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Editorial

Anastomotic dehiscence and recurrence of colorectal cancer: an association that strengthens the prognostic value of the surgeon in the oncological outcome

Dehiscencia de anastomosis y recurrencia del cáncer colorrectal: una asociación que refuerza el valor pronóstico del cirujano en el resultado oncológico

Although mortality from colorectal cancer has demonstrated a downward tendency in recent years, the mean 5-year survival rates in Spain and Europe is only 52.5% and 54%, respectively.[1] The most important determining factor for survival among patients that are able to undergo curative surgery is local and distant tumour recurrence, which, combined, range between 30% and 40%. Likewise, tumour relapse mainly depends on lymph node involvement. However, besides the tumour stage, there are other variables with prognostic value which affect oncological outcome, such as certain pathological characteristics of the primary tumour, the administration of adjuvant therapy and, of course, the quality of surgery. It has been widely shown that surgery, such as the total mesorectal excision, is one of the most important prognostic factors in rectal cancer surgery[2] and it probably plays a no less significant role in colon cancer surgery.[3,4]

One of the most important complications in colorectal cancer surgery is anastomotic dehiscence. Different series have shown incidences ranging between 0.5% and 30%, depending on the location of the tumour and the definition of the dehiscence.[5] This complication is more common after rectal cancer surgery and is associated with high rates of morbidity and mortality.[6] Several cohort and case control studies published in recent years suggest that anastomotic dehiscence and the resulting peritoneal infection are associated with higher recurrence rates and increased cancer-related mortality.[7-10] A study of 1722 consecutive patients undergoing surgery for colon and rectal cancer reported that the overall 5-year survival in patients presenting with dehiscence was 45%, compared with 64% in those without this complication.[7] Furthermore, anastomotic dehiscence showed a negative independent association with cancer-related survival. More recently, in a series of 1741 patients undergoing surgery for rectal cancer, Ptok et al found that patients with dehiscence requiring surgical treatment had a higher 5-year local recurrence rate and lower disease-free survival rates than patients without dehiscence.[10] Although unconfirmed by other authors,[11] there are many studies reporting the influence of anastomotic dehiscence and peritonitis on cancer outcome. This has also been observed when the peritoneal infection occurs after the resection of hepatic metastases.[12] It has even been suggested that the negative affect on long-term cancer outcome is not limited to peritoneal infections, but also includes other infectious[12] and non-infectious[13,14] complications after different operations on patients with gastrointestinal cancer. Although most studies supporting this association have been published in recent years, it is interesting to note that, even back in 1983, Nowacki and Szymendera showed that post-operative fever lasting longer than 2 days was the most unfavourable prognostic factor in a series of 224 patients undergoing surgery for colorectal cancer.[15]

Several hypotheses have been proposed to explain the mechanisms responsible for the association between anastomotic dehiscence, infection, and recurrence. It has been suggested that the inflammatory response, which is greater in patients with postoperative infection, causes the inactivation of apoptosis, promoting the proliferation of implanted tumour cells and hidden metastases.[7] Other researchers have suggested that dehiscence could promote the implantation of exfoliated cells deposited outside the intestinal lumen in the pelvis.[8] However, these hypotheses

have not been proven, so other factors involved in tumour growth must be studied.

Angiogenesis plays a key role in tumour recurrence and the development of metastases. In the absence of angiogenesis, tumour growth is limited to 1-2 mm.[16] Vascular endothelial growth factor (VEGF) is the most potent angiogenic cytokine, stimulating the proliferation of endothelial cells and microvascular permeability. Increases in angiogenesis and serum VEGF levels have been associated with a shorter disease-free time and lower overall survival rates in patients with colorectal cancer.[17] One of the main inducers of angiogenesis is the inflammatory response to surgical aggression, a response that increases when there is peritoneal infection. Although the activation of angiogenesis in the postoperative period must be considered part of the healing process, an increased response could have a negative effect on cancer patients. An experimental model combining colon cancer and intra-abdominal infection carried out by our research group confirmed that postoperative infection leads to greater tumour recurrence, and that it is associated with increased angiogenesis and VEGF expression.[18] The preliminary results of a clinical case-controlled matched-pair cohort study of patients with colorectal cancer confirmed that increased postoperative angiogenesis is involved in the higher rates of recurrence among patients with dehiscence.[19]

The relationship between anastomotic dehiscence, peritoneal infection and recurrence strengthens the prognostic value of the surgeon in patients undergoing surgery for colorectal cancer, and makes it even more important for postoperative morbidity to be maintained within the required quality standards.[20] In view of the impact that this complication seems to have on the oncological outcome, adjuvant therapy should be considered in these patients, regardless of the tumour stage. Lastly, more in-depth knowledge of the mechanisms involved in this association could facilitate the choice of targeted therapy, such as antiangiogenic antibodies and drugs, which would make it possible to reduce the risk of recurrence.

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