



0959-8049(95)00250-2

Developments in Colorectal Cancer Surgery

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The developments in colorectal cancer since the 19th century are reviewed. Local recurrence of colorectal cancer after curative surgery is a major problem and may occur because of inadequate removal of the primary tumour and lymph node metastases, or intra-operative spill of tumour cells. Colorectal surgeons differ with regard to postoperative mortality. The best surgical technique has not yet been determined; there have been only two prospective randomised trials on surgical technique. However, it is predicted that laparoscopic surgery will have an important place in colorectal surgery.

Key words: curative surgery, laparoscopy
Eur J Cancer, Vol. 31A, Nos 7/8, pp. 1379–1381, 1995

INTRODUCTION

IN THE 19th century, the operative plan for colorectal cancer was mainly determined by the presence of the primary tumour. Its resection was a major procedure so that other factors such as the possible preoperative induction of metastases and peri-operative promotion of metastatic growth, seemed remote and were not considered. Morbidity and mortality following colorectal resections were high. Local recurrence occurred in a very high percentage and in 1907 Moynihan wrote: "We have not yet sufficiently realised that surgery of malignant disease is not the surgery of organs: it is the anatomy of the lymphatic system that counts". It is amazing that at such an early time it was realised that lymph node metastases were so important. It is even more astonishing that presently we still do not have an adequate answer to this important question. The main topic that will run through this brief overview is that cancer surgery is a double-faced procedure: it may not only benefit but also harm the patient.

METASTATIC PATHWAYS

Local recurrence of colorectal cancer after "curative" surgery is a major problem. Approximately 10–40% of patients undergoing curative surgery will develop local recurrence. Local recurrence may either be a consequence of inadequate removal of the primary tumour and its lymph node metastases, or be caused by intra-operative spill of tumour cells. Obviously, it is important to perform a radical resection of the primary tumour and to avoid spill of tumour cells. However, it is not clear how much of the lymph node area should be resected. This depends very much on the pattern of lymphatic metastasis. If lymphatic spread is a centripetal and stepwise process, in which tumour cells are filtered from lymph node to lymph node, then it is important to remove even the last positive lymph node. It is known, however, that lymphatic venous communications do exist, indicating that lymphatic metastases may develop in conjunction with systemic venous dissemination. Furthermore, skip lesions are often found in lymphatic spread. Thus, it is not clear when lymphatic spread

can be regarded as locoregional spread or at which stage it represents distant seeding. It is known that lymphatic spread in colorectal cancer occurs mainly in an upward direction, but in rectal disease lateral spread may also be present. This should be taken into account when considering lymph node dissection.

INTRA-OPERATIVE DISSEMINATION

Another possible cause of local recurrence is spill of tumour cells during surgery. Malignant cells in the abdominal cavity have been demonstrated during operation. These cells may survive and grow in the abdominal cavity or in the lumen of the bowel. Many surgeons perform lavage of the abdominal cavity. It is, however, not proven that such methods are of any use.

Besides intra-operative spill of tumour cells in the abdominal cavity, dissemination may occur via the venous pathway. Tumour cells can be found in the portal blood in up to 67% of patients. This may particularly be true in case of angio-invasive growth of the tumour. Angio-invasive growth is related to a decreased disease-free survival, and it has been postulated that handling of the tumour during operation may dislodge tumour cells. Tumour cells may even be found in the bone marrow, as has recently been demonstrated by Lindemann and associates [1]. In 32% of the patients with colorectal cancer, micrometastatic tumour cells were found in the bone marrow. Those patients had a significantly poorer survival than patients without tumour cells in the bone marrow.

Collectively, these deliberations on the causes of local (and distant) recurrence indicate that the surgical knife is double edged. Although surgery is the only treatment which can cure a cancer patient, it may also have adverse side effects: the surgeon may spill tumour cells locally during the operation; induce systemic release of tumour cells and furthermore, induce immunosuppression and stress by inflicting a large operative trauma in the patient. Immunosuppression, induced by blood transfusion in relation to colorectal cancer prognosis, has been an important issue in the last decade. Interestingly, it appeared that this aspect of surgery was more related to the surgical knife than had been anticipated.

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BLOOD TRANSFUSIONS AND CANCER PROGNOSIS

When it became apparent from results in the field of kidney transplantation that blood transfusions could induce immunosuppression, it was questioned whether transfusions might also have an effect on tumour growth. The notion that this indeed might be the case was instigated by our own experimental studies, which showed an adverse effect of blood transfusions on tumour growth, particularly when combined with surgical trauma. Subsequently, an adverse association between perioperative blood transfusion and cancer prognosis was demonstrated in numerous retrospective studies. In order to investigate whether this association might be causal, three randomised studies on colorectal cancer have been performed thus far. Two studies, including the one by our group, compared autologous blood with allogeneic blood [2, 3]. In the third study, leucocyte-depleted allogeneic packed cells were compared with non-depleted red cells [4].

In none of the trials could a significant difference in survival time between the two randomised groups be demonstrated. Yet, when we performed a multivariate analysis on the results of our trial, comparing non-transfused patients with transfused patients, it appeared that transfused patients (irrespective of the type of blood received), had a shorter disease-free survival time than the non-transfused patients. Since there were no differences between the outcome of patients who had received autologous or allogeneic blood, our reasoning was that not the blood transfusions themselves, but rather the circumstances necessitating transfusions were the real determinants of prognosis in colorectal cancer. The sobering conclusion, therefore, is that the blood transfusion phenomenon is an epiphenomenon of the adverse effects produced by operative trauma and stress, which mainly are determined by the skill of the surgeon.

