

CAPÍTULO xxvi

Validity of current experimental evidence on laparoscopic surgery for colorectal cancer

Roberto Bergamaschi.

Experimental animal studies can provide crucial evidence for the evaluation and refinement of the controversial area of many areas of surgery. Recently, during the surge in interest in laparoscopic surgery, in particular for colorectal cancer, 72 animal studies have been published between 1995 and 2001. However, the question remains as to which of these data can be suitably extrapolated to the human population. Forty-five of 47 studies, which use cell suspensions, relied on percutaneous intraperitoneal injection of cancer cells to induce peritoneal carcinomatosis. One study described a laparotomy-based model with injection of tumor cells into the cecal lumen while a different study [3] presented the cancer cells via enema. In this study, sigmoid resection was performed before colorectal solid tumor growth.

Overall 25 manuscripts have described solid tumor models, 21 of which used extra-colonic tumors to draw conclusions on laparoscopic surgery for intracolonic colorectal carcinoma. The remaining 4 studies did at least utilize colorectal sites including anastomosis, cecum and rectum. Three of these 4 studies, however, did not include resection [1, 7] or included performance of resection prior to development of solid tumor [5]. One [7] of these studies utilized subserosal cecal injection for induction of the tumor, whereas the latter [5] used cancer cell enema. Transmural injection to create submucosal blister with contralateral rectotomy was performed in one study as the method of tumor tissue implantation [1], while yet another model described resection of the solid cecal tumor derived from human cells growing in nude mice [6].

Currently available experimental models of laparoscopic surgery for colorectal cancer are unlikely to be valid. They have included models with tumors remote from the primary disease, which they are expected to reflect in the host. Specifically, extra-colonic sites, absence of colonic solid tumor at the time of resection, and nude mice, all fail to meet the criteria of extrapolation to the human model. Other studies have involved significant modifications of primary colorectal carcinoma by using peritoneal carcinomatosis induced by intraperitoneal cell injection or cell implantation on colonic serosa by laparotomy. There

is a dire need for a solid tumor model that does not involve initial laparotomy or laparoscopy for tumor induction [2]. The model should comprise a single intramural tumor derived from the same species, which can grow in immunocompetent animals. The tumor should grow in the colon at a site that is amenable to conventional or laparoscopic resection with minimal morbidity and mortality. An example might be resection of the long cecum in the rat, which would avoid the need for an anastomosis making cecum the preferred site for induction by total colonoscopy [4]. Such a model would allow a valid comparison of cecal cancer resection by laparotomy and laparoscopy. It may also reduce animal subject mortality, thereby decreasing the number of animals necessary to be used in research projects. It might make studies more ethically and fiscally responsible and allow the model to be reproducible for other investigators.

References

1. Balague C, Braumann C, Fuhrer K, Guski H, Jacobi CA (2001) Validation of a new experimental model of colon cancer. *Surg Endosc* 15: 833-836
2. Bergamaschi R, Yavuz Y, Marvik R. Toward the development of a murine cancer model induced by total colonoscopy. *Preliminary Report Dis Colon Rectum* (in press)
3. Gutt CN, Riemer V, Kim ZG, Jacobi CA, Paolucci V, Lorenz M (1999) Impact of laparoscopic colonic resection on tumor growth and spread in an experimental model. *Br J Surg* 86: 1180-1184
4. Hull CC, Stellato TA, Ament AA, Gordon N, Galloway P (1990) Endoscopic and radiographic evaluation of the murine colon. *Cancer* 66: 2528-2532
5. Pauwels M, Lauwers P, Hendriks J, Hubens A, Eyskens E, Hubens G (1999) The effect of CO₂ pneumoperitoneum on the growth of a solid colon carcinoma in rats. *Surg Endosc* 13: 998-1000
6. Pocard M, Debruyne P, Bras-Goncalves R, Mareel M, Dutrillaux B, Poupon MF (2001) Single alteration of p53 or E-cadherin genes can alter the surgical resection benefit in an experimental model of colon cancer. *Dis Colon Rectum* 44: 1106-1112
7. Tomita H, Marcello PW, Milsom JW, Gramlich TL, Fazio VW (2001) CO₂ pneumoperitoneum does not enhance tumor growth and metastasis: study of a rat cecal wall inoculation model. *Dis Colon Rectum* 44: 1297-1301