Correlation between the Standard Pancreatic Elastase-1 Enzyme-Linked Immunosorbent Assay Test and the New, Rapid Fecal Pancreatic Elastase-1 Test for Diagnosing Exocrine Pancreatic Insufficiency

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(Fig. 1F). The Ki-67/MIB-1 proliferation index was less than 1%. The postoperative course was uneventful. The patient was discharged on the ninth postoperative day and underwent adjuvant chemotherapy with gemcitabine 1700 mg (total dose/die), with administration on day 1, 8, and 15 of a q28-day schedule. Currently, the patient shows no disease recurrence. Intraductal papillary mucinous neoplasm is an exocrine pancreatic tumor characterized by papillary and mucinous proliferation of the epithelium of the main pancreatic duct and its branches.[1] Intraductal papillary mucinous neoplasm is widely considered a precursor lesion of invasive pancreatic adenocarcinoma[2] but is often associated with other neoplasms, both pancreatic and extrapancreatic, possibly because of the microsatellite instability of this tumor.[3] Pancreatic neuroendocrine tumors arise from pluripotent pancreatic cells of the ductal/acinar system[4] and represent 1% to 2% of all pancreatic tumors[5] and 7% to 9% of all gastroenteropancreatic neuroendocrine tumor.[6] The incidence of concomitant IPMNs and NETs is reportedly 9%, suggesting a nonrandom association and possibly shared risk factors for both diseases.[7] The frequency of small, incidental, nonfunctioning Pan-NETs is higher, and in some autopsy series, it has been reported to be close to 10%.[8] This is why the same tumorigenesis for these two tumors has been postulated, but the hypothesis that both exocrine and endocrine cells could arise from the same progenitor seems unlikely because the two tumors are often located in different sites, as was the case in our patient.[9] In conclusion, the association of IPMN, ductal adenocarcinoma, and glucagonoma is very rare. Based on our own case and on a review of the literature, IPMN and Pan-NETs can occur simultaneously and ductal adenocarcinoma can obviously derive from IPMN cancerization, but the association of these two conditions is uncommon. Our findings highlight the difficulty of the preoperative radiologic diagnosis of small, asymptomatic, incidental Pan-NETs and the importance of intraoperative examination of the pancreas to detect synchronous neoplasms.

The authors declare no conflict of interest.

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Correlation Between the Standard Pancreatic Elastase-1 Enzyme-Linked Immunosorbent Assay Test and the New, Rapid Fecal Pancreatic Elastase-1 Test for Diagnosing Exocrine Pancreatic Insufficiency

To the Editor:

Exocrine pancreatic insufficiency (EPI) is a common complication in patients with pancreatic diseases such as chronic pancreatitis, pancreatic resection, and pancreatic cancer. In this vulnerable patient group, EPI causes maldigestion with symptoms of weight loss, steatorrhea, and flatulence.[1] In current clinical practice, the fecal pancreatic elastase-1 (PE-1) enzyme-linked immunosorbent assay (ELISA) test is mostly used for diagnosing EPI. However, a certain pitfall of the PE-1 ELISA test is that results are only available after 3 to 4 weeks. Recently, a rapid fecal PE-1 test became available to diagnose EPI, the Quick test (ScheBo Biotech AG, Giessen, Germany). The Quick test is based on the same immunochemical reaction as the PE-1 ELISA test and can be analyzed without the use of a laboratory, and results are available within a few minutes.[2] One recently published study compared the diagnostic accuracy of the Quick test with the PE-1 ELISA test in 126 subjects, mostly (n = 90) with cystic fibrosis, showing high sensitivity and specificity (92.8% and 96.6%, respectively).[3]

DIAGNOSTIC ACCURACY OF THE QUICK TEST

We performed a prospective study to compare the accuracy of the Quick and PE-1 ELISA test on consecutive patients with potential EPI in the gastrointestinal and surgical pancreaticobiliary outpatient clinic. Patients were asked to obtain one stool sample, and both tests were performed from the same sample. Pancreatic elastase-1 ELISA test results are continuous; PE-1 <200 μg/g was considered insufficient. Quick test results are dichotomous based on the presence (sufficient) or absence (insufficient) of a test line; this line was scored by 3 observers (P.F., J.E.v.H., and M.G.B.). In case Quick test outcome was not scored unanimously, we applied the outcome with 2 of 3 votes for comparison with the PE-1 ELISA test. Diagnostic accuracy of the Quick test was evaluated based on the agreement between both tests, calculated using Cohen κ. Fleiss κ was applied to evaluate the interobserver variability of scoring the Quick test outcome.

