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Original Article

Early Oncological Results of Abdominoperineal Resection For Rectal Cancer: The Challenge After The Introduction of Total Mesorectal Excision

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Abstract

Objectives: This study was designed to evaluate oncological results of abdominoperineal resection (APR) after introduction of total mesorectal excision. The final end-points were local recurrence and survival curves. The results were compared with anterior resection (AR). **Methods:** Seventy-one patients (54 percent males; median age, 59.5 – range, 29-82 – years) with rectal cancer were submitted to surgery with curative intention from May 1999 to December 2004 at the Division of Coloproctology and Small Bowel of Alfa Institute of Gastroenterology at Federal University of Minas Gerais Hospital. Operative procedures were classified as either abdominoperineal resections or anterior resections with coloanal or low rectal anastomosis. Total mesorectal excision was routinely performed for carcinomas of the lower middle and lower third of the rectum. Data were tracked prospectively. Local recurrences and cancer-related survival rates were estimated. **Results:** Twenty patients had tumor located in the lower third of rectum (28 per cent) and 11 of them (55 per cent) were submitted to APR. Overall, 15.5 percent of patients with rectal tumor were treated by APR. Estimated rates of local recurrence were 6 percent for AR patients and 23 percent for APR patients ($p = 0.0778$). Estimated rates for cancer related survival in patients submitted to APR was 67 percent and for AR patients was 78 percent ($p = 0.2910$). **Conclusion:** There is an important trend to poor oncological results of APR when compared with AR in patients with rectal cancer submitted to total mesorectal excision. This clinical observation elicits the necessity of a different approach for low rectal tumors, probably using a more radical APR and routine preoperative radiotherapy.

Key words: Rectal cancer; Total mesorectal excision; Abdominoperineal resection; Anterior resection.

Introduction

Rectal cancer represents now a days an important health problem around the world, including developing countries. In Brazil, in spite of the lack of official data, rectal cancer may account for approximately 35 percent of large bowel tumors. In the last two decades, an annual average increase of 3.5 percent has been observed in the incidence of rectal cancer, with 7,000 new cases being diagnosed each year.[1,2]

Optimal surgical resection is considered of paramount importance to achieve local control of disease, mainly in tumors of the middle and lower thirds of rectum. Unfortunately, a great diversity of oncological results has been reported after rectal resection.[3-8] Local recurrence usually ranges from 30 to 70 percent for patients submitted

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to conventional resection with high-risk tumors (stages II and III).

In contrast, after the introduction of total mesorectal excision (TME) in specialized centers around the world, a very important decrease on local recurrence rates was noted. Most studies obtain a rate consistently lower than 10 percent. In addition, TME has improved overall 5-year survival rates from an average of 45 percent to 80 percent.[8] Therefore, TME is considered now the gold standard in rectal cancer surgical treatment.

in spite of this, in the TME era, patients with lower rectal cancer submitted to abdominoperineal resection (APR) have had higher rates of local recurrence and lower rates of overall survival when compared to patients submitted to sphincter-saving low anterior resection. Heald et al reported a rate of only 1 percent of local recurrence after curative low anterior resection (LAR) and 33 percent after curative APR in patients with same stage tumors[8].

The present study aims to evaluate oncological results of abdominoperineal resection in comparison to results of low anterior resection in patients with rectal cancer submitted to surgery with the technical principles of TME.

Patients and Methods

Seventy-one consecutive patients with rectal adenocarcinoma were treated, with curative intent, by total mesorectal excision between May 1999 and December 2004 at Colorectal Section of Alfa Institute of Gastroenterology at Federal University of Minas Gerais Hospital. All primary cancers were biopsy confirmed. Data were colleted prospectively in a database at Alfa Institute of Gastroenterology. Follow-up was completed for all patients and the median follow-up time was 26 months (range: 9-49).

Patients submitted to an extensive preoperative diagnostic protocol, including digital examination, rigid rectosigmoidoscopy, colonoscopy and biopsy, computed tomography of abdomen and pelvis, and chest X-ray. Endoanal ultrasound was performed whenever it was possible in patients with lower third rectal tumors. Diagnostic studies also comprised complete blood count and serum chemistry including carcinoembryogenic antigen (CEA). Clinical and pathological data were retrieved from the protocol of TME patients and the tumors were classified according to TNM system.[9]

The operation was performed in modified Lloyd-Davies position after standardized bowel preparation and antibiotic prophylaxis. A complete dissection of the rectum and mesorectum down to the pelvic floor was performed by direct vision. Sharp dissection with scissors or diathermy in the avascular plane between the mesorectum and the surrounding paries was performed in all patients treated by TME. The aim is obtaining an intact mesorectum with no tearing of the surface and no circumferential margin involvement. The whole mesorectum is always excised this way, except for tumors of the upper third, when it may be safely divided 5 cm below the lower edge of the tumor. The reconstruction after TME has been performed using stapled straight or colonic J pouch anastomosis. Handsewn coloanal anastomosis is performed when intersphincteric resection was done.

