Polarization gating spectroscopy of normal-appearing duodenal mucosa to detect pancreatic cancer

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Background: According to the field effect theory, by detecting microvasculature changes such as early increase in blood supply (EIBS) in the surrounding tissue, neoplastic lesions can be identified from a distance.

Objective: To determine the feasibility and efficacy of a fiberoptic probe containing novel polarization gating spectroscopy technology to identify patients with pancreatic adenocarcinoma (PAC) by the field effect theory.

Design: Prospective cohort (pilot) study.

Setting: Outpatient tertiary care center.

Patients: Adult ($\geq$18 years) patients undergoing EGD-EUS were screened. Patients with PAC were included in the "cancer" group and patients without PAC were included in the "control" group. We excluded patients with other known malignancies and gastroduodenal premalignant lesions.

Interventions and Main Outcome Measures: Spectroscopic measurements of EIBS variables, such as deoxyhemoglobin concentration (DHb) and mean blood vessel radius (BVR), were obtained from 5 periampullary locations. The Mann-Whitney rank sum test was used for the statistical analysis ($P \leq .05$).

Results: Fourteen patients (mean age 72 years, 79% male) in the cancer group and 15 patients (mean age 63 years, 60% male) in the control group were included in the final analysis. At the ampullary site, both DHb ($P = .001$) and BVR ($P = .03$) were higher in PAC patients than in the control subjects. The DHb alone (92% sensitivity, 86% specificity) or in combination with BVR (92% sensitivity, 79% specificity) can differentiate PAC from control subjects with high accuracy.

Limitations: Small sample size, unmatched control subjects.

Conclusions: Spectroscopic measurements of EIBS by fiberoptic probes are feasible. Preliminary evidence suggests that in vivo measurement of normal-appearing duodenal tissue can differentiate PAC patients from a distance with high accuracy. (Gastrointest Endosc 2014;80:786-93.)

(footnotes appear on last page of article)

INTRODUCTION

Pancreatic cancer is the fourth leading cause of cancer death in the United States and is associated with a poor prognosis. The mortality rate is approximately 74% at 1 year and 94% at 5 years.[1] The average life expectancy after the diagnosis is approximately 5 to 8 months.[2] At present, successful surgical resection is the only curative therapy that can improve long-term survival. However, long-term survival can be achieved only when a tumor is detected at an early stage.[3] Unfortunately, because of nonspecific symptoms associated with pancreatic cancer, it is commonly detected in the later stages of the disease.[4]

In the past decade, there has been significant improvement in the quality of imaging studies (eg, CT, MRI, and EUS) and development of disease-specific molecular markers (eg, CA 19-9). However, their use has failed to significantly improve the mortality rate of the pancreatic

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cancer.[5] Unfortunately, fewer than 20% of patients are considered eligible candidates for curative surgical resection at the time of diagnosis.[6] This suggests that although modern imaging methods may define the diagnosis of pancreatic cancer with more precision, they have failed to improve the prognosis associated with it. Therefore, identifying patients with early pancreatic cancer and developing screening strategies for high-risk patients are of immense importance.[7,8] To date, no definite biomarkers or imaging techniques have proven to be safe, sensitive, and cost-effective strategies for pancreatic cancer screening in the general population. However, technologic advances have been able to detect early neoplastic changes in the field of tissue surrounding the pancreas and other solid tumors.[9-12]

In this study, we hypothesized that pancreatic adenocarcinoma (PAC) could be detected by measuring the changes in the early increase in blood supply (EIBS)[13] found in the surrounding normal-appearing duodenal tissue with Polarization Gating Spectroscopy (PGS) technology. Our goal was to evaluate the feasibility and efficacy of PGS measurements in the duodenum during endoscopy procedures and to evaluate EIBS markers, deoxyhemoglobin concentration (DHb), and average blood vessel radius (BVR) in patients with PAC versus control subjects.

Take-home Message

- Detection of the field effect changes such as early increase in blood supply surrounding the malignant lesion can potentially be useful to detect a malignant lesion from a distance. We can detect variables of early increase in the blood supply with a simple through-the-endoscope fiberoptic probe and can predict the presence of pancreatic adenocarcinoma with high accuracy.
- Such technology may bring additional tools to stratify the malignant potential of the pancreatic lesion.

METHODS

Study design and sample size

This pilot study was a single-center, open-label, prospective cohort study performed at the Mayo Clinic in Jacksonville, Florida, in partnership with the Biomedical Engineering Department of Northwestern University in Evanston, Illinois. We planned to recruit a total of 15 patients with pathologically confirmed PAC (cancer group) and 15 patients without PAC (control group) to compare spectroscopic measurements. The sample size was based on both feasibility and the primary aim to gain sufficient pilot data to provide reasonable point estimates for each measurement to plan future studies. The Institutional Review Board of the Mayo Clinic approved the study, and all patients signed the informed consent documentation. (Clinical trial registration number: NCT01015820.)

Study patients

We screened all patients prescheduled to receive EGD with upper EUS. Patients with a known, recent history of PAC (untreated) were included in the cancer group, and patients without a known history of PAC were included in the control group. Patient eligibility in the cancer group or the control group was determined based on the inclusion and exclusion criteria of our study (Table 1). All patients in the cancer group were diagnosed with PAC. Patients with pancreatic neuroendocrine tumors were excluded from the study. As described in the exclusion criteria, patients in the control group had no malignant or premalignant lesions in the pancreas or gastroduodenal area. Patients with chronic pancreatitis were excluded from the PAC group but not from the control group. All patients with visible inflammatory conditions in the upper GI tract were excluded from both the PAC group and the control group. Patients in the control group received an upper EUS for the indication of abdominal pain. Patients with EGD/upper EUS findings who did not meet the exclusion criteria were considered a "screen failure" and were excluded from the final study analysis.

Polarization gating spectroscopy

PGS is an optical method that measures the intensity of light scattering with the help of both polarization and wavelength (λ) (Fig. 1). The polarization dependence of the scattered light allows depth-selective interrogation of tissue. The collection of polarized light parallel ($I_{\|}$) and perpendicular ($I_{\perp}$) to the incident beam allows the analysis of the $I_{\|}$, $I_{\perp}$ and difference between $I_{\|}$ and $I_{\perp}$ signals.[14] PGS light signals interrogate progressively deeper into the tissue at estimated maximum penetration depths of 200, 270, and 400 μm. Analysis of the wavelength dependence of these signals allows measurements of oxyhemoglobin concentration, DHb, and the mean BVR via a modified Beer-Lambert algorithm (see Supplement 1 for details, available online at www.giejournal.org).[14-16]

The measurement method with a PGS fiberoptic probe was described previously in detail.[16,17] The PGS measurement unit consists of the following components: (1) a mobile cart with a light source, spectrometer, computer processor, monitor, keyboard, and calibration equipment (Fig. 2A) and (2) a fiberoptic probe (Fig. 2B). The reusable fiberoptic probe was sterilized and reprocessed with Cidex solution (Ethicon Endo-surgery Inc., Cincinnati, Ohio) in a similar standardized fashion as with other endoscopes.

Procedural details

Each patient received EGD with upper EUS as scheduled by an experienced endoscopist participating in the study (M.W., M.R., or T.W.). All patients were sedated with monitored anesthesia under the guidance of an anesthesiology provider.