RESULTS

Overall, 101 patients were included in the study (mean [standard deviation] age, 62 [13.5] years; 53% female), with 70% EPI according to PE-1 ELISA. Underlying condition was pancreatic surgery in 52%, chronic pancreatitis in 17%, pancreatic cancer in 13%, recurrent acute pancreatitis in 2%, and autoimmune pancreatitis or von Hippel–Lindau disease in 1%.

Independent scoring of the Quick test results revealed a calculated Fleiss κ for agreement of 0.70 ($P < 0.01$), indicating only "substantial" agreement between the

TABLE 1. Accuracy of the Fecal PE-1 Quick Test Compared With the Fecal PE-1 ELISA Test for Different Subgroups

	n	Cohen κ	*P*
PE-1 <200 μg/g vs normal PE-1	101	0.27	<0.01
PE-1 <100 μg/g vs normal PE-1	82	0.40	<0.01
PE-1 ≤15 μg/g vs normal PE-1	64	0.56	<0.01

Agreement between the Quick test and the PE-1 ELISA test calculated with Cohen κ slightly increased in patients with lower fecal PE-1 values.

observers. Agreement between the observers did not increase in patients with lower PE-1 concentrations.

Calculated Cohen κ was 0.27 ($P < 0.01$), suggesting "fair" agreement between the PE-1 ELISA and the Quick test. If we would consider the PE-1 ELISA test as the criterion standard for diagnosing EPI, the Quick test would have an accuracy of 0.60, a sensitivity of 0.50, a specificity of 0.84, a positive predictive value of 0.88, and a negative predictive value of 0.43. Agreement between the PE-1 ELISA test and the Quick test slightly increased in patients with lower PE-1 concentrations (Table 1).

DISCUSSION

This prospective study clearly demonstrates that the new fecal PE-1 Quick test for EPI is associated with frequent disagreement among observers and poor accuracy, which makes it clearly inferior to the PE-1 ELISA test. Although Quick test results are based on the presence or absence of a test line, results were frequently ambiguous and therefore hard to interpret (Fig. 1). The fact that we did not compare the Quick test with the "true gold standard" (secretin-CCK test) can be considered as a limitation.[2,4] However, the fecal PE-1 ELISA is usually used as a standard test to diagnose EPI in most centers worldwide because is it less invasive, less time consuming, and less expensive as the secretin-CCK test and does not require a specific diet. Furthermore, one could criticize the fact that we did not have optimal control on the collection of stool for the Quick test by the patients. This step may indeed be vulnerable for errors. However, this is how the Quick test is intended to be used, thus mimicking clinical practice.

In conclusion, the fecal PE-1 Quick test for diagnosing EPI is inferior to the PE-1 ELISA-test, despite the fact that both tests are based on the same immunochemical reaction.

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S.J.L. and S.A.H. contributed equally to the work. M.G.B. and J.E.v.H. share senior authorship.

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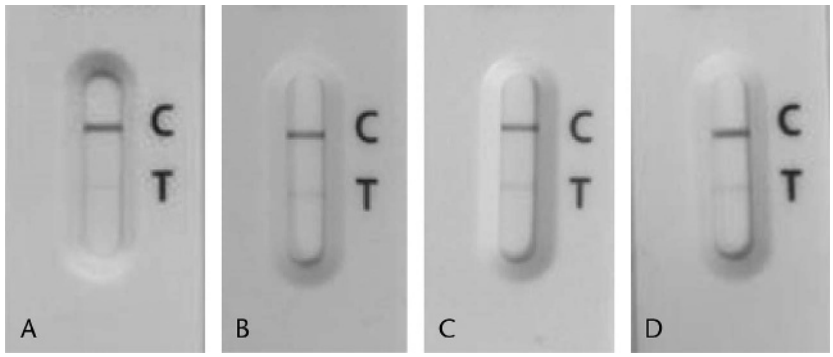

FIGURE 1. Four examples of ambiguous results of the Quick Test. PE-1 299 μg/g (A), PE-1 173 μg/g (B), PE-1 327 μg/g (C), and PE-1 ≤15 μg/g (D).

Challenges in Diagnosis and Management of Pancreatic Inflammatory Myofibroblastic Tumors in Children

To the Editor:

Pancreatic neoplasms in childhood are rare. The Surveillance, Epidemiology and End Results data from 2009 to 2013 showed that the age-adjusted and age-specific incidence of patients younger than 20 years with pancreatic cancer in the United States is less than 0.1% of all new cancer cases in the United States.[1] In a single institutional study at Boston Children's Hospital, only 18 cases were found during a 90-year period. The rarity and histopathologic diversity of primary pancreatic tumors in children have made it very challenging to predict prognosis and develop evidence-based