



REVIEW ARTICLE

Surgical safety margin of gastroenterological cancer surgery: A truth or a dream?



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Summary Most surgeons dream about performing an extensive resection with a wide resection margin and extensive lymph nodes dissection, which will yield a favorable prognosis. Previous studies have reported varying lengths of the margins based on different clinical profiles. The so-called safety margin is not completely safe because limited scientific evidence exists for nonrecurrence, even after the patient has had a pathological examination to prove a negative cancer invasion at the resection margin. The safety margins for malignancy are different in the esophagus, stomach, colorectum, liver, and others because of the different modes of carcinogenesis and variable paths of recurrence. However, a minimally acceptable margin length can be defined because the margin is destroyed during operative dissection or shortened after formalin fixation for tissue assessment during pathological diagnosis. The currently available data for supporting the reality of a true negative or true positive invasion at the resection margin could be presumed by gross findings of a solid tumor. A safety margin for esophageal, gastric, liver, and colorectal cancer could be 0.1, 2–4, 2, and 1–3 cm, respectively. A dream to have a real safety surgical margin to achieve better surgical outcome is a challenge for any gastroenterological surgeon. However, a complete safety margin may not always be realized because it is impossible to have a true negative margin from surgical equipment and pathological tissue process.

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1. Introduction

The role of a surgical margin in surgical oncology has always been discussed with regard to the tumor recurrence and survival rate in gastrointestinal cancer surgery. Previous reports have suggested that extensive operation with a wide resection margin and extensive lymph node dissection will probably result in a better prognosis.^{1–4} According to

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the “seed-and-soil theory”, during the carcinogenesis of liver tumor, less liver parenchyma will mean less likelihood of recurrence. As a result, extensive liver resection for primary liver cancer is usually encouraged if liver function is preserved.^{5–7} In the report by Poon et al,⁸ extended hepatic resection for hepatocellular carcinoma (HCC) with cirrhosis needed to be justified depending on the preserved liver function. Besides, there were no significant differences in the incidence of hepatic failure, complication rate, and resection margin width between the groups undergoing extended or lesser extended hepatectomy for HCC. The role of the surgical margin width in a hepatectomy for HCC was explained by Shimada et al,⁹ and it was suggested to secure a surgical margin >10 mm in young patients without hepatitis C virus infection and/or a tumor size of 25 mm or larger after a macroscopic curative hepatectomy to achieve long-term disease-free survival.

However, differences exist with regard to the role of surgical margin. For example, the “1-cm rule” for distal rectal cancer surgery refers to distal bowel margin as measured by surgeons on the fresh anatomically restored *ex vivo* condition, as reported by Bujko et al.¹⁰ The bias in measurement could be induced by the measuring pathologist on either the fresh tissue or on formalin-fixed specimens. Because of the bowel shrinkage occurring soon after the removal from the patient’s abdomen and the additional shrinkage occurring after fixation, correction factors have been proposed to account for the shrinkage of the distal margin. In addition, because the measurements were based on histological assessment during pathologic evaluation and not routinely by the surgeon’s operative findings, the results of the previous report¹⁰ should be considered taking this limitation into account, which may induce a potential source of bias.

Safety surgical margin of each organ in gastroenterologic cancer will have different recurrence and/or survival rates. In addition, the length of safety surgical margin cannot be firmly set with regard to the various organs. Actually, no impairment in the oncologic safety margin is expected owing to the differences that exist, as a negative or an ultraclosed negative will yield a totally different surgical outcome.

2. Surgical margin in esophagus cancer

The prognostic role and definition of the circumferential resection margin (CRM) involvement in operable esophageal cancer remain controversial. The College of American Pathologists and Royal College of Pathologists define CRM involvement as a tumor found at the cut resection margin and a tumor within 1 mm of the cut margin, respectively. A systematic review and meta-analysis was performed to determine the influence of CRM involvement on survival in operable esophageal cancer.¹¹ In this previous study by Chan et al, 2433 patients with esophageal cancer who had undergone potentially curative esophagectomy were analyzed in 14 reports. The CRM involvement between 0.1 and 1 mm was associated with a significantly higher 5-year mortality rate than the CRM-negative status ($p < 0.001$). Thus it was concluded that CRM involvement is an important predictor of esophageal cancer prognosis. Microscopic

tumor infiltration of the resection margin after esophageal resection is implicated to influence anastomotic leakage, tumor recurrence rates, and long-term survival. Law et al compared patients with tumor infiltration of resection margin (RM+) and those without infiltration (RM-).¹² Of the total 604 patients analyzed in the study, anastomotic recurrences developed in 10.3% of the patients in the RM+ group and in 4.9% of the patients in the RM- group without significant difference. Although a positive margin did not increase anastomotic recurrence, median survival time was significant different. However, in another study by Dexter et al,¹³ the odds ratio for the risk of dying from esophageal cancer was 2.08 when the CRM was involved ($p = 0.013$). Therefore, the presence of tumor within 1 mm of the circumferential margin following potentially curative resection for esophageal carcinoma is an important independent prognostic variable, and thus, it should be routinely reported.

3. Surgical margin in gastric cancer

The effect of positive or negative resection margin on the prognosis of gastric cancer was recognized and debated for decades. In a retrospective study by Chen et al,¹⁴ 64 advanced gastric cancer patients with positive resection margin after potentially curative resection were investigated for the prognostic effect of postoperative resection margin status for intraoperative positive resection margins. The survival between those patients who were re-excised to a negative resection margin and those who were left with positive resection margin was compared. The median survival in the positive resection margin group was 17.0 months as compared with 23.0 months in the negative resection margin group ($p = 0.045$). Thus, re-excision for an intraoperatively positive margin to a negative margin as a standard, can improve the prognosis of the patients with advanced gastric cancer. Therefore, routine frozen section examination of the resection margins should be made mandatory in all advanced gastric cancer patients undergoing potentially curative surgery. However, it is necessary to discuss how far is adequate to avoid the positive resection margin. In fact, the incidence of infiltration of the proximal edge was significantly higher when the tumor penetrated the serosa layer or spread beyond it than when the lesion was confined to the mucosal, submucosal, or muscular layer.¹ With reference to the length of the resection margin, no involvement was found when the cranial distance between the lesion and the line of resection was ≥ 6 cm. Proximal or distal infiltration for a distance >3 cm did not occur in patients with lesions confined to the mucosal, submucosal, and muscular layers. With regard to the length of the resection margin, no involvement was found when the cranial distance between the lesion and the line of transection exceeded 2 cm in patients with orally well-defined-type esophageal invasion. However, in patients with orally ill-defined type, transection with a distance >4 cm commonly guarantees safety of the proximal margin, except for cases with lymphatic invasion.¹⁵ These data provide a gastric surgeon with a rational basis for assessing the extent of resection while performing gastrectomy for gastric cancer.

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