 2013 | 139 | Data improved by ENPD (P = 0.0001) |
| Conventional | 79 | Sensitivity 39%, specificity 100%, PPV 100%, NPV 40%, accuracy 57% |
| ENPD for 3 days | 60 | Sensitivity 80%, specificity 100%, PPV 100%, NPV 71%, accuracy 87% |
| Conventional | 79 | Sensitivity 78%, specificity 93%, PPV 88%, NPV 88% |
| Monzen et al., 2013 | 23 | Cell block cytology sufficient for typing/grading of IPMN in 20 patients, 95% of typing and 80% of grading consistent with histology |
| Hara et al., 2013 | 36 | Histological subtype accurately diagnosed in 42% of cases; rate improved to 89% with MUC staining (P < 0.01). HGD/invasive IPMN diagnosed with 77.2% sensitivity, 85.7% specificity, and 80.5% accuracy |
| Ohtsuka et al., 2014 | 70 | Accuracy 77%; 3 of 11 concomitant PDAC could be diagnosed only by pancreatic juice cytology |

ENPD, endoscopic nasopancreatic drainage; HGD, high-grade dysplasia; IPMN, intraductal papillary mucinous neoplasm; NPV, negative predictive value; PDAC, pancreatic ductal adenocarcinoma; PPV, positive predictive value.
documented a 2–10% incidence of concomitant pancreatic cancer in patients with IPMN. Uehara et al. reported that even ≤1-cm BD-IPMN were associated with an 8% risk of distinct pancreatic cancer during surveillance. The yearly incidence of distinct pancreatic cancer in patients with BD-IPMN is reportedly 0.41–1.10%. More effective and efficient surveillance strategies for early detection of concomitant pancreatic cancer in patients with IPMN are needed. The intervals of the imaging surveillance proposed in the Fukuoka guidelines are now questioned because even surveillance done at 6-month intervals may miss the diagnosis of pancreatic cancer at a sufficiently early stage.

Kamata et al. conducted EUS and other imaging examinations at 6-month intervals in 102 patients with obviously benign BD-IPMN and found distinct pancreatic cancer in seven patients (7%), but found no cases of malignant transformation of BD-IPMN. Interestingly, CT and magnetic resonance imaging (MRI) carried out immediately after the detection of pancreatic cancer by EUS demonstrated the lesion in only 43% of cases. This suggests the crucial role of EUS, especially contrast-enhanced harmonic EUS, in the early detection of pancreatic cancer despite its inherent weakness of observer dependency.

A few studies have investigated the characteristics of IPMN associated with distinct pancreatic cancer. Ideno et al. investigated the histological subtypes of IPMN in patients with concomitant pancreatic cancer and found a high frequency of the gastric subtype without GNAS mutation within codon 201. The epithelial subtypes of IPMN may be identified by ERCP cytology as described later and would help to predict the tendency of malignant transformation (most likely the intestinal type) and development of concomitant pancreatic cancer (mostly the gastric type).

Distinct pancreatic cancer may exist in the pancreatic segment to be left in place after pancreatectomy for IPMN or pancreatic cancer concomitant with IPMN. This can be examined by preoperative ERCP cytology or intraoperative irrigation cytology of the MPD. Moreover, pancreatic cancer may develop even after resection of IPMN. Ohtsuka et al. reported that 17 (9.9%) of 172 patients who underwent resection of IPMN subsequently developed distinct pancreatic cancer. If this condition is to be detected at a very early stage of development, patients who undergo IPMN resection by distal pancreatectomy should subsequently undergo ERCP cytology. The time interval between these cytological examinations should be determined in future studies.

Familial pancreatic cancer provides another opportunity for the early detection of pancreatic cancer. Patients with a strong family history of pancreatic cancer may develop multiple BD-IPMN as well as pancreatic cancer during surveillance. The Fukuoka guidelines advocate the lower threshold for total pancreatectomy in such patients. However, because total pancreatectomy necessitates lifelong treatment of both pancreatogenic diabetes and exocrine deficit, ERCP cytology with or without balloon segmental cytology may help to decide whether to carry out pancreatic resection and, if done, determine the segment and extent of pancreatic resection before the uniform application of total pancreatectomy.