Patients with tumors with evidence of infiltration of either internal or external sphincter muscles in the pelvic imaging or digital examination were submitted to abdominoperineal resection. Decision-making was done before radiotherapy, when it was indicated.

Surgery was deemed curative only on the basis of clinical grounds. The absence of macroscopic residual tumor after resection was the definition of curative surgery. Postoperative mortality was defined as death occurring during the first 30 postoperative days.

Local recurrence was present if the tumor was detected in pelvis regardless of whether or not new metastases were found elsewhere. Local examination with biopsy or CT imaging with or without biopsy was needed to determine local recurrence. Distant recurrence was defined as evidence of tumor in any other area.

Radiotherapy was used preoperatively associated with chemotherapy (2 cycles of 5-fluorouracil plus leucovorin at the beginning and at the end of radiotherapy course), if image exams showed a T3 or T4 lesion or N1 disease. In patients with histologically proven lymph-node positive involvement adjuvant chemotherapy with 5-fluorouracil and leucovorin was applied during six months. Postoperative radiotherapy was indicated for pT3 or pT4 tumors after the

specimen examination if no irradiation was applied in preoperative period.

For estimating time, a Kaplan-Meier analysis was performed. SPSS® software, version 11.0 (SPSS Inc., Chicago, IL) was used to analyze data. The following survival functions were calculated: overall survival, cancer-specific survival and local recurrence-free survival. The operative deaths were included. In overall survival, observations were considered as complete if patients died of any cause in the follow-up period. In cancer-specific survival, observations were considered only when patients died as a direct result of rectal cancer. Deaths from all other causes were suppressed. In local recurrence-free survival, observations were complete if patients had died of any cause in the follow-up period or if they were identified as having local recurrent disease during the follow-up period. All survival times were calculated from the date of operation until they were suppressed or patients remained alive and/or disease-free by March 2005.

Data were treated by the Kaplan-Meier product limit estimate and a log-rank test. Confidence intervals were taken at the 95 percent level.

Results

In the inclusion period, 71 patients with rectal cancer were submitted to total mesorectal excision with curative intention. There were 38 males (54 percent) with median age of 59.5 years (range, 29-82 years). Twenty patients had tumor located in the lower third of rectum (28 per cent) and 11 of them were submitted to abdominoperineal resection (55 per cent) (Table 1). Overall, 15.5 per ent of patients with rectal tumor were treated by APR.

There were no significant differences between AR and APR patients regarding sex and age, as well as pathological findings (Table 1), except for tumor level, that was lower in APR patients. Blood transfusion was more frequent in patients submitted to APR than AR (p = 0.016), but length of hospital stay was not different. There was a trend to worst UICC stages in patients submitted to APR, with the majority staged as II and III (77.7 per cent). Mesorectal tumor foci were more common in patients submitted to APR than AR (44 *versus* 17 per cent), but the difference did not reach statistical significance (p = 0.144). The mean lymph nodes harvest was slightly higher in AR patients (not significant). Otherwise, the mean of metastatic lymph nodes tended to be higher in APR patients (5.0 *versus* 1.2; p = 0.124) and with more N2 cases (not significant).

Table 1 - Clinical and pathological features in 71 patients underwent anterior resection and abdominoperineal resection with total mesorectal excision

Variable	AR	APR	*p*
Sex (male/female)	33/27	5/6	*0.398*
Age (mean)	59,27	60,64	*0.756*
Location (lower third)	9/60	11/11	
Differentiation			
well	13	3	
mod	45	7	
poor	2	1	*0.600*
Mucinous tumor	4/61	1/11	*0.581*
Lymphatic invasion	18/60	2/11	*0.344*
Perineural invasion	13/60	1/11	*0.308*
Vascular invasion	9/60	1/11	*0.515*
Radial margin invasion	5/60	1/9	*0.582*
UICC			
I	22	2	
II	14	2	
III	16	2	
IV	3	5	*0.419*
Mesorectal foci	10/59	4/9	*0.144*
Blood transfusion	18/59	8/11	***0.011***
Hospital period	15,48	10,27	*0.528*
Lymph nodes (mean)	17,5	14,4	*0.650*
Metastatic			
lymph nodes (mean)	1.2	5.0	*0.124*
N			
0	38	4	
I	9	1	
II	10	4	*0.096*
Local recurrence	3/60	2/11	*0.169*
Systemic recurrence	9/60	2/11	*0.542*
Radiotherapy	24/60	8/11	*0.870*

The crude local recurrence rate was lower in AR patients than in APR patients (5 percent *versus* 18 per cent), but again this difference did not reach statistical significance (p = 0.169). Systemic recurrence was similar between groups (AR = 15 percent and APR = 18 per cent; p = 0.542) (Table 1).

