THE ROLE OF TRANSANAL ENDOSCOPIC MICROSURGERY IN THE TREATMENT OF T1N0 RECTAL CANCER – CASE SERIES AND REVIEW OF THE LITERATURE

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ABSTRACT

Background: Currently, there has been an increasing trend toward transanal endoscopic microsurgery as a definitive treatment of T1 rectal cancer. Despite the promising results from the earlier series, the more recent studies reported a higher rate of local recurrences. Methods: A retrospective analysis of 20 patients with T1 rectal cancer managed by transanal endoscopic microsurgery is presented. Results: The patients were followed-up for mean 39.3 months. Local recurrences occurred in 5.3% of low-risk, 50% of high-risk T1 cases. The 3-year and 5-year cancer-specific survival in T1 group were 94.4% and 73.5%, respectively with mean time without LR was 81.5 months (90.5 months in the low-risk and 21 months in the high-risk group). Conclusion: The results corroborate the excellent prognosis for low-risk T1 cancers treated by TEM alone. For a high-risk T1 cancer adjuvant radiotherapy or conventional resection is highly recommended. KEYWORDS: early rectal cancer, transanal endoscopic microsurgery, risk factors, adjuvant radiotherapy

Introduction

Colorectal cancer (CRC) is the third most common malignancy in the world with an annual incidence of 20/100 000 and the fourth most common cause of cancer death [1]. Rectal cancer accounts for approximately 34-38% of all CRCs. The conventional treatment includes anterior resection or abdominoperineal extirpation with total mesorectal excision (TME). Although the introduction of TME led to a significant reduction of the local recurrence rate, the standard resection is still associated with several complications such as intraoperative bleeding, bladder and sexual dysfunctions (30-50%), fecal incontinence, permanent stomy (up to 30%) and mortality up to 5% [2, 3]. To avoid these complications, transanal excision (TAE) introduced during 60th of the past century. Subsequently, the development and implementation of transanal endoscopic microsurgery (TEM) considerably improved the results from the local treatment of the rectal lesions. Although TEM offers a significant advantage in comparison to TAE and conventional resection regarding the benign lesions, the results from the treatment of rectal cancer are still contradictory [4].

Material and methods

The present study was designed to evaluate the effectiveness of TEM as a radical treatment for early rectal cancer in medically qualified patients. It includes a retrospective analysis of 20 pa-
patients with T1 rectal cancer. The procedure performed to avoid the possible complications from low anterior resection in four or as a personal choice of the rest. Informed consent obtained from all patients. They treated according to a standardized protocol by a multidisciplinary team consisting of a colorectal surgeon, gastroenterologist, pathologist, radiologist, and oncologist. All patients were staged preoperatively by digital examination, full colonoscopy, endorectal ultrasound (ERUS) or magnetic resonance tomography (MRT) and biopsy. All of them were treated by full-thickness TEM by one team from January 2008 to December 2014. All the patients refused additional treatment. The specimens were pinned on a cork plate, measured and examined by two experienced pathologists with particular attention to the resection margins and the presence of risk factors for recurrence. The patients divided into two groups according to the risk. As a low-risk were considered the cases with well-differentiated tumor size < 3 cm with the absence of lymphatic, vascular invasion and mucin production. In the presence of one risk factor, the cases were considered as a high-risk. The follow-up spanned the period from 1 Jan 2008 to 15 Jan 2015. It was performed according to a protocol by physical examination, abdominal US, chest X-ray, ERUS/MRT and rectoscopy at six months in the first three years and yearly after that. The endpoints were the rates of local recurrences (LR), distant spreading and cancer-specific survival. Statistical analysis performed with SPSS v.20. Descriptive statistics with numbers and proportions for qualitative variables and means (ranges and standard deviations – SD) for significant ones performed. The survival rate was calculated using Kaplan-Meier analysis. The comparison between groups made by using Log-Rank test (Mantel-Cox). P values < 0.05 were considered statistically significant.

Results

The results summarized in Table 1. There were 20 patients with T1 cancer – 8 women and 12 men. The mean age was 66.3 years (range 45-86, SD 12.3). The average size of the lesions was 3.5 cm (range 1-8, SD 1.7) with a mean distance from the anal border 8.1 cm (range 4-16, SD 2.6). Three cases (15%), initially diagnosed with villous adenoma, appeared to have T1 cancer after TEM. Microscopically negative margins (R0) obtained and confirmed by pathological examination in all cases. Complications occurred in 2 cases (10%) – postoperative bleeding and suture insufficiency. There was no postoperative mortality. All cases except two were with a small risk. The patients were followed-up for mean 39.3 months (range 3-96, standard deviation 23.1). LR occurred in 1/18 (5.3%) in the low-risk and 1/2 (50%) in the high-risk group. The mean time without LR was 81.5 months (95% CI 66.7-96.2) – 90.5 months in the low-risk and 21 months in the high-risk group (p<0.001, Log-Rank test). One of the low-risk cases (5%) developed distant liver and lung metastases after two and four years which treated by liver resection and lung metastasectomy.