GOOD AND MODERATE SURGEONS

It follows from the previous arguments that a good surgeon is a surgeon who operates with the least surgical trauma possible. Is there any evidence that "good surgeons" have a better record with regard to cancer prognosis than "bad surgeons"? The impact of the variability in surgical skill among surgeons has been studied by several groups. In a multicentre study by Reinbach and colleagues [5], it was found that there was a significant difference between colorectal surgeons with regard to postoperative mortality, which varied from 8 to 30%. The anastomotic leakage rate ranged from 0 to 25%, wound sepsis from 6 to 35% and the local recurrence rate from 0 to 29%. The 10-year survival rate varied from 0 to 63%! A significant difference in anastomotic leakage rate and local recurrence was also noted in the studies by Fielding and associates and Phillips and colleagues [6, 7]. There are now too many studies to ignore the fact that there exists a variability among surgeons, which was suspected earlier from results of retrospective studies. Reinbach and associates concluded from their study that: "A considerable improvement in overall survival might be achieved if such surgery were undertaken by surgeons with a special interest in colorectal surgery or surgical oncology". I tend to disagree with this statement, because a well trained general surgeon, aware of the importance of delicate tissue handling, will also be a good oncological surgeon, whereas a surgeon with a specific interest may still be a moderate surgeon.

In this respect, a few notable surgeons should be mentioned, who changed the scope of surgery. Halsted stressed the importance of taking the submucosa in the suture for a safe anastomosis. In 1947, Turnbull published his data on the no-touch isolation

technique. He anticipated that by not touching the tumour and ligating the vascular pedicle before resection, tumour seeding via the venous pathways during operation would not occur and survival would improve. From the results of a retrospective trial, he claimed that the no-touch technique improved survival in the case of Dukes' stage C. However, a prospective trial performed in The Netherlands demonstrated that the no-touch technique did not lead to further surgical complications, or lead to a better 10-year survival rate, but seemed to abolish the deteriorating effect on disease-free survival of angio-invasive growth [8].

Extended lymph node dissection has been highly recommended by Japanese surgeons, starting with a publication by Hojo and colleagues in 1982 [9]. They focused their attention on lateral spread of rectal cancer and advocated wide dissection of the pelvic lymph nodes and of the upper lymph node area. They made a significant contribution to increasing knowledge of the lymphatic drainage area and the possible locations of positive lymph nodes. Increased survival has been claimed, especially in the case of Dukes' stage C, but prospective randomised studies have not been performed.

In 1986, Heald published his excellent results of rectal cancer surgery [10], advocating resection of the mesorectum. In doing so, the local recurrence rate in his series was below 10%. Total mesorectal excision is less demanding than extensive lymph node resection and, therefore, probably will lead to lower morbidity and mortality.

LAPAROSCOPIC RESECTION OF COLORECTAL CANCER

Laparoscopic surgery is a recent development and has been undertaken for colorectal disease since 1991. Laparoscopic surgery is claimed to have many favourable effects such as: less pain, faster recovery, reduced wound infection, a favourable effect on cell-mediated immunity, neutrophil function and the induction of oxidants and cytokines and reduced blood loss. In the early years 1991–1994 laparoscopic colorectal resection was difficult, because of the relative clumsiness of the first generation instruments. From the results published in those years, a series of 460 patients could be reviewed [11]. The morbidity in that series was 17%, the mortality rate was only 1%, and patients could be discharged after 6 days. Although these results are very good, the proceedings in laparoscopic colorectal resection have been slow as compared with the popularity of laparoscopic cholecystectomy. The reasons for this are two-fold. Firstly, adequate tumour and lymph node resection may be a problem. It still has to be demonstrated that laparoscopic surgery does not compromise these sound surgical principles. A second problem is the occurrence of portsite recurrences, which have been reported in a number of cases. These local recurrences appear in the small openings of the abdomen and are an unexpected and troublesome feature in laparoscopic colorectal cancer surgery. These issues should be resolved before laparoscopic colorectal cancer surgery can be regarded as a routine and safe procedure. It is to be expected that experienced laparoscopic surgeons will be able to remove an adequate resection specimen in colorectal cancer. The portsite recurrence is a bigger problem. The cause of this recurrence is still unknown but currently is under investigation by our group using a laparoscopic rat model [12].

CONCLUSION

More questions than answers have been forwarded in this brief review. Questions posed at the beginning of this century on the issue of lymph node resection have not yet been completely

solved. Furthermore, there is still no information about the best surgical technique as only two prospective randomised trials on surgical technique have been performed thus far. One concerned the trial on the no-touch isolation technique [8], and the other by Rouffet and associates dealt with segmental resection versus hemicolectomy [13]. More prospective randomised studies have to be performed before we really know how to operate for colorectal cancer.

It is anticipated that laparoscopic surgery will capture an important place in colorectal surgery. Laparoscopic instruments will improve and learning curves will be shortened. The portsite recurrence problem undoubtedly will be solved. According to our surgical principles, there should be no local tumour remnant, no local spill, no distant seeding and no large operative trauma. This will improve the prospects of colorectal cancer patients. The patients will participate in choosing this direction. They will plead for a less traumatic procedure and may want to have the best surgeon. Before a "Michelin guide" for surgeons is composed by our patients, we should organise health care in such a way that adequate surgical care is provided by the right surgeon at the right moment. If we continue to perform well designed studies on colorectal cancer surgery, the future for colorectal cancer patients will definitely become brighter.

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