DIFFERENTIATION OF EPITHELIAL SUBTYPES OF IPMN

As reported by Furukawa et al., IPMN is classified into four histological subtypes (gastric, intestinal, pancreatobiliary, and oncocytic) based on the histomorphological features of papillary proliferation and the immunohistochemical characteristics of mucin glycoproteins. Differentiation of these histological subtypes is achieved...
by postoperative histological examination of resected specimens of IPMN. Differentiation also has significance in predicting the prognosis, as previously described in several reports.\textsuperscript{44–47} Colloid carcinoma derived from intestinal-type IPMN and invasive oncocytic IPMN have far better prognoses,\textsuperscript{45} whereas tubular carcinoma derived from the gastric and pancreatobiliary types resembles ordinary pancreatic cancer.\textsuperscript{46,47}

In view of these observations, it is ideal to differentiate the subtypes preoperatively to consider the surgical indication and predict the prognosis. In a preliminary study by Hibi et al.,\textsuperscript{8} the cytological subclassification of pancreatic juice was consistent with the histological subtype of resected IPMN in 79% of cases. A subsequent study by Hara et al.\textsuperscript{12} explored the possibility of preoperatively determining IPMN histological subtypes in combination with mucin immuno-histochemical cell staining of the pancreatic juice. The authors evaluated 36 patients who underwent preoperative pancreatic juice cytology and subsequent surgical resection of IPMN. Histological subtyping of cytological samples was consistent with the postoperative subtypes in 42% of patients without MUC staining and in 89% of patients with MUC staining ($P < 0.01$) and showed a significant correlation with the rate of malignancy. Preoperative pancreatic juice cytology with MUC staining may be useful for identification of the histological subtype of IPMN.

The above-mentioned study also showed that the histological subtype is correlated with the $GNAS$ mutational frequency.\textsuperscript{48} However, preoperative evaluation of the histological subtypes of IPMN is still in an investigational phase. Future studies involving mucin immunohistochemistry and analysis of specific genes may lead to the exploration of more definitive preoperative diagnoses of histological subtypes of IPMN. Endoscopic sampling of the pancreatic juice would likely play a crucial role in this context.

Cyst fluid obtained by EUS-FNA may be another useful sample for histological subtype determination. However, differentiation of histological subtypes in FNA aspirates of IPMN has not yet been investigated.

**DISADVANTAGES OF ENDOSCOPIC EXAMINATION OF IPMN**

The disadvantages of endoscopic examination of IPMN are shown in Table 1. Acute pancreatitis remains a major disadvantage of ERCP cytology, as in other ERCP procedures, occurring in 10–14% of patients.\textsuperscript{49–51} Although most of cases of post-ERCP acute pancreatitis shortly subside, up to 20% of patients may develop severe pancreatitis, which is sometimes fatal. Thus, great caution must be exercised when carrying out ERCP cytology.

Disadvantages of cyst fluid analysis for the diagnosis of malignant BD-IPMN include acute pancreatitis, bleeding, and, although rare, gastric wall seeding and peritoneal dissemination of malignant cells. Anecdotal reports have described gastric wall invasion secondary to needle track seeding, or peritoneal dissemination as a result of leakage of cyst contents through needle holes.\textsuperscript{52,53} A large cohort study compared 175 patients who underwent resection of IPMN after EUS-FNA with 68 patients who underwent the resection without undergoing FNA.\textsuperscript{54} Although the study did not demonstrate a significant difference in the frequency of peritoneal seeding (2.3% vs 4.4%, respectively; $P = 0.403$), Japanese endosonographers refrain from EUS-FNA in patients with possibly malignant BD-IPMN because of concern regarding peritoneal dissemination and gastric wall seeding secondary to cyst fluid spillage and needle track implantation of malignant cells.

