PROGNOSTIC FACTORS IN RECTAL CANCER

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Nearly 50% of patients operated for rectal cancer die of recurrent or metastatic disease, despite approximately 75% of them have undergone resection with curative intent. Trie difficulty to know the real prognosis of the disease has stimulated many studies aiming to establish some factors influencing its outcome. Three are the components to consider in the prognosis of a patient with a rectal cancer: the tumor, the host and the surgeon.

THE TUMOR

An unquestionable prognostic factor is the stage of the tumor at the moment of the diagnosis and treatment. A careful clinical and instrumental preoperative evaluation permits a precise macroscopical staging of the disease and, in most cases, a consequent proper approach. Digital examination, transanal ultrasound, pelvic CT permit a good preoperative evaluation while other investigations (colonoscopy, abdominal US, MR) can exclude syncronous cancers or metastatic spread (1,2).
Dukes' classification with its variants and T N M are generally accepted and numberless are the studies about their prognostic validity. A careful histological evaluation of the tumor is the essential step to know the stage of the disease and to evaluate the utility of an adjuvant treatment.
Regarding the micrometastasis in the lymph nodes in rectal cancers Dukes A and B, a recent study has demonstrated that they cannot be considered as a prognostic marker and their presence don't imply different strategies for additional theraphy or follow-up (3).
Many authors have published studies about factors considered as expression of biological malignancy of the disease. Tumor D N A content has been described as having a prognostic significance in patients with colorectal cancers. It's unclear whether tumor ploidy as a prognostic factor is indipendent of various standard prognostic variables such as depth of invasion and lymph nodes involvement by the tumor. Nevertheless some studies seem to demonstrate that the marker plays an important role in indicating a biologic aggressiveness of the disease (4,5).
P53 expression has demonstrate no prognostic value for overall survival or local control in a recent accurate study (6), while the Urokinase type plasminogen activator (uPA) seems to be a promising prognostic factor in Dukes B and C rectal cancers (7). Same results has been achieved using the Thymidylate Synthase (TS): patients with colorectal cancer and TS positive tumor seem to have a poorer prognosis(8).

THE HOST

The immunologic response of the patient with rectal cancer doesn't seem to have a direct influence on (he outcome of the disease. Hypoalbuminemia, loss of weight, need for blood transfusions, concomitant systemic diseases certainly can have a negative influence on the outcome of the disease but the results of many studies about these factors don't permit to consider any of them as an indipendent variable in the prognosis of patients with rectal cancer.

THE SURGEON

Local recurrences after resection for rectal cancer can vary between 0 and 21%. Also if some of these variations can depend on selection of patients it is likely that the surgical

technique is the most important variable. Many technical factors are involved in the resection of a rectal cancer and can play an important role in the outcome of the disease.

1-High or low ligation of the inferior mesenteric artery: there are no prospective controlled study on this subject but seems that a high tie is not necessary and can increase the risk of nerve injury.(9)

2- Total mesorectum excision (T E M) Studies on the local spread of rectal cancer have demonstrated that continuous or discontinuous extensions of the tumor involve the mesorectum and that its excision with envelope of fascia intact can highly reduce the incidence of local recurrence. (10,11,12)

This finding has led the concept that a T E M must be an indispensabile step in the surgery for rectal cancer. Spread of the tumor distally within the mesorectum rarely exceeds 2 cm and it's probably unnecessary to remove the whole mesorectum for tumors of the upper third of the rectum. If the tumor is found by the pathologist at the circumferential resection margin, this can be considered as a factor of poor prognosis in terms of distant metastasis and survivals 13)

3- Extended lymphadenectomy: The Japanese are the main proponents of this technique that provides the removal of the lateral and superior lymphatic systems. This means the high ligation of the inferior mesenteric artery and an extended periaortic and pelvic lymph node dissection from the duodenum to the periaortic and lateral iliac lymph nodes. The main disadvantage of the technique is the increase of morbidity, particularly regarding the pelvic nerve injuries.(i4)

Up to date we don't know if the technique is likely to result in an improvement in survival.(15)

4- Irrigation of the rectal stump: Although we know that many neoplastic cells are shed into the lumen during a rectal excision, their viability has been a contentious subject. Recent data confirm this possibility: even so this mechanism of local recurrence is thought to be quite rare. It's therefore a good idea to irrigate the rectal stump with a cancercidal agent prior performing the anastomosis.

5- Resections of contiguous structures: A tumor that involves other structures has a worse prognosis than a tumor that's confined to the rectum. Nevertheless some studies have reported encouraging results after extended procedures. (16,17)

Probably the best results in these cases depend on a careful selection of patients. It's unknown if a less aggressive surgery combined with pelvic radiotherapy can achieve similar results.

In a recent prospective study 10 prognostic factors were correlated with recurrence and tumor-related mortality:

Patient factors: age, gender, preoperative C E A;

Tumor factors: location from the anal verge, stage, intratumoral blood vessel invasion (BVI), intratumoral lymphatic vessel invasion, tumor ulceration, histologic differentiation;

Surgical treatment: extent of surgical resection.

Indipendent predictors of recurrence were male gender and B V I. Indipendent predictors of tumor-related mortality were male gender, B V I and poorly differentiated tumors.(18)

Up to date the outcome of a patient with rectal cancer is the result of the host response in addition to the macroscopic and histologic findings of the tumor related to the volume of mesorectum excised by a good surgeon.

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