Local recurrence-free survival in 50 months in patients submitted to abdominoperineal resection was 23 percent and for anterior resection was 6 percent (p = 0.0778) (Figure 1). There was no difference regarding systemic recurrence between APR and AR patients (p = 0.542).

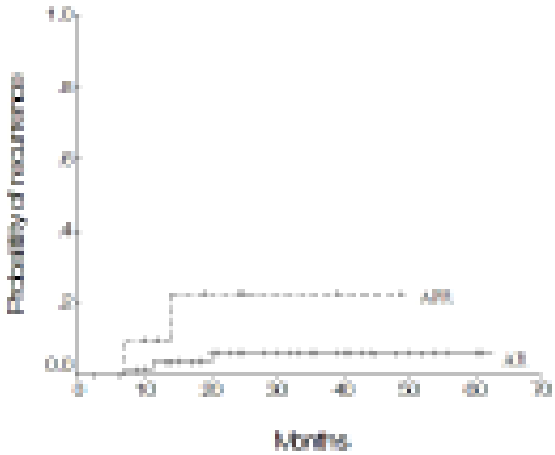

Figure 1 - Local recurrence-free survival in patients underwent abdominoperineal resection (APR) and anterior resection (AR).
Estimated rate in 5 years: AR = 6 per cent; APR = 23 per cent (p = 0.0778).

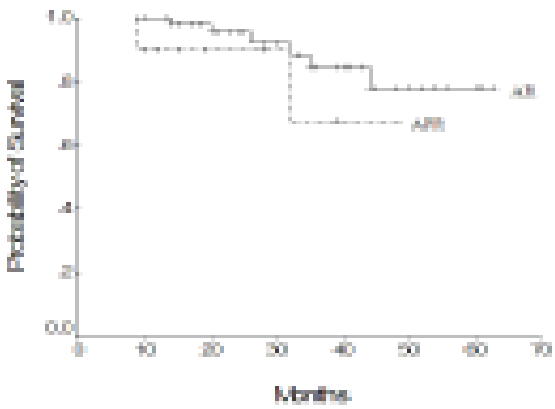

Figure 2 - Cancer-specific survival in patients underwent abdominoperineal resection (APR) and anterior resection (AR).
Estimated rate in 50 months: AR = 78 per cent; APR = 67 per cent (p = 0.2910; log rank) (p = 0.1754; Breslow)

Cancer-specific survival in patients submitted to APR was 67 percent and for AR patients was 78 percent (p = 0.2910) (figure 2). The overall survival in 50 months for patients submitted to APR was 67 percent and for AR patients was 64 percent (p = 0.9887).

Discussion

Until 25 years ago, abdominoperineal resection (APR) was accepted as the gold standard in the treatment of tumors located within 8 cm of the anal verge, despite of its mutilative results. Since them, the observation that the surgical treatment of low rectal tumors most of time by APR provides higher local recurrence and lesser overall survival rates when compared with high rectal tumors leads to an important concern related to suboptimal oncologic results of this kind of surgery.[10,11]

Due to the knowledge of tumor biological behavior with its lymphatic dissemination pathways and the knowing of limited intramural distal spread of tumor, the indications for conventional sphincter-saving procedures (SSP) for treatment of rectal cancer were progressively extended. In spite of improving the functional results with sphincter-saving procedures, the oncological results were not better than those obtained with APR.