**DECISION OF STRATEGY FOR MANAGEMENT OF BD-IPMN**

Endoscopy plays a pivotal role in decision-making in the management of BD-IPMN. Whether to observe or operate on a BD-IPMN depends on the presence and size of mural nodules within the BD-IPMN (Fig. 3). Uehara et al.\textsuperscript{55} reported that a mural nodule of 10 mm was an appropriate indicator for immediate surgery. Mural nodules can be distinguished from mucus aggregates within the IPMN with the use of Doppler EUS and more definitively by contrast-enhanced harmonic EUS to demonstrate the presence of a blood supply. Therefore, EUS is now essential in determining the optimal strategies with which to manage BD-IPMN.
INNOVATIVE TECHNOLOGY IN ENDOSCOPY

MORE RECENT INNOVATIONS in modern technology have been applied to endoscopy and contribute to the management of IPMN. First, pancreatoscopy can allow for visualization of the papillary growths of IPMN in the MDP and help to accomplish targeted sampling of neoplastic cells for cytology and biopsy. Second, the ability of EUS-elastography to provide supplementary information, mainly regarding pancreatic mass lesions, has also been investigated to distinguish mucinous (potentially malignant) from serous (mostly benign) cystic lesions by quantifying acoustic radiation force impulses from the cyst. Third, confocal laser endomicroscopy combined with EUS-FNA can be used to enable real-time microscopic and molecular imaging, demonstrating the presence of epithelial villous structures in cystic lesions of the pancreas, including IPMN. The utility, safety, and clinical significance of these new modalities need further evaluation.

CONFLICT OF INTERESTS

AUTHOR DECLARES NO conflict of interests for this article.

REFERENCES

1 Tanaka M, Chari S, Adsay V et al. International consensus guidelines for management of intraductal papillary mucinous neoplasms and mucinous cystic neoplasms of the pancreas. Pancreatology 2006; 6: 17–32.
2 Ohashi K, Tajiri H, Gondo M et al. A case of cystadenocarcinoma of the pancreas forming biliary-pancreatic fistula. Prog. Dig. Endosc. 1980; 17: 261–4. (in Japanese with English abstract.)
3 Ohashi K, Murakami F, Maruyama M et al. Four cases of mucous secreting pancreatic cancer. Prog. Dig. Endosc. 1982; 203: 348–51. (in Japanese with English abstract.)
4 Tanaka M, Fernández-del Castillo C, Adsay V et al. International Association of Pancreatologists: International consensus guidelines 2012 for the management of IPMN and MCN of the pancreas. Pancreatology 2012; 12: 183–97.
5 Tanaka M. Intraductal Papillary Mucinous Neoplasm, 1st edn. Tokyo: Springer, 2014.
6 Yamaguchi K, Nakamura M, Shirahane K et al. Pancreatic juice cytology in IPMN of the pancreas. Pancreatology 2005; 5: 416–21.
7 Yamaguchi T, Shirai Y, Ishihara T et al. Pancreatic juice cytology in the diagnosis of intraductal papillary mucinous neoplasm of the pancreas. Significance of sampling by peroral pancreatoscopy. Cancer 2005; 104: 2830–36.
8 Hibi Y, Fukushima N, Tsuchida A et al. Pancreatic juice cytology and subclassification of intraductal papillary mucinous neoplasms of the pancreas. Pancreas 2007; 34: 197–204.
9 Mikata R, Ishihara T, Tada M et al. Clinical usefulness of repeated pancreatic juice cytology via endoscopic naso-pancreatic drainage tube in patients with pancreatic cancer. J. Gastroenterol. 2013; 48: 866–73.
10 Sai JK, Suyama M, Kubokawa Y, Watanabe S, Maehara T. Pancreatic-duet-lavage cytology in candidates for surgical resection of branch-duct intraductal papillary mucinous neoplasm of the pancreas: Should the International Consensus Guidelines be revised? Gastrointest. Endosc. 2009; 69: 434–40.
11 Monzen M, Shimizu K, Hatori T, Furukawa T, Shiratori K. Usefulness of cell block cytology for preoperative grading and typing of IPMNs. Pancreatology 2013; 13: 369–78.
12 Hara T, Ikebe D, Odaka A et al. Preoperative histological subtype classification of intraductal papillary mucinous neoplasms (IPMN) by pancreatic juice cytology with MUC stain. Ann. Surg. 2013; 257: 1103–11.
13 Genevay M, Mino-Kenudson M, Yaege K et al. Cytology adds value to imaging studies for risk assessment of malignancy in pancreatic mucinous cysts. Ann. Surg. 2011; 254: 977–83.
14 Ono J, Yaege KA, Genevay M, Mino-Kenudson M, Brugge WR. Cytological analysis of small branch-duct IPMNs provides a more accurate risk assessment of malignancy than symptoms. Cytojournal 2011; 8: 21.
15 Pitman MB, Michaels PJ, Deshpande V, Brugge WR, Bounds BC. Cytological and cyst fluid analysis of small (< or =3 cm) branch duct intraductal papillary mucinous neoplasms adds value to patient management decisions. Pancreatology 2008; 8: 277–84.
16 Hirono S, Tani M, Kawai M et al. The carcinoembryonic antigen level in pancreatic juice and mural nodule size are predictors of malignancy for branch duct type intraductal papillary mucinous neoplasms of the pancreas. Ann. Surg. 2012; 255: 517–22.
17 Ohno E, Hirooka Y, Itoh A et al. IPMNs of the pancreas: Differentiation of malignant and benign tumors by endoscopic ultrasound findings of mural nodules. Ann. Surg. 2009; 249: 628–34.
18 Ohno E, Itoh A, Kawashima H et al. Malignant transformation of branch duct-type intraductal papillary mucinous neoplasms of the pancreas based on contrast-enhanced endoscopic ultrasonography morphological changes: Focus on malignant transformation of IPMN itself. Pancreas 2012; 41: 855–62.
19 Kitano M, Sakamoto H, Komaki T, Kudo M. New techniques and future perspective of EUS for the differential diagnosis of pancreatic malignancies: Contrast harmonic imaging. Dig. Endosc. 2011; 23 (Suppl 1): 46–50.
20 Tanaka M, Yokohata K, Konomi H, Yamaguchi K, Chijiwa K, Ohta M. Segmental balloon cytology for preoperative localization of in situ pancreatic cancer. Gastrointest. Endosc. 1997; 46: 447–9.
21 Yamaguchi K, Nakamura K, Yokohata K, Shimizu S, Chijiwa K, Tanaka M. Pancreatic cyst as a sentinel of in situ carcinoma of the pancreas. Report of two cases. Int. J. Pancreatol. 1997; 22: 227–31.

