Development of a secretin-stimulated, catheter-assisted method for the early detection of pancreatic cancer during esophagogastroduodenoscopy

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Abstract

Pancreatic cancer remains one of the most lethal malignancies, largely due to the difficulty of early detection. We developed a novel, minimally invasive diagnostic approach that enables detection of early-stage pancreatic cancer during routine upper esophagogastroduodenoscopy. Synthetic human secretin was intravenously administered to stimulate pancreatic fluid secretion, followed by insertion of a newly designed catheter through the endoscope to wash and collect fluid from the major duodenal papilla. DNA extracted from the recovered lavage was analyzed using high-sensitivity technology for analyzing *KRAS* mutations. The method identified early pancreatic cancer with excellent diagnostic accuracy. This secretin-stimulated duodenal lavage test represents a powerful molecular diagnostic tool for the early detection of pancreatic cancer and may contribute to improved prognosis through earlier therapeutic intervention.

Background & Results

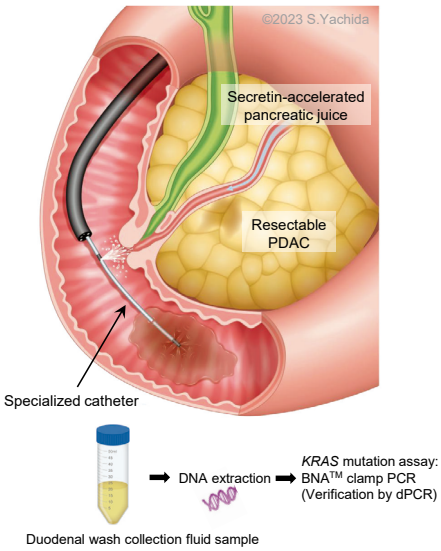
In pancreatic cancer, the limited efficacy of current chemotherapeutic regimens underscores the urgent need for early detection and curative surgical intervention. Patients diagnosed at an early stage and treated with resection followed by adjuvant chemotherapy achieve a five-year survival rate of approximately 50%, highlighting the crucial importance of early diagnosis.

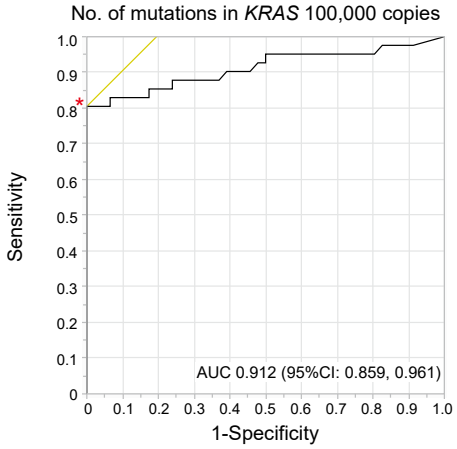
Almost all pancreatic cancers harbor *KRAS* mutations as the earliest genetic alteration, making this mutation an ideal biomarker. However, conventional blood-based liquid biopsies detect *KRAS* mutations only in advanced or metastatic disease, necessitating the development of a diagnostic strategy suitable for early-stage detection.

To address this challenge, we conducted a multicenter study involving ten institutions, enrolling 75 healthy controls and 89 patients with surgically resectable pancreatic cancer. During routine esophagogastroduodenoscopy, synthetic human secretin was administered intravenously to stimulate pancreatic secretion, followed by duodenal lavage using a specially designed catheter. DNA extracted from the collected fluid was analyzed with the BNA^{TM} clamp PCR assay to quantify *KRAS* mutations. Mutations were detected at significantly higher frequency in patients with pancreatic cancer than in healthy controls, achieving 80.9% sensitivity, 100% specificity, and an AUC of 0.912—demonstrating superior diagnostic accuracy over conventional tumor markers such as CEA and CA19-9.

Significance of the research and Future perspective

To date, no reliable screening method has been established for the early detection of pancreatic cancer. Unlike indirect serum tumor markers such as CEA and CA19-9, this assay directly detects *KRAS* mutations derived from pancreatic cancer cells, providing a highly specific molecular signature. Incorporating this minimally invasive test into routine esophagogastroduodenoscopy screening programs—such as the biennial upper esophagogastroduodenoscopy recommended in Japan—could allow efficient identification of individuals at high risk for pancreatic cancer. This innovative diagnostic platform offers a promising foundation for early detection, enabling curative surgical intervention and potentially improving survival outcomes in patients with this devastating malignancy.





Specificity: 100% [95%CI: 92.3%, 100%]
Sensitivity 80.9% [95%CI: 65.1%, 91.2%]

Patent

Treatise Yachida, Shinichi; Yoshinaga, Shigetaka; Shiba, Satoshi et al. *KRAS* mutations in duodenal lavage fluid after secretin stimulation for detection of pancreatic cancer. Annals of Surgery. 2025 Feb 4. doi: 10.1097/SLA.0000000000006645. Online ahead of print.

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