As a result of these data, Heald and his co-workers studied the spread of tumor into distal mesorectum. The authors identified discontinuous microscopic foci of tumor into mesorectum until 4cm below to the distal margin of carcinoma independently of lymph nodes involvement. Therefore, they argued that resection of the entire posterior, distal and lateral mesorectum within its visceral layer, a procedure denominated total mesorectal excision (TME), would remove all potential foci of residual disease and would reduce the rates of local recurrence.[12]

In 1986, Heald and Ryall published their first results of TME. The authors studied 188 patients with rectal cancer operated by a single surgeon. Local recurrence occurred in only 2.6 percent of patients submitted to curative sphincter-saving resections, without adjuvant therapy.[7] APR was performed in only 11 percent of cases, a slightly lower result than the observed in the present study (15.5 per cent). In recent years, many studies have related percentages ranging from 10 to 30 percent of Miles operation in rectal cancer treatment.[12-14]

Because of an excellent initial oncological results of TME, many specialized centers around the world have published studies with rates of local recurrence lesser than 10 percent and 5-year overall survival around 80 per cent, much better than the average of 45 percent before the introduction of TME.[13,15,16]

Total mesorectal excision has led to improvement of SSP with no impairment of

oncological principles of radical resection.[17] In this situation, the whole mesorectum is removed intact, as a large cylinder, with no residual tissue on lateral pelvic walls, independently of intramural distal spread. In the other hand, in conventional anterior resection the rectum and mesorectum are transected 2cm below the tumor and surgeons usually performs an inverted cone shaped dissection and mesorectal tissue is left on pelvic walls. This fact justifies the high rates of local recurrence after conventional resections for rectal cancer.

Nowadays, it may be stated that sphincter preservation is the rule in surgical treatment of rectal cancer and APR is the exception. McAnema et al in a study of 81 patients submitted to to TME with SSP for distal rectal cancer observed 3.5 percent of local recurrence and 81 percent of 5-year overall survival, supporting the fact that reduction of distal margin did not affect these rates.[18]

Recently, Rullier et al have published their results with intersphincteric resection of distal rectal tumors (1.5cm to 4.5cm from anal verge).[17] Patients with two or more years of follow-up presented 2 percent of local recurrence and 81 percent of 5-year overall survival. Therefore, the distance the tumor is from the anal verge does not figure as a limitation for sphincter preservation since the external sphincter is not invaded.[17] Despite the great success of SSP, in some situations APR is the only curative surgical option to be offered for patients with tumors located near the dentate line, with gross sphincter invasion or for very obese patients or those who have a very narrow pelvis. In these cases, despite the whole mesorectal dissection, many studies have demonstrated higher rates of local recurrence and lesser rates of overall survival for patients submitted to APR when compared to patients submitted to AR.[19-22] The present study shows an important trend in this direction. When large numbers of patients be available for study, it is possible that APR will bring about more local recurrences when compared to AR, with statistically significant differences.

Heald in 1997 observed local recurrence rates of 1 percent for curative TME anterior resection in comparison to 33 percent for curative TME abdominoperineal resection in patients with same stage tumors.[8] Enker et al also observed at that time an overall survival rate of 60 percent for patients submitted to APR/TME and 81 percent for patients submitted to AR/TME. Prognostic features related to higher recurrence rates were lymph nodes involvement and lymphatic and perineural invasion.[13]

The reasons for higher local recurrence following APR are not fully understood. Insufficient distal margin, higher rates of tumoral invasion of circumferential radial margin (CRM) and lymphatic lateral spreading in low rectum are possibilities. In addition, it has been considered the high likelihood of implantation of exfoliated tumoral cells in perineal wound.[11]

Inadequate lateral margin at tumor level may be the leading reason determining the worst

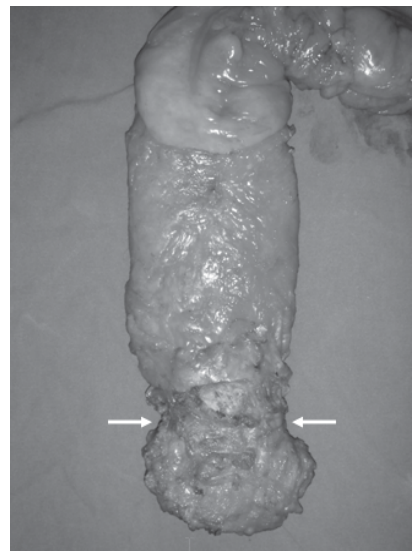

Figure 3 - Abdominoperineal specimen with total mesorectal excision showing an hour-glass shape with an evident "waist" (arrows)