© 2015 The Author
Digestive Endoscopy published by Wiley Publishing Asia Pty Ltd on behalf of Japan Gastroenterological Endoscopy Society
22 Yamaguchi K, Ohuchida J, Ohtsuka T, Nakano K, Tanaka M. Intraductal papillary-mucinous tumor of the pancreas concomitant with ductal carcinoma of the pancreas. *Pancreatology* 2002; 2: 484–90.

23 Tada M, Kawabe T, Arizumi M et al. Pancreatic cancer in patients with pancreatic cystic lesions: A prospective study in 197 patients. *Clin. Gastroenterol. Hepatol.* 2006; 4: 1265–70.

24 Uehara H, Nakaizumi A, Ishikawa O et al. Development of ductal carcinoma of the pancreas during follow-up of branch duct intraductal papillary mucinous neoplasm of the pancreas. *Gut* 2008; 57: 1561–5.

25 Ingkakul T, Sadakari Y, Ienaga J, Takahata S, Tanaka M. Predictors of the presence of concomitant invasive ductal carcinoma in intraductal papillary mucinous neoplasm of the pancreas. *Ann. Surg.* 2010; 251: 70–5.

26 Tanno S, Nakano Y, Koizumi K et al. Pancreatic ductal adenocarcinomas in long-term follow-up patients with branch duct intraductal papillary mucinous neoplasms. *Pancreas* 2010; 39: 36–40.

27 Tanno S, Nakano Y, Sugiyama Y et al. Incidence of synchronous and metachronous pancreatic carcinoma in 168 patients with branch duct intraductal papillary mucinous neoplasm. *Pancreatology* 2010; 10: 173–8.

28 Ikeuchi N, Itoi T, Sofuni A et al. Prognosis of cancer with branch duct type IPMN of the pancreas. *World J. Gastroenterol.* 2010; 16: 1890–5.

