News Release

Is surgery really necessary? Precisely diagnosing the cancer risk of pancreatic cysts (IPMN) with endoscopic ultrasonography

Key Points

•Reevaluating the Surgical Indications for Pancreatic Precancerous Lesions (IPMN)

Intraductal Papillary Mucinous Neoplasm (IPMN) (*1), a type of pancreatic cystic tumor, carries a risk of malignancy. However, it has not been clear whether all high-risk cases (*2) necessarily require surgery.

•Endoscopic Ultrasound (EUS) as a Key Diagnostic Tool

EUS (*3) has been proposed as a more precise diagnostic method than conventional CT, capable of detecting "invasive nodules" (*5), a sign of invasive cancer (*4) in IPMN.

•The Presence of Invasive Nodules Significantly Affects Survival Rates

Patients with invasive nodules tend to have lower survival rates, whereas those without them have demonstrated favorable prognoses even without surgery.

•Impact on Older Adults or Those with Comorbidities

If no invasive nodules are present, it may be possible to avoid surgery while ensuring safe monitoring and follow-up.

Contributing to Improved Pancreatic Cancer Diagnosis and Treatment Choices

By enabling a more precise assessment of tumor invasion, this approach can help reduce unnecessary surgeries while facilitating appropriate treatment decisions.

Summary

A research group consisting of Ryohei Kumano, a graduate student at the Department of Gastroenterology, Graduate School of Medicine, Nagoya University, Professor Hiroki Kawashima from the same department, and Professor Eizaburo Ohno from the Department of Gastroenterology, Fujita Health University, has proposed a new evaluation criterion for the surgical indications of intraductal papillary mucinous neoplasm (IPMN).

This study demonstrated that high-precision imaging with endoscopic ultrasound (EUS) may enable a more accurate assessment of the risk of invasive cancer in IPMN.

IPMN is a cystic lesion (a fluid-filled sac) that forms in the pancreas, and some

cases have the potential to become cancerous, making appropriate treatment decisions crucial. Previously, surgical resection was recommended for patients with "High-risk stigmata (HRS)," a set of findings associated with a high risk of malignancy. However, it remained unclear whether all patients with HRS necessarily required surgery. Given that pancreatic surgery is highly invasive and poses significant risks, especially for older adults or those with comorbidities, a more precise diagnostic approach was needed to avoid unnecessary surgeries.

In this study, 257 IPMN patients considered for surgery were evaluated using EUS to determine the presence of "invasive nodules (IN)," a sign of progressive cancer. The results revealed that the presence or absence of IN significantly influenced patient survival rates.

- Patients with IN showed improved prognoses following surgery, indicating the necessity of surgical intervention in such cases.
- Patients without IN often had favorable outcomes even without surgery, suggesting that some patients could safely undergo monitoring instead of immediate surgery.
- Particularly, in older adults or those with comorbidities, the overall survival rate was nearly the same whether or not surgery was performed in the absence of IN. The findings suggested that approximately 20% of the overall study population and about 50% of older adults or those with comorbidities could avoid surgery without compromising outcomes.

This study provides a more individualized approach to IPMN treatment, potentially reducing unnecessary surgeries. In particular, for older adults or those with comorbidities, a new treatment strategy could be proposed, wherein the decision to undergo surgery or opt for careful monitoring is based on the presence or absence of invasive nodules. The findings from this research are expected to contribute to future clinical guidelines for IPMN, leading to more accurate pancreatic cancer diagnoses and optimized treatment selection.

Research Background

Intraductal Papillary Mucinous Neoplasm (IPMN) (*1) is a mucin-producing cystic lesion (a fluid-filled sac-like abnormality) that develops in the pancreas. Some cases have the potential to progress to pancreatic cancer. Therefore, surgery is recommended for patients deemed to be at high risk of malignancy. In particular, IPMN patients who meet the criteria for "High-Risk Stigmata (HRS) (*2)" are generally considered to have a high likelihood of cancer progression and are typically indicated for surgical intervention.

However, it has not been clearly proven whether all patients who meet the HRS

criteria should actually undergo surgery. In fact, among patients who underwent surgery, there have been many cases where pathological examination results diagnosed them with "low-grade dysplasia (*6)," meaning that the condition was still benign and had not progressed to cancer. This suggests that some of these patients could have been adequately managed with careful observation instead of surgery.

Furthermore, the natural history of IPMN (the pattern of disease progression) remains largely unknown. While it is generally recognized that IPMN progresses relatively slowly, the exact rate of malignant transformation and which patients are at particularly high risk have not been sufficiently studied. As a result, there has been ongoing debate about whether all patients who meet the HRS criteria should undergo surgery uniformly.

Additionally, pancreatic surgery is highly invasive and places a significant burden on patients. Recovery after surgery requires a long period, and there is a high risk of complications. Particularly for older adults or those with comorbidities, the surgery itself may pose a life-threatening risk. Moreover, it has not been sufficiently verified whether surgery truly improves prognosis in these patients.

Given these concerns, determining whether all IPMN patients with HRS should undergo surgery and whether surgery is indeed the best treatment option for older adults or those with comorbidities has been a crucial clinical issue. This study aimed to address these challenges by utilizing more precise diagnostic methods to appropriately assess the surgical indications for IPMN patients. The goal was to reduce unnecessary surgeries while ensuring that high-risk patients receive the most suitable treatment, minimizing surgical burden for those for whom surgery may pose significant risks.

Research Results

In this study, we evaluated the impact of assessing the presence or absence of invasive nodules (IN) within the cysts of intraductal papillary mucinous neoplasm (IPMN) using endoscopic ultrasound (EUS) (*3) on patient prognosis. IN refers to a nodule within the cyst that exhibits invasive characteristics, and when IN is detected, it is considered highly indicative of Invasive Carcinoma (* 4). The results revealed that the presence or absence of IN is a crucial factor in determining the indication for surgery in IPMN patients.

