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Screening for Pancreatic Ductal Adenocarcinoma: Are We Asking the Impossible? – Letter

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Caldwell et al(1) highlight several challenges associated with employing a pancreatic cancer screening test. Several questionable assumptions in their study, especially regarding individuals at high-risk of pancreatic cancer, limit their conclusions.

First, patients with a positive screening test would not proceed immediately to EUS/FNA. Before clinical implementation, the main causes of false-positive screening tests would need to have been determined. Before broad-scale implementation of a screening test, studies would be undertaken to evaluate strategies to limit complications that arise from aggressively pursuing positive screening tests, such as identifying comorbidities that cause false-positives and/or repeating screening tests. Furthermore, a test with 90% specificity would generate too many false-positives and would be unlikely implemented for pancreatic cancer screening. If a 99%-specificity test was used, patients testing positive could proceed to EUS, where an FNA, which is the main cause of EUS-related complications, would only be performed if a suspicious lesion was detected. Even with a high specificity

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test, many positive screening tests would be false-positives; therefore suspicious-looking, false-positive lesions would rarely be seen on EUS. Second, the authors oversimplify by imposing a scenario whereby all patients with a positive EUS, including false-positives, would proceed directly to surgical resection. Pancreatic surgeons do not resect the pancreas indiscriminately. In some cases, pancreatic surveillance imaging identifies worrisome lesions, but clinicians are well-aware of the risk-benefits of proceeding to surgery. In this setting, the decision to undertake surgery is best decided in a multi-disciplinary fashion. As a result, the authors overestimate the morbidity of pancreatic cancer screening. Third, the authors assume all high-risk individuals with germline mutations would undergo pancreatic cancer screening. Pancreatic cancer surveillance is not recommended until middle age (age 50+ for most mutation carriers) when the incidence of pancreatic cancer is greater than the 0.2% the authors estimate.

Currently, high-risk individuals typically undergo annual surveillance with pancreatic imaging, with acceptable morbidity, as outlined in the most recent CAPS consensus conference(2). This surveillance strategy is associated with down-staging to resectable disease of diagnosed pancreatic cancers(3,4), including the detection of stage I cancer, with preliminary evidence of improved survival(3). The pursuit of early detection of pancreatic cancer is still a work in progress, but patients diagnosed with stage I pancreatic cancer who undergo surgical resection have excellent 5- and 10-year survival(5). Therefore, early detection research remains an important strategy to improve the prognosis of pancreatic cancer, especially amongst high-risk individuals.

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