Is It Time to Expand the Role of Total Pancreatectomy for IPMN?

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Key Words

IPMD · Intraductal papillary mucinous neoplasm · Multifocal IPMN · IPMN recurrence · Total pancreatectomy · Pancreatic cancer · PDAC · Field defect

Abstract

Intraductal papillary mucinous neoplasms (IPMN) are cystic precursors to pancreatic cancer believed to arise within a widespread neoplastic field defect. The tendency for some patients to present with multifocal disease and/or develop additional lesions over time argues in favor of a field defect and complicates surgical management decisions. Surgery usually consists of partial pancreatic resection, which leaves behind a pancreatic remnant at risk for recurrent disease and progression to cancer. As an alternative, total pancreatectomy (TP) provides the most complete oncologic resection, but postoperative morbidity and quality of life (QoL) issues have generally limited its use to only the highest risk patients. Significant progress has been made in the management of the post-TP apancreatic state and studies now show less morbidity with acceptable QoL comparable to type 1 diabetic and post-pancreaticoduodenectomy patients. These improvements do not yet justify the routine use of TP, but they have opened the door for expansion to additional subsets of non-invasive IPMN. Here, we have identified several groups of patients that we believe would benefit from TP over partial resection based on the most current literature.

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Introduction

Intraductal papillary mucinous neoplasms (IPMN) are mucin-producing cystic lesions of the pancreas and precursors to pancreatic ductal adenocarcinoma (PDAC). In recent years, they have attracted a great deal of attention as targets for early intervention because they are easily detected on routine imaging and offer a unique opportunity for pre-emptive resection. The importance of early intervention is highlighted by 5-year survival rates after resection ranging from 77 to 100% in patients with non-invasive lesions compared to 34–62% in patients with associated invasive carcinoma [1].

Management of these lesions is often complicated due to their significant clinicopathological heterogeneity and wide range of malignant potential. The decision to operate is based upon the perceived risk for progression to cancer with the goal of avoiding unnecessary surgeries in low-risk patients. Unfortunately, accurately predicting future malignancy remains an imprecise science and consensus resection guidelines continue to evolve.

Management decisions are complicated further by the presence of multifocal disease and the concept of a widespread neoplastic field defect believed to underlie IPMN development [1–4]. Patients may present with multiple lesions involving the pancreas diffusely or in non-contiguous surgical regions that prevent resection through one of the standard segmental anatomical techniques. This

presents the surgeon with the difficult choice of either leaving behind known disease or committing the patient to the morbidity of total pancreatectomy (TP). Even if all gross disease can be resected via partial pancreatectomy, there is still the unresolved question of the field defect and the extent to which it leaves the pancreatic remnant at risk for recurrent disease.

For most lesions meeting resection criteria, current management guidelines recommend limited segmental resection followed by ongoing surveillance of the pancreatic remnant postoperatively [1]. However, from an oncologic perspective, multifocal disease and the likelihood of a widespread field defect argue in favor of radical resection of all pancreatic tissue via TP. Unfortunately, the magnitude of the attendant postoperative morbidity related to the apancreatic state is generally considered too severe for all but those at greatest risk for recurrence. While complete endocrine and exocrine pancreatic insufficiency (EPI) certainly pose the potential for significant long-term morbidity, there is new evidence emerging to suggest that they can now be managed safely and with a reasonable quality of life (QoL). The ongoing progress in this area is narrowing the gap of acceptable risk such that TP once again deserves reconsideration for an expanded role in the management of IPMN disease.

In this review, we will evaluate the most recent and pertinent literature to determine if there are any subsets of IPMN beyond those already recognized by the current guidelines that would benefit from TP over partial resection. We will start by discussing the basic features of IPMN disease including classification, pathogenesis and management practices per the most recent consensus guidelines. We will also discuss the controversial topics of the pancreatic field defect and multifocal disease as they relate to surgical management and disease recurrence. Next, we will evaluate the current status of TP with an emphasis on long-term outcomes and QoL. Finally, we will use this information to determine the role TP should have in the current management of IPMN.

Clinicopathological Features of IPMN

IPMN are usually diagnosed between 60 and 70 years of age with a slight male preponderance. Patients are often asymptomatic, but may experience symptoms related to obstruction of the pancreatic ductal system such as abdominal pain, weight loss and recurrent episodes of pancreatitis [5]. The rate of diagnosis for asymptomatic, incidentally discovered IPMN is currently increasing due to the improving resolution and expanded utilization of high-quality cross-sectional imaging. A review of 2,832

asymptomatic patients undergoing multi-detector CT discovered previously undiagnosed pancreatic cysts in 2.6% of study participants, the majority of which were believed to be IPMN [6].