29 Kanno A, Satoh K, Hirota M et al. Prediction of invasive carcinoma in branch type intraductal papillary mucinous neoplasms of the pancreas. *J. Gastroenterol.* 2010; 45: 952–9.

30 Maguchi H, Tanno S, Mizuno N et al. Natural history of branch duct intraductal papillary mucinous neoplasms of the pancreas: A multicenter study in Japan. *Pancreas* 2011; 40: 364–70.

31 Tanaka M. Controversies in the management of pancreatic IPMN. *Nat. Rev. Gastroenterol. Hepatol.* 2011; 8: 56–60.

32 Tamura K, Ohtsuka T, Ideno N et al. Unresectable pancreatic ductal adenocarcinoma in the remnant pancreas diagnosed during every-6-month surveillance after resection of branch duct intraductal papillary mucinous neoplasm: A case report. *JOP* 2013; 14: 450–3.

33 Kamata K, Kitano M, Kudo M et al. Value of EUS in early detection of pancreatic ductal adenocarcinomas in patients with intraductal papillary mucinous neoplasms. *Endoscopy* 2014; 46: 22–9.

34 Sakamoto H, Kitano M, Komaki T et al. Small invasive ductal carcinoma of the pancreas distinct from branch duct intraductal papillary mucinous neoplasm. *World J. Gastroenterol.* 2009; 15: 5489–92.

35 Ideno N, Ohtsuka T, Kono H et al. Intraductal papillary mucinous neoplasms of the pancreas with distinct pancreatic ductal adenocarcinomas are frequently of gastric subtype. *Ann. Surg.* 2013; 258: 141–51.

36 Ohtsuka T, Ideno N, Aso T et al. Role of endoscopic retrograde pancreatography for early detection of pancreatic ductal adenocarcinoma concomitant with intraductal papillary mucinous neoplasm of the pancreas. *J. Hepatobiliary Pancreat. Sci.* 2013; 20: 356–61.

37 Mori Y, Ohtsuka T, Tamura K et al. Intraoperative irrigation cytology of the remnant pancreas to detect remnant distinct pancreatic ductal adenocarcinoma in patients with intraductal papillary mucinous neoplasm undergoing partial pancreatectomy. *Surgery* 2014; 155: 67–73.

38 Ohtsuka T, Kono H, Tanabe R et al. Follow-up study after resection of intraductal papillary mucinous neoplasm of the pancreas; special references to the multifocal lesions and development of ductal carcinoma in the remnant pancreas. *Am. J. Surg.* 2012; 204: 44–8.

39 Iglesias-Garcia J, Lariño-Noia J, Domínguez-Muñoz JE. Early diagnosis of pancreatic cancer, time to screen high-risk individuals? *Minerva Gastroenterol. Dietol.* 2011; 57: 205–12.

40 Bartsch DK, Dietzel K, Bargello M et al. Multiple small ‘imaging’ branch-duct type IPMNs (IPMNs) in familial pancreatic cancer: Indicator for concomitant high grade pancreatic intraepithelial neoplasia? *Fam. Cancer* 2013; 12: 89–96.

41 Shi C, Klein AP, Goggins M et al. Increased prevalence of precursor lesions in familial pancreatic cancer patients. *Clin. Cancer Res.* 2009; 15: 7737–43.

42 Poley JW, Klavijt I, Gouma DJ et al. The yield of first-time endoscopic ultrasonography in screening individuals at a high risk of developing pancreatic cancer. *Am. J. Gastroenterol.* 2009; 104: 2175–81.

43 Furukawa T, Klöppel G, Adsay NV et al. Classification of types of intraductal papillary-mucinous neoplasm of the pancreas: A consensus study. *Virchows Arch.* 2005; 447: 794–9.

44 Sadakari Y, Ohuchida K, Nakata K et al. Invasive carcinoma derived from the nonintestinal type intraductal papillary mucinous neoplasm of the pancreas has a poorer prognosis than that derived from the intestinal type. *Surgery* 2010; 147: 812–7.

45 Nakata K, Ohuchida K, Aishima S et al. Invasive carcinoma derived from intestinal-type IPMN is associated with minimal invasion, colloidal carcinoma, and less invasive behavior, leading to a better prognosis. *Pancreas* 2011; 40: 581–7.