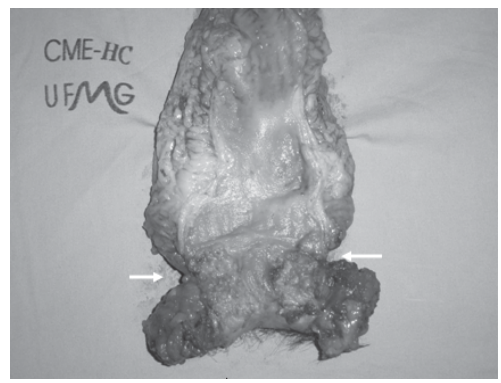

Figure 4- Opened abdominoperineal specimen showing the abrupt ending of mesorectal fat and the paucity of tissue at level of tumor (arrows)

prognosis after APR. Recently, Marr et al have evaluated prospectively 561 patients with rectal cancer submitted to exclusive TME. Higher rates of local recurrence after APR (22.3 percent) than after AR (13.5 percent) and better rates of overall survival after AR than APR (59 percent *versus* 48 percent) were reported[22]. They argued that higher rates of involved CRM in APR patients (41 percent *versus* 12 per cent) are associated with inadequate tissue excision beyond *muscularis propria* plane at the level of maximal invasion of tumor and this is the main cause of this disappointing outcome.[22]

Some authors argue that mesorectum coning down e caused by its natural tapering at the level of pelvic floor is the main reason for inadequate excision in APR. In these cases, the plane of surgical resection most frequently followed mesorectal fascia and then passed over the surface or into the sphincter muscles. Only a tiny tissue protects the surgical margin from direct spread of tumor circumferentially.[11] The delivered specimen shapes like an hourglass with an evident waist, probably the point of oncologic vulnerability (Figures 3 and 4).

Despite this, Salerno et al described prominent rates of local recurrence in low rectal cancer independently of resection modality (AR or APR) due to CRM involvement.[21] They emphasized the importance of preoperative chemoradiotherapy in cases of low rectal tumors according to an adequate identification of level of parietal tumor invasion and lymph node involvement by means of magnetic resonance imaging.[21]

Regarding neoadjuvant therapy for low rectal tumors, Nagtegaal et al, from the Dutch Radiotherapy plus Total Mesorectal trial, working with Dr. Quirke from Academic Unit of Pathology from Leeds, UK have demonstrated that local recurrence and overall survival rates of APR patients were significantly worse when compared to AR patients, both groups submitted to preoperative radiotherapy.[11] They have demonstrated that in one third of cases, the plane of surgical resection lies within the mural sphincter muscle or the submucosa. In cases with perforation, it is probable that surgical plane has passed through all the layers of the bowel wall into the lumen or that the mechanical manipulation of removing the rectum has led to tearing of the rectum in areas where the plane of excision has entered into the muscle or submucosa.[11]

Lymphatic lateral spreading might be considered as one reason for lower results of APR in the treatment of low rectal cancer, ranging in literature from 7 percent to 30 per cent, mainly in T3 and T4 tumors. According with this point, Japanese surgeons have performed pelvic lateral lymphadenectomy achieving lesser local recurrence rates. They argued that such lymph nodes are located beyond of resection limits of TME/APR.[23,24]

In this way, Takahashi et al identified neoplastic dissemination to pelvic lateral lymph nodes in 8.6 percent of patients, predominantly in low rectal cancer (16.4 per cent). 5 overall survival was 42.4 per cent, but 75 percent in cases of no evidence of invasion of superior lymphatic pathways.[23] A great concern in this situation is related to the type of surgical resection usually performed in Japan, which consists of wide ileopelvic lymphadenectomy frequently causing lesions to autonomic pelvic nerves. This damage leads to urinary and sexual dysfunctions, compromising dramatically these patients quality of life. In order to reduce the extent of this lesion, Morya et al have described a technique of lymphadenectomy with preservation of autonomic nerves, but at this moment, there is no uniformity in terms of surgical technique and functional results.[25]

Preoperative radiotherapy has been used as an alternative treatment for wide pelvic lymphadenectomy in patients with locally advanced low rectal cancer in order to improve oncological and functional results. Recent Japanese studies comparing lateral pelvic dissection *versus* TME with preoperative radiotherapy have demonstrated that lymphadenectomy may be replaced by irradiation followed by TME in the treatment of patients with advanced low rectal tumors.[26, 27]

Other important pathological features have been considered regarding local recurrence of rectal cancer in addition to TNM classification, such as involvement of circumferential radial or distal margins and localization of tumor in low rectum, mainly into the anterior wall.[11,22,28,29] The use of APR is applied fairly in these cases, and this explains the high rates of local failure this traditional operation presents. Therefore, another

surgical approach for low rectal tumors is crucial and there are proponents of a "new APR" with a more radical perineal dissection including coccyx and levator muscles with their natural relationships intact, as is performed by some Swedish surgeons.[22] In these cases, an adequate oncological specimen with cylindrical shape may be delivered as fashioned by anterior resection with TME

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