1. Correlation Between the Presence of Invasive Nodules (IN) and Surgical Indication

We evaluated the presence or absence of IN using EUS in 257 IPMN patients

with HRS who were indicated for surgery. The results demonstrated that patients with IN showed improved survival rates after undergoing surgery. On the other hand, even among patients who met the HRS criteria, those without IN were often able to maintain a good prognosis without surgery, suggesting that careful monitoring might be a viable alternative in such cases.

2. Impact on Older Adults or Those with Comorbidities

Particularly among older adults or those with comorbidities, there was little difference in survival rates between patients who underwent surgery and those who did not, provided they did not have IN. Given that pancreatic surgery is highly invasive, requires a long recovery period, and carries a high risk of complications, avoiding surgery in patients without IN appears to be a reasonable treatment strategy.

The findings of this study suggest that approximately 20% of all IPMN patients and about 50% of older adults or those with comorbidities may be eligible for observation instead of immediate surgery.

3. The Superior Diagnostic Accuracy of EUS

Furthermore, EUS demonstrated higher sensitivity in detecting IN compared to CT scans. EUS was able to identify IN that CT could not detect, enabling more precise diagnosis and potentially leading to a new standard for determining surgical indications in IPMN patients.

4. Significance of the Study

The results of this study indicate that rather than relying solely on traditional HRS criteria, incorporating EUS-based evaluation of IN allows for a more precise treatment strategy for IPMN patients.

In particular, for older adults or those at high surgical risk, using IN as a criterion could help avoid unnecessary surgeries while still ensuring that high-risk patients receive appropriate treatment.

The findings of this study could serve as a valuable reference for clinical decision-making in IPMN treatment and are expected to contribute to future clinical guidelines.

Research Summary and Future Perspective

This study demonstrated that the evaluation of invasive nodules (IN) using endoscopic ultrasound (EUS) could serve as a new criterion for determining the surgical indication for IPMN. The application of this IN-based criterion has the potential to help many patients avoid unnecessary surgery. Moving forward, the challenge lies in further establishing this diagnostic standard and promoting its implementation in more clinical settings.

1. The Need for Large-Scale Studies

Since this study was a single-center retrospective study, future research should involve multi-center collaborative studies to rigorously validate the effectiveness of EUS-based IN assessment. In particular, it is crucial to analyze IN size, shape, and invasiveness in greater detail to establish criteria that enhance diagnostic accuracy.

2. Further Investigation of the Natural History of IPMN

Many aspects of the risk factors for malignant transformation of IPMN remain unclear. Future research should focus on long-term observational data to identify patients at higher risk more precisely. This will allow for more accurate classification of patients who genuinely require surgery and those for whom observation is a more appropriate approach.

3. Revision of Treatment Guidelines and Clinical Application

The findings of this study suggest the clinical utility of EUS-based IN assessment, which may contribute to future clinical guidelines. Since the current HRS criteria alone may not always provide the optimal surgical indication, further investigation is needed to assess the effectiveness of treatment algorithms incorporating IN evaluation.

In particular, for older adults or those with comorbidities, the establishment of guidelines for carefully determining surgical indications remains a critical issue.

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Glossary

(*1) Intraductal Papillary Mucinous Neoplasm (IPMN) A mucin-producing cystic tumor that develops within the pancreatic duct. While some cases remain benign, others may progress and become malignant.

(*2) High-Risk Stigmata (HRS)

Refers to features in IPMN that indicate a particularly high risk of malignant transformation. Criteria for assessment include pancreatic duct dilation, cyst size, and the presence of nodules within the cyst.

(*3) Endoscopic Ultrasound (EUS)

A diagnostic method that combines an endoscope with an ultrasound probe, allowing for high-resolution imaging of the pancreas and surrounding tissues from the stomach or duodenum. It enables detailed evaluation of small lesions that may not be easily detected by CT or MRI.

(*4) Invasive Carcinoma

A condition in which cancer cells have spread beyond the walls of the pancreatic duct into surrounding tissues. Once IPMN reaches this stage, it is classified as progressive pancreatic cancer.

(*5) Invasive Nodule (IN)

A nodule within IPMN that, when evaluated using EUS, is determined to have spread beyond the cyst wall into pancreatic tissue. The presence of IN suggests a high likelihood of progressive pancreatic cancer.

(*6) Low-Grade Dysplasia

A condition in which cellular morphology and characteristics remain close to normal, indicating a low risk of malignant transformation. If IPMN is at this stage, observation rather than immediate surgery may be considered.

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Author Names and Affiliations:

Ryohei Kumano, MD,¹ Eizaburo Ohno, MD-PhD,² Takuya Ishikawa, MD-PhD,¹ Kentaro Yamao, MD-PhD,¹ Yasuyuki Mizutani, MD-PhD,¹ Tadashi Iida, MD-PhD,¹ Kota Uetsuki, MD-PhD,¹ Takeshi Yamamura, MD-PhD,¹ Kazuhiro Furukawa, MD-PhD,¹ Masanao Nakamura, MD-PhD,³ Takashi Honda, MD-PhD,¹ Hiroki Kawashima, MD-PhD,¹

¹Department of Gastroenterology and Hepatology, Nagoya University Graduate

School of Medicine, Nagoya, Aichi, Japan.

²Department of Gastroenterology and Hepatology, Fujita Health University, Toyoake, Aichi, Japan.

³Department of Endoscopy, Nagoya University Hospital, Nagoya, Aichi, Japan.

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