It was with great interest that we read the article published by Yip-Schneider and colleagues on which we would like to comment. The authors demonstrated that vascular endothelial growth factor (VEGF-A) was considerably elevated in patients with serous cystic neoplasm (SCN), providing 100% sensitivity and 97% specificity; VEGF-C had the same sensitivity but inferior specificity (90%). Pancreatic fluid samples were analyzed for VEGF-A by ELISA and correlated with the surgical pathologic diagnosis. It is crucial to clarify whether all these lesions were eventually resected; otherwise, the alternative tissue sampling method should be described in order to exclude a potential sampling error.

The authors used 8,500 pg/mL as cut-off for VEGF-A and 200 pg/mL for VEGF-C, calculated from a study of only 87 patients; these cut-offs need to prove reproducible in bigger cohorts before deemed valid.

Both VEGF and its receptors (VEGFR2) are overexpressed in pancreatic cancer, with VEGF acting as a strong mitogen, participating in tumor spread. High VEGF levels are correlated with disease progression and dismal prognosis. Perhaps understandably, the authors suggest that VEGF abundance in the SCNs is related to the high vascularity of their walls; nonetheless, this novel finding of VEGF overexpression in SCNs, when associated with the established knowledge of VEGF’s relationship to disease progression in pancreatic cancer, stands out as intriguing to say the least.

Von Hippel-Lindau (VHL) disease is related to multiple micro- and macrocystic adenomas as well as cystic and solid neuroendocrine and diffuse pancreatic tumors. Given VHL’s protean nature and its demonstrated tendency to overexpress VEGF, cyst fluid VEGF-A positivity might provide false assurance and hinder the timely diagnosis of a VHL-related evolving malignancy.

REFERENCES

Disclosure Information: Nothing to disclose.

Vascular Endothelial Growth Factor
In Reply to Giorgakis and colleagues

Michele Yip-Schneider, PhD, C Max Schmidt, PhD, MD, MBA
Indianapolis, IN

We appreciate the insightful comments raised by Emmanouil Giorgakis and colleagues. In response, we confirm that all lesions included in the vascular endothelial growth factor (VEGF) analysis were resected and pathologically confirmed. We agree that the reported results and cutoff values do need to be validated further before they can be applied with confidence in clinical practice. To that end, our results have been independently validated in a separate group of patients at Massachusetts General Hospital, Boston, MA (personal communication, Cristina R Ferrone, MD). Few institutions have sufficient pancreatic cyst fluid specimens banked and available to confirm our
findings because resected serous cysts are relatively uncommon; therefore, we have combined resources with other institutions through support of the Lustgarten Foundation and are hopeful this will facilitate further validation.

We agree that elevation of VEGF-A and VEGF-C in serous cysts, although intriguing, is only part of the puzzle and that the results must be interpreted with caution when translated to the clinic. If a threshold VEGF cut-off is determined for clinical use, there will likely be patients whose VEGF levels are close to the cut-off value. In those cases, it will be important to have additional information to aid in clinical decision making. We envision that determination of VEGF will be one component of a diagnostic biomarker panel; together the selected biomarkers will be able to differentiate benign serous cysts from other pancreatic lesions that may require monitoring or surgery. In this manner, diagnosis will not depend on VEGF-A or VEGF-C positivity alone but rather on a panel of suitable markers to provide the necessary accuracy. We believe that patients with asymptomatic benign serous cysts will be spared surgery, while those with premalignant or malignant lesions will be identified for further monitoring or surgical intervention.

REFERENCE


Disclosure Information: Dr Schmidt is a paid consultant for Redpath IP, Inc and Asuragen, Inc. He is founder and employed at B9, Inc, and has a patent pending for VEGF-A use. Dr Yip-Schneider has nothing to disclose.

Treatment of Anastomotic Leak

Kenneth A Heisler, MD, FACS
Falmouth, MA

I was troubled that, in the intriguing article on treatment of anastomotic leak by Krarup and colleagues,1 no data were presented enumerating what anastomotic techniques were used in the original 9,333 operations—593 of which proved leaky.

What proportion of these original anastomoses was stapled? What proportion was hand sewn? Did one technique fare better than the other?

I would very much like to know. After all, the best way to manage an anastomotic leak is not to have had it at all.

REFERENCE


Disclosure Information: Nothing to disclose.

Management of Anastomotic Leakage

In Reply to Heisler

Peter-Martin Krarup, MD
Copenhagen, Denmark

We thank Dr Heisler for his interest in our article on management of anastomotic leakage in patients with colonic cancer.1 It is correct that information on the type of anastomosis at the primary operation would add considerably to the assessment of risk factors for anastomotic leakage, but such data were unfortunately not available in the national database of the Danish Colorectal Cancer Group. A previous Cochrane review did not report any statistically significant differences in leak rates between stapled or sutured colorectal anastomoses at any level.2 The meta-analysis was updated in 2012 with the same conclusion.3 In a meta-analysis including patients with ileocolic anastomoses, stapled functional end to end anastomoses were associated with a lower rate of anastomotic leakage compared with sutured anastomoses in a subset of patients with colonic cancer, and no significant difference was found in patients without cancer.4

Anastomotic leakage is an inevitable part of colorectal surgery, for which detailed knowledge on preventive measures and management of this complication is essential to decrease morbidity and mortality.

REFERENCES


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