46 Mino-Kenudson M, Fernández-del Castillo C, Baba Y et al. Prognosis of invasive intraductal papillary mucinous neoplasm depends on histological and precursor epithelial subtypes. *Gut* 2011; 60: 1712–20.

47 Yopp AC, Kataki N, Janakos M et al. Invasive carcinoma arising in intraductal papillary mucinous neoplasms of the pancreas: A matched control study with conventional pancreatic ductal adenocarcinoma. *Ann. Surg.* 2011; 253: 968–74.

48 Kang MJ, Lee KB, Jang JY, Han IW, Kim SW. Evaluation of clinical meaning of histological subtypes of intraductal papillary mucinous neoplasm of the pancreas. *Pancreas* 2013; 42: 959–66.

49 Ohtsuka T, Matsunaga T, Kimura H et al. Role of pancreatic juice cytology in the preoperative management of intraductal papillary mucinous neoplasm of the pancreas in the era of international consensus guidelines 2012. *World J. Surg.* 2014; 38: 2994–3001.
50 Jones WB, Blackwell J, McKinley B, Trocha S. What is the risk of diagnostic endoscopic retrograde cholangiopancreatography before cholecystectomy? Am. Surg. 2014; 80: 746–51.
51 Dumonceau JM, Andriulli A, Elmunzer BJ et al. Prophylaxis of post-ERCP pancreatitis: European Society of Gastrointestinal Endoscopy (ESGE) Guideline – Updated June 2014. Endoscopy 2014; 46: 799–815.
52 Yamao K, Yanagisawa A, Takahashi K et al. Clinicopathological features and prognosis of mucinous cystic neoplasm with ovarian-type stroma: A multi-institutional study of the Japan Pancreas Society. Pancreas 2011; 40: 67–71.
53 Hirooka Y, Goto H, Itoh A et al. Case of intraductal papillary mucinous tumor in which endosonography-guided fine-needle aspiration biopsy caused dissemination. J. Gastroenterol. Hepatol. 2003; 18: 1323–7.
54 Yoon WJ, S Dalgilar E, Castillo CF, Mino-Kenudson M, Pitman MB, Brugge WR. Peritoneal seeding in intraductal papillary mucinous neoplasm of the pancreas patients who underwent endoscopic ultrasound-guided fine-needle aspiration: The PIPE Study. Endoscopy 2014; 46: 382–7.
55 Uehara H, Ishikawa O, Katayama K et al. Size of mural nodule as an indicator of surgery for branch duct intraductal papillary mucinous neoplasm of the pancreas during follow-up. J. Gastroenterol. 2011; 46: 657–63.
56 Miura T, Igarashi Y, Okano N, Miki K, Okubo Y. Endoscopic diagnosis of intraductal papillary-mucinous neoplasm of the pancreas by means of peroral pancreatoscopy using a small-diameter videoscope and narrow-band imaging. Dig. Endosc. 2010; 22: 119–23.
57 Nagayoshi Y, Aso T, Ohtsuka T et al. Peroral pancreatoscopy using the SpyGlass system for the assessment of intraductal papillary mucinous neoplasm of the pancreas. Hepatobiliary Pancreat. Sci. 2014; 21: 410–7.
58 D’Onofrio M, Crosara S, Canestrini S et al. Virtual analysis of pancreatic cystic lesion fluid content by ultrasound acoustic radiation force impulse quantification. J. Ultrasound Med. 2013; 32: 647–51.
59 Nakai Y, Shinoura S, Ahluwalia A, Tarnawski AS, Chang KJ. In vivo visualization of epidermal growth factor receptor and survivin expression in porcine pancreas using endoscopic ultrasound guided fine needle imaging with confocal laser-induced endomicroscopy. J. Physiol. Pharmacol. 2012; 63: 577–80.
60 Konda VJ, Meining A, Jamil LH et al. A pilot study of in vivo identification of pancreatic cystic neoplasms with needle-based confocal laser endomicroscopy under endosonographic guidance. Endoscopy 2013; 45: 1006–13.