Microscopically, IPMN are characterized by intra-ductal papillary proliferation of mucin-producing epithelium in the main pancreatic duct or its branches [7]. They are categorized into 3 morphological types based on location of involvement derived from imaging studies and/or histology: main duct IPMN (MD-IPMN), branch duct IPMN (BD-IPMN) and mixed-type IPMN (MT-IPMN) [1, 5, 7]. Main duct involvement is associated with the highest rates of invasive disease, which are reported to be 43.1 and 45.3% for MD- and MT-IPMN, respectively. Disease limited to the branch ducts has a lesser, though still significant rate of 17.7% [1].

IPMN are classified further into 4 epithelial subtypes based upon mucin expression and morphology: gastric, intestinal, pancreatobiliary and oncocytic [8–10]. The gastric subtype is the most common overall and is generally found in the periphery of the pancreas in the form of BD-IPMN. These usually exhibit low- to intermediate-grade dysplasia, but may rarely progress to an aggressive tubular-type adenocarcinoma. Although progression to cancer is rare compared to their overall prevalence, one large study found that they made up 74% of IPMN-associated cancers and had significantly worse survival compared to other IPMN-derived cancers [8]. The remaining subtypes generally affect the main duct and are associated with higher grades of dysplasia and higher rates of malignant transformation. Intestinal type is the most common form of MD-IPMN and correlates with progression to colloid carcinoma. The pancreatobiliary type carries the highest prognostic risk of the 4 subtypes because of its high rate of progression to the same invasive tubular adenocarcinoma as gastric type. Finally, the oncocytic subtype is rare and correlates with progression to oncocytic carcinoma.

In aggregate, the reported 5-year survival for resected invasive IPMN is 34–62%, which is significantly better than that of classic PDAC at 9–21% [1]. Epithelial subtyping helps to explain this well documented survival advantage through the observation that each has a distinct path and rate of progression to a specific form of pancreatic cancer. Subtype analysis of these specific cancers reveals that much of the overall survival advantage is due to the more favorable prognoses of colloid and oncocytic carcinoma compared to tubular adenocarcinoma, which has a similar overall survival to classic PDAC [8, 10, 11].

Current Management Strategies

In 2006, an international panel of experts published the 'Sendai Consensus Guidelines' as a standardized set of instructions for managing IPMN [12], followed by an updated version in 2012 [1]. These guidelines strongly encourage the resection of MD- and MT-IPMN in all surgically fit patients due to the established risk of malignancy. A more conservative approach consisting of close monitoring and surveillance is recommended for BD-IPMN, unless the lesions show evidence of specific 'high-risk stigmata' (main duct dilatation ≥ 10 mm, enhancing solid component within a cyst, cystic lesion in the head of the pancreas causing obstructive jaundice) or 'worrisome features' (lymphadenopathy, cyst > 3 cm, main duct dilatation between 5 and 9 mm). If any of these factors are present, resection is again warranted in surgically fit patients.

Surgical management is generally carried out through segmental anatomical resection using pancreaticoduodenectomy (PD) for lesions of the head, neck and uncinate and distal pancreatectomy (DP) for body and tail lesions. Current series report that PD is performed in 50–71% of IPMN resections and DP is performed in 12–31% [13]. However, TP is currently performed in up to 23% of IPMN resections, which accounts for nearly half of all TPs performed [2, 14]. In these cases, the indication is generally extensive multifocal disease, diffuse main duct involvement or inability to clear margins of high-grade dysplasia [15]. One recent retrospective study found IPMN was the indication in 56% of planned elective total pancreatectomies, 54% of completion pancreatectomies and 36% of unplanned total pancreatectomies [14].

Multifocal Disease and the Pancreatic Field Defect

IPMN likely result from a pancreatic 'field defect' comprised of diffusely unstable ductal epithelium prone to malignant degeneration [1–4]. The nature of this field defect and the factors driving it are yet to be established, but its existence is supported by the well-documented tendency for some patients to present with multifocal disease and/or develop new cysts over time [3, 16, 17]. The fact that IPMN have an association with certain inherited genetic syndromes such as Peutz-Jeghers syndrome, familial adenomatous polyposis and familial pancreatic cancer as well as an association with extrapancreatic malignancies such as colorectal cancer lends additional support to this theory [16, 18].

