HHS Public Access

Author manuscript

*JAMA Surg*. Author manuscript; available in PMC 2022 July 26.

Published in final edited form as:

*JAMA Surg*. 2021 July 01; 156(7): 661–662. doi:10.1001/jamasurg.2021.1814.

# Evidence-Based Guidelines for Branch-Duct Intraductal Papillary Mucinous Neoplasm Management:

## Still a Lot of Room to Grow

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**The goal of surveillance** for pancreatic neoplasms, such as branch-duct intraductal papillary mucinous neoplasms (BD IPMNs), is to resect high-grade dysplasia (HGD) before invasive cancer develops. Because most patients with BD IPMN will not develop invasive cancer, patient selection is paramount. Clinical- and imaging-based guidelines seek to identify patients for whom surveillance is safe and those with HGD/invasive cancer for whom surgery is recommended.[1] However, the low specificity of guidelines leads to unnecessary surgery.[2-4] The presence of mural nodules of at least 5 mm is the best indicator of HGD/invasive cancer, but they are difficult to identify because cross-sectional imaging section thickness borders that threshold.[5] Contrast-enhanced endoscopic ultrasonography is more sensitive, but it is operator dependent and unavailable at most centers.

In this issue of *JAMA Surgery*, Marchegiani et al[6] report a large (n = 292) retrospective cohort of patients who underwent surgery for BD IPMN after at least 12 months of surveillance. Their main finding was that development of additional risk factors, including new high-risk stigmata (HRS; highest risk factors) or worrisome features (other risk factors), was associated with HGD. Among HRS, jaundice was associated with development of invasive cancer. Two large multi-institutional studies[2,4] have also shown that cysts with more risk factors are associated with unfavorable pathological findings. These results are not surprising but provide insight into progression of BD IPMNs and reinforce the expected outcome from surveillance: intervention after progression.

However, the results reported by Marchegiani et al[6] demonstrate that even at expert centers, current guidelines fail to meet the goals of surveillance. In their study, HGD was found in less than one-quarter (63 [21.6%]) of patients. Most (185 [63.4%]) had low-grade dysplasia and were over-treated, but the authors do not address why those with low-risk lesions underwent surgery. The remaining patients (44 [15.1%]) were found to have invasive cancer

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**Additional Contributions:** Pam Derish, MA, Department of Surgery, UCSF, assisted with manuscript editing. Ms Derish was not financially compensated by our group for her contribution.

**Conflict of Interest Disclosures:** None reported.

and were undertreated with surveillance, but the authors do not say who constituted this group. Did it include the 16 patients with HRS at baseline, and, if so, why did they not undergo surgery for more than 1 year after diagnosis? Strikingly, 6 of the 33 patients with low-risk cysts that were stable until the time of surgery had invasive cancer. What led to the surgery? Can we identify these patients earlier?

Consensus-based guidelines for BD IPMNs have been invaluable for sparing numerous patients from unnecessary surgery.[1,2] These evidence-based guidelines use the best available evidence interpreted by experts. However, aside from the HRS, other risk factors (ie, worrisome features) combined with further evaluation/surveillance are inadequate to select patients for surgery. This study and others suggest that each additional risk factor increases the chances of HGD/invasive cancer. Consideration of new risk factors, such as uncinate duct dilatation, cyst fluid analysis, and others, may help. There is no doubt that identifying HGD before surgery is incredibly difficult. As such, future efforts by Marchegiani et al[6] and others are desperately needed.

## REFERENCES

1. Tanaka M, Fernández-Del Castillo C, Kamisawa T, et al. Revisions of international consensus Fukuoka guidelines for the management of IPMN of the pancreas. Pancreatology. 2017;17(5):738–753. doi:10.1016/j.pan.2017.07.007 [PubMed: 28735806]
2. Pulvirenti A, Margonis GA, Morales-Oyarvide V, et al. Intraductal papillary mucinous neoplasms: have IAP consensus guidelines changed our approach? results from a multi-institutional study. Published online December 5, 2019. Ann Surg.
3. Sharib JM, Fonseca AL, Swords DS, et al. Surgical overtreatment of pancreatic intraductal papillary mucinous neoplasms: Do the 2017 International Consensus Guidelines improve clinical decision making? Surgery. 2018;164(6):1178–1184. doi:10.1016/j.surg.2018.07.014 [PubMed: 30170819]
4. Wilson GC, Maithel SK, Bentrem D, et al. Are the current guidelines for the surgical management of intraductal papillary mucinous neoplasms of the pancreas adequate? a multi-institutional study. J Am Coll Surg. 2017;224(4):461–469. doi:10.1016/j.jamcollsurg.2016.12.031 [PubMed: 28088598]
5. Izumo W, Higuchi R, Furukawa T, et al. Importance of each high-risk stigmata and worrisome features as a predictor of high-grade dysplasia in intraductal papillary mucinous neoplasms of the pancreas. Pancreatology. 2020;20(5):895–901. doi:10.1016/j.pan.2020.06.011 [PubMed: 32624417]
6. Marchegiani G, Pollini T, Andrianello S, et al. Progression vs cyst stability of branch-duct intraductal papillary mucinous neoplasms after observation and surgery. Published online May 19, 2021. JAMA Surg. doi:10.1001/jamasurg.2021.1802