Laparoscopic colorectal surgery and vascular endothelial growth factor

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The paper “Persistent elevation of plasma VEGF levels during the first month following minimally invasive colorectal resection” [1] increases our understanding of the impact that surgery has on the complex universe of tissue-derived growth factors, which are critical for wound healing but also have an impact on various malignant tumors. The “dark side” of these healing factors, of which there are several classes, is that overexpression, at least theoretically, can promote the implantation or growth of metastatic cancers. Vascular endothelial growth factor (VEGF) is one of the most potent and well studied of the tissue-derived angiogenic factors, and as such has been closely investigated, particularly for its role in tumor implantation and growth. One of the most important recent chemotherapeutic developments for colon cancer, in fact, has been antiangiogenic therapy, and drugs such as the recombinant humanized anti-VEGF monoclonal antibody bevacizumab are rapidly becoming an important element in chemotherapeutic regimens for advanced colon cancers.

At the same time that our knowledge of the relationship between angiogenesis and cancer growth has grown we have seen renewed interest in the use of minimally invasive approaches to gastrointestinal cancers, with multiple studies showing improved short-term outcomes and equivalent cancer outcomes. Such quality-of-life issues are, of course, important, but nonetheless, the primary goal of surgery is one of effective treatment and even cure. The question currently before the surgical community is whether laparoscopy will eventually be shown to improve cancer outcomes. If it does, it will certainly become the absolute

standard of practice, to the benefit of all cancer patients. In the past, improved cure rates from surgery were a result of better resection techniques; this is unlikely to be the explanation of any improvements resulting from the use of laparoscopy, as the mechanics of the surgery are seldom altered. Instead it will come from alteration of the physiological impact of the surgery, the effects of which are mediated by tissue-generated and blood-borne factors such as VEGF.

So, what is known about colorectal cancer, surgery, and VEGF? We know that colon cancer patients have higher levels of circulating VEGF than comparable patients with benign disease – a finding confirmed by the present study. We know that higher plasma levels of VEGF can predispose patients to tumor implantation and growth [2]. We know that any trauma, including surgery, can increase circulating and tissue levels of VEGF. Minimally invasive surgery may cause less of an increase in circulating VEGF, possibly as a result of smaller incisions generating less tissue-derived VEGF, although the data on this is somewhat mixed in the literature [3,4]. And now, thanks to the present study by Dr Whelen et al., we know that these higher levels of circulating VEGF can remain elevated for days and even weeks after the surgery — a finding that may be important when considering the optimal timing of adjuvant chemotherapy using antiangiogenic therapies.

We do not know, however, why some patients, almost a third of those in this study, show no or a very transient rise in VEGF after surgery. Whether this is a flaw in study design, variable expression in individuals or a difference in surgical technique is unknown, but obviously it is of interest from a clinical standpoint as it may turn out to correlate with wound complications, cancer recurrence or choice of adjuvant chemotherapeutic agents. In their discussion, the authors nicely summarize these unknowns and

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possibilities and outline future research to increase our knowledge in this critical field.

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