Multifocal disease refers to the presence of ≥ 2 discrete, synchronous lesions present in the same gland, but its interpretation is inconsistent in the literature due to the various methodologies used for assessment. Some authors rely on imaging alone or in combination with pathological evaluation, some limit discussion to multifocal BD-IPMN only, and some include multifocal MT- and MD-IPMN in their totals. This has resulted in a widely variable reported prevalence of 0–83%, but most current series estimate a more conservative range of 18–41% [17–20].

Multifocal Branch Duct Disease

Several studies investigating BD-IPMN report radiographic evidence of multifocal disease in 14.5–64% of cases [17–20]. The true rate may actually be higher since Rodriguez et al. [18] demonstrated that imaging alone underestimates multifocal involvement. In this study, pathological confirmation of 145 resected BD-IPMN identified multifocal disease in 25.5% of cases versus 14.5% using imaging. Despite the increased number of lesions, most series show no difference in rates of invasive carcinoma for multifocal (7–15%) compared to unifocal (12–18%) branch duct disease [17–19, 21]. Fritz et al. [16] reports a higher rate of invasiveness at 33.3%, but this is based on a relatively small sample size of 15 cases without comparison made to the unifocal BD-IPMN in the study.

As it currently stands, multifocal BD-IPMN present a very challenging management situation because in 17–67% of cases, gross disease is not confined to a single surgical region [19, 21]. This means that surgery cannot fully address the risk of malignancy without also committing the patient to the attendant morbidity and lifestyle changes of TP. Furthermore, even if gross disease is confined to one surgical region, the unpredictable recurrence patterns for BD-IPMN mean that surveillance may not be effective in preventing progression to cancer. In a study by Uehara et al. [22], 60 low-risk BD-IPMN were followed clinically for a mean of 87 months. Over the course of follow-up, 12% (7 of 60) of patients developed invasive cancer and 71% of these (5 of 7) occurred at a site distinct from the index lesion. Another study of 168 BD-IPMN reported similar results based on 9 (5.4%) invasive cancers identified within the group [23]. Of the 9 cancers, 5 were diagnosed synchronously with the BD-IPMN and 4 were diagnosed metachronously during the surveillance period. This illustrates that point that IPMN are markers of risk and the macroscopic disease does not always correlate with the site of worst disease.

Multifocal Main Duct Involvement

Multifocal disease is common among MT-IPMN, usually presenting as multiple BD-IPMN with varying degrees of main duct involvement [24]. Schmidt et al. [19] reported multifocal disease in 65% of MT-IPMN, while Fritz et al. [16] reported that 61% of all multifocal diseases in their series were due to MT-IPMN. As with multifocal BD-IPMN, multifocal MT-IPMN does not appear to carry any increased risk of invasiveness compared to its unifocal counterpart [16, 19].

Multifocal MD-IPMN are also described in the literature, though usually in reference to multisegmental involvement of the main pancreatic duct. Tamura et al. [25] reviewed 57 MD-IPMN and observed 7 (12.8%) with multisegmental involvement. Fritz et al. [16] reported that 5 (9.8%) of 51 cases of multifocal IPMN were pure multisegmental main duct disease. Despite the small sample sizes, the rates of invasive carcinoma in both cohorts of multisegmental MD-IPMN were very similar (range 57.1–60%) and consistent with the usual rate reported for MD-IPMN [16, 25].

Recurrence Following IPMN Resection: Who's at Risk?

Recurrence following IPMN resection may be classified as local, regional or distant (metastatic), the latter being well documented following resection of invasive IPMN [2, 26, 27]. In these cases, reported recurrence is 40–65%, generally occurs within 3 years of resection and presents as invasive cancer with primarily distant metastatic spread [2]. This kind of recurrence is thought to result from early extrapancreatic dissemination via micrometastases from the original cancer rather than new or progressive disease in the pancreatic remnant.

Recurrence also occurs in the setting of noninvasive disease, where the pancreatic remnant remains at risk for metachronous development of new lesions or progression of previously unrecognized synchronous disease [28]. In the study by Chari et al. [2], 5 of 60 (8%) non-invasive IPMN recurred following partial resection (median follow-up 37 months). Three of the recurrences were noninvasive, while the last 2 presented as unresectable cancers. White et al. [29] reported very similar results when they observed recurrence in 6 of 72 (8.3%) patients that underwent partial resection for non-invasive IPMN (median follow-up 40 months). These included 4 cancers, 3 of which were unresectable. Together, these 2 studies concluded that recurrence in the setting of non-invasive

disease is a relatively rare event occurring locally in the pancreatic remnant, but warrants ongoing surveillance postoperatively.

More recently, several studies have reported much higher rates of recurrence. In a follow-up to White et al. [29] by the same group, Frankel et al. [30] reviewed a larger series of 192 non-invasive IPMN, and this time observed a recurrence rate of 21% (40 patients) after median follow-up of 46 months. Of these, 6 met criteria for re-resection and were found to be non-invasive, while 3 presented as unresectable cancers. Compared to their earlier study, overall recurrence was greater, but there was not a similar increase in malignant recurrence.

He et al. [3] reported a higher overall recurrence rate of 17% in their review of 130 non-invasive IPMN following partial resection (median follow-up 38 months). Of the 22 patients who developed radiographic evidence of new or progressive disease, 11 went on to have completion pancreatectomies. In total, 5 recurrences were found to be invasive cancer and were unresectable in 2 cases.

Miller et al. [31] took a slightly different approach to evaluating recurrence by investigating the impact of known residual disease in the pancreatic remnant. They divided 191 non-invasive IPMN into 2 groups based on the presence (remnant positive) or absence (remnant negative) of residual disease, which was defined as one or more unresected synchronous lesions and/or surgical margins positive for any grade of IPMN. The remnant negative group demonstrated radiographic evidence of recurrence in 31 of 153 (20%) patients, 3 of which were cancer. The remnant positive group demonstrated recurrence in only 1 of 38 patients (2.6%), which was an invasive carcinoma. Though somewhat puzzling, these results at least seemed to indicate that the presence of residual disease in the remnant did not confer any additional risk of recurrence. Of note, the mean follow-up time was significantly greater in the remnant negative group (73 months) compared to the remnant positive group (41 months), which may have contributed to the unexpected difference in recurrence rates. Overall, in this group of 191 non-invasive IPMN, 32 (17%) had recurrence, 11 (5.8%) underwent re-resection and 4 (2.1%) recurred with cancer.

Clinical Significance of Recurrence

Based on the presented studies, recurrence occurs in up to 21% of patients who undergo resection of non-invasive IPMN [30]. However, not all patients who recur will ultimately progress to cancer or even require re-resection. In these 5 studies, overall re-resection rates ranged from 3.1 to 8.5% and overall malignant recurrence rates ranged

from 1.6 to 5.6%, many of which were unresectable. This translated to generally favorable 5-year survival rates of 81–88% [2, 3, 31]. However, most studies had a median follow-up time of 3–5 years for what is known to be a slowly progressive disease, meaning the long-term risk is likely much higher. With this in mind, He et al. [3] calculated the Kaplan–Meier projections for 5- and 10-year risks of recurrence, which were 25 and 62% for IPMN, respectively, and 7 and 38% for invasive cancer, respectively. These figures suggest that IPMN recurrence may actually prove more common and pose a more significant clinical burden over time than studies currently indicate.

Unfortunately, the full clinical impact of recurrence is unclear since long-term data, especially prospective data, is still lacking. There are several factors that could potentially diminish the clinical importance of recurrence, the first of which is patient age. Since patients undergoing resection for IPMN are often elderly, it is reasonable to consider that for some, recurrence is unlikely to occur within the timeframe of their projected lifespan. Moreover, many studies report that IPMN is associated with an increased prevalence of extrapancreatic malignancies, especially colorectal, renal cell and thyroid carcinomas [32]. He et al. [3] even noted that in their study of 130 patients, more died of extrapancreatic malignancies than pancreatic cancer. However, for patients that present at a younger age and are otherwise healthy, TP should be considered due to the greater likelihood that recurrence could occur and have significant clinical impact over the course of their lifetime.

Risk Factors for Recurrence

Margin Status

Results are mixed with regard to the influence of margin status on recurrence, in part due to the lack of a consensus definition for what constitutes margin positivity following IPMN resection [28]. Frankel et al. [30] defined a positive margin as the presence of any grade of IPMN or PanIN, which correlated with a 3-fold increased risk of recurrent disease on multivariate analysis ($p = 0.02$). White et al. [29] defined positive as any grade of IPMN present at the margin, but excluded PanIN-1 and -2 and demonstrated recurrence in 17% of positive margins versus 2% of negative margins ($p = 0.02$). A meta-analysis comprising 12 studies with a total of 701 non-invasive IPMNs defined a positive margin as any grade of dysplasia present, excluding PanIN-1A and 1B. This yielded a recurrence rate of 9.6% in margin positive resections compared to 3.7% for margin negative ($p = 0.01$) [33]. Most authors speculate that positive margins do not rep-

resent a local oncological failure of resection, since the resulting recurrence rarely occurs at the margin itself [27, 34]. Instead, it likely serves as a marker for more diffuse or advanced disease and is indicative of a field defect [30].

High-Grade Dysplasia

Some studies have identified an association between recurrence and the presence of high-grade dysplasia in the initially resected IPMN [3, 31, 35]. In one study, recurrence was significantly higher following resection of high-grade versus low- and intermediate-grade IPMN (13.3 vs. 4.0%; $p = 0.027$). The authors went on to identify this on multivariable analysis the single most important predictor of recurrence with an OR of 3.9 (95% CI 1.3–11.9; $p = 0.018$) [35]. Another study observed that 10.3% of high-grade IPMN recurred as cancer compared to 0.6% among low and intermediate-grade lesions [31]. High-grade dysplasia also resulted in lower rates of overall 5-year survival ranging from 72 to 83% compared to 85–90% for those with low and intermediate grade dysplasia [3, 35]. Similar to positive margin status, the presence of high-grade dysplasia may serve as an indicator of more diffuse involvement or advanced progression of disease and indicate the potential for unrecognized foci of high-grade dysplasia in other regions of the pancreas as well [35].

Histological Subtype

As previously discussed, the various histological subtypes of IPMN have variable degrees of malignant potential and progress to distinct cancer subtypes [8, 10, 11]. Furthermore, the different histological subtypes of IPMN tend to recur at different rates. Among non-invasive IPMN, reported recurrence rates are 3.4, 9.8, 11.1 and 0% for gastric, intestinal, pancreatobiliary and oncocytic types, respectively [35]. Preoperative identification of pancreatobiliary or intestinal type would be beneficial for risk stratification and planning the type and extent of resection best suited for a patient. In a recent study by Hara et al. [50], histological subtype was successfully diagnosed preoperatively by pancreatic juice cytology with MUC stain in 89% (32 of 36; $p < 0.01$). The sensitivity, specificity and overall accuracy of this method were 86, 100 and 94% for intestinal subtype, respectively.

Family History

The increased risk of developing PDAC in the setting of a positive family history is well established, with a 2.3-fold increased risk for 1 first-degree relative and 6.4-fold increased risk for 2 first-degree relatives [36]. With regard to IPMN, the most recent consensus guidelines recommend-

ed a lower threshold for TP in patients with a family history of PDAC due to the likelihood of increased risk of malignancy [1]. This recommendation was based on the report of increased IPMN prevalence in association with familial PDAC [37]. In the study by He et al. [3], multivariable analysis identified family history of pancreatic cancer as a significant risk factor for IPMN recurrence with an OR of 4.2 (95% CI 1.3–14.1; $p = 0.02$). Of note, family history was defined as at least 1 first or second-degree relative with PDAC, which is a much more liberal definition than is typically used and encompasses a wider demographic of patients.

Discussion: Who Should Undergo TP for IPMN?

Most experts agree that the only way to definitively eliminate all IPMN-associated risk for pancreatic cancer is through prophylactic resection of the entire gland [2, 34, 38, 39]. However, they also agree that the relatively low overall risk of IPMN recurrence does not justify routine use of the procedure due to its potentially significant long-term sequelae. TP is already indicated in cases of diffuse main duct involvement, multifocal disease in high risk patients and persistent high-grade dysplasia at the resection margin because the established risk for recurrence and/or cancer in these patients makes the morbidity of TP more acceptable [14, 28, 29, 40]. This illustrates the inverse relationship between postoperative QoL and magnitude of survival benefit. For TP to be an acceptable intervention, it must either improve survival significantly or with a favorable enough QoL to justify a smaller benefit.

Fortunately, postoperative outcomes have already improved greatly over the past 25 years. A recent review of 100 patients who underwent TP for pancreatic adenocarcinoma observed a decline in operative mortality from 40% prior to 1989 to just 1.9% between 2000 and 2007, which was comparable to patients who underwent PD during the same period (1.9 vs. 1.2%; $p = 0.17$) [41]. Although perioperative morbidity remains as high as 66%, the majority of these are generally minor grades I–II complications by Clavien–Dindo classification and require minimal or no intervention.

Today, the primary focus of concern has shifted from perioperative complications to postoperative QoL and long-term morbidity from insulin-dependent diabetes and EPI. Many believe these to be insurmountable barriers to expanding the role of TP, but ongoing advances in technology, pharmaceuticals and management strategies are changing the outlook for life after pancreatectomy. Once considered to be ‘brittle’ diabetics, many studies

now show that TP patients experience no difference in diabetes-specific complication rates or long-term glyce-mic control compared to type 1 diabetics [42–44]. Moreover, pancreatic enzyme replacement therapy has improved GI symptoms and largely resolved nutritional deficiency in appropriately managed patients [38, 45]. As a result, post-TP QoL is now reported to be comparable to that of regular type 1 diabetics, post-PD patients and even the age-matched general population [44, 46–49].

Despite these significant improvements, TP still requires major lifestyle modifications and poses a QoL burden significant enough in comparison to the overall risk of IPMN recurrence that we cannot recommend it for routine surgical management at this time. Rather, the decision to pursue TP should be on a case-by-case basis that includes an exhaustive risk assessment of the patient in relation to stated goals of care and QoL expectations. This should be used to determine, based on surgeon experience, if the QoL cost of TP is commensurate with the risk of clinically significant recurrence without TP. At this time, without even considering QoL, the operative mortality of TP (0–8.5%) approaches total re-resection rates (3.1–8.5%) and overall malignant recurrence rates (1.6–5.6%) when considering all-comers and does not justify routine use [2, 3, 29–31]. However, high-risk subsets of IPMN with higher rates of malignant transformation and greater potential for clinically significant recurrence should be identified and considered for TP. While there still remains a great deal of work to be done in identifying these high-risk groups, what follows is our list of patients that should be given greater consideration for TP based on the most recent literature.

The first group to consider for TP is patients with high-grade dysplasia or positive surgical margins due to their association with higher rates of recurrence, often as unresectable cancer [3, 29–31, 35]. This finding appears to be a general marker of worse or more advanced disease in the setting of a multicentric field defect. The concern is that the patient could harbor unrecognized synchronous disease elsewhere in the pancreas that does get removed if surgery is limited to a partial resection.

Young and otherwise healthy patients who present with IPMN should also be considered for TP. Even in the absence of an inherited syndrome, these patients are inherently at greater risk for recurrence due to their much longer potential life span after resection. The counterargument can be made that because of their longer life span they should have a partial resection with surveillance to avoid the apancreatic state as long as possible. This would require an in-depth discussion to determine what is most important to the patient in terms of QoL and goals of care.

This should also be framed with the acknowledgement that postoperative surveillance is not infallible, and disease is known to occur in the form of cancer remote from locations of known disease and in the absence of evidence on imaging [22, 23].

Patients with a family history of pancreatic cancer likely have a higher risk of progression to PDAC as well as developing recurrence in the remnant after partial resection [1, 3, 36, 37]. Current consensus guidelines already recommend lowering the threshold for TP in these patients when there is multifocal disease [1]. Given the fact that IPMN is likely a diffuse process even in the absence of gross multifocal disease, the threshold for TP should be lowered in all of these patients, especially in the setting of any of any additional factors such as those discussed above.

Finally, recent advances with histological subtyping in combination with endoscopic techniques are allowing for what may be a reliable means of preoperatively risk stratifying patients [50]. Pancreatobiliary type IPMNs usually affect the main duct and demonstrate higher rates of high-grade dysplasia, higher rates of malignant transformation and higher rates of recurrence, even when resected as non-invasive neoplasms. Though the diagnosis of subtype from cytology still needs additional study and validation, preoperatively diagnosed pancreatobiliary type IPMN may also serve as a potential target for TP.

Conclusion

Since Ohashi et al. [51] first described what would later come to be known as IPMN in 1982, these lesions have become the focus of intense research given their identification as precursors to pancreatic adenocarcinoma. Studies have shown that the risk of recurrence with subsequent IPMN or invasive carcinoma is not insignificant following partial resection, but we do not yet fully understand which patients are at greatest risk. Several of the currently recognized high-risk patient groups are presented here for consideration of TP over partial resection to eliminate the potential for disease progression. TP has come a long way since its original inception, but there are still QoL drawbacks that currently make this procedure inappropriate in lower risk patients. There are certainly additional high-risk patients who would benefit from TP, but further research is needed to better understand the clinicopathological and genetic factors associated with the highest risk of recurrence in order to best stratify patients for aggressive management.

Disclosure Statement

The authors have no conflicts of interest to disclose.

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