| T (n) | Follow-up, months (mean) | LR %, (n) | Time without LR, months (mean) | Survival (%) |
|-------|--------------------------|-----------|--------------------------------|--------------|
|       |                          |           |                                | 3-year       | 5-year       |
| T1 (20)| 39.3                     | 10 (2)    | 81.5                           | 94.4         | 73.5         |
|       |                          |           |                                |              |              |
| - low-risk (18) | 5.3 (1)     | 90.5     |                                |              |              |
| - high-risk (2)  | 50 (1)        | 21       |                                |              |              |
Table 2 An overview of the results after treatment of T1 rectal cancer with TEM.

| Author             | N  | Follow-up (months) | Local recurrences (%) | 5-year survival (%) |
|--------------------|----|--------------------|-----------------------|---------------------|
| †Dixon, 2007⁴     | 618| 40                 | 5.5                   | -                   |
| Bretagnol, 2007⁹  | 31 | 34                 | 9.7                   | 76                  |
| Zacharakis, 2007¹⁰| 14 |                    | 7.1                   | -                   |
| Whitehouse, 2008¹¹| 23 | 34                 | 26                    | -                   |
| Baastrup, 2009¹²  | 72 |                    | 13                    | 76                  |
| Jeong, 2009¹³     | 17 | 37                 | 0                     | 96                  |
| Tsai 2010¹⁴       | 51 | 54                 | 9.8                   | -                   |
| Doornebosch, 2010¹⁵| 88 |                    | 20.5                  | ‡31                 |
| Ramirez, 2011¹⁶   | 54 | 71                 | 4                     | 98                  |
|                    | 28 |                    | 10                    | 93                  |
| Allai, 2011¹⁷     | 38 |                    | 0                     | 100                 |
| Morino, 2011¹⁸    | 48 | 54                 | 10.4                  | 86                  |
| Aman, 2012¹⁹      | 41 | 34                 | 9.8                   | -                   |
| Kogler, 2013²⁰    | 29 | 58                 | 10.3                  | 83                  |

†Cumulative analysis of 33 series to 2007,
‡3-year survival after salvage surgery,
§ High-risk T1 and low-risk T2 in combination with adjuvant radiotherapy

The patient is still alive without LR 6 years after TEM. Distant metastases also noted in one high-risk case. Two patients in the low-risk group died, one of which due to concomitant advanced pancreatic cancer. The mean survival time was 81 months (95% CI 66.3-95.8), 3-year and 5-year cancer-specific survival were 94.4% and 73.5%, respectively (Fig. 1, 2). No significant difference between high and low-risk cases was proven (p>0.05, Log-Rank test) probably due to small sample size (mean survival time for little risk was 84.9 months and 48 for high-risk cases).

Discussion

A nationwide study in the USA with 35 179 cases showed a considerable increase of the use of transanal excision of stage I rectal cancer during 1989-2010 (TEM used in 65% of the cases) [5, 6]. The increase is from 26.6% to 43.7% for T1 and from 5.8% to 16.8% for T2. In this study, the local excision of T1 cancer was associated with significantly lower morbidity (5.6% vs. 14.6%) and shorter hospital stay (2 vs. 8 days) than anterior resection, but with significantly higher five-year LR~12.5% vs. 6.9% [5]. On other hand, in comparison to the conventional transanal excision, TEM have been associated with higher rate of intact and non-fragmented specimen (94 vs. 65%), clear margins – 95-98% vs. 63-81% in cancer and 83-88% vs. 50-61% in adenomas, lower frequency of local recurrences – 3% vs. 22% for cancer and 3% vs. 32% for adenomas and lower 3-year mortality (2% vs. 29%) [7, 8].

The cumulative analysis of 33 studies revealed LRs in 5.5% (4-50%) of the cases after a mean follow-up of 40 months [4]. However, several recent studies [9-20] reported significantly higher recurrence rate varying between 5% and 26% (Table 2). On another hand, several studies, directly comparing TEM with the conventional resection in T1 cancer, reported significantly higher rate of recurrences [20, 21]. The lack of stratification according to the risk has been thought to be the main reason for this finding. In the present series, only 1 LR in the low-risk group (5.3%) vs. 1/2 (50%) in the high-risk T1 were found. It was in unison with Heintz et al., who reported no difference between TEM and conventional resection in low-risk (4% vs. 3%) in contrast to high-risk lesions (33% vs. 18%) [22]. In a recent prospective series, Ramirez et al. reported 4% LR for low-risk T1 vs. 10% in the group with high-risk T1 and low-risk T2 cancers after adjuvant radiotherapy [16].

The lack of mesorectal excision has been thought to be the primary cause for the higher recurrence rate after local excision. Lymph node metastases occur in 8-20% of T1 cancer and 12-28% in T2 [23, 25]. The results from the treatment of the recurrences are worst irrespectively of salvage surgery and adjuvant radiotherapy [15, 26]. Doornebosch et al. reported only 31% 3-years survival for the patients with LR, who underwent salvage surgery [15]. LRs also associated with higher rate of abdominoperineal extirpation due to the presence of postoperative fibrosis, which hampers the orientation about the resection margins. These factors highlight the need for a careful selection of the cases to achieve the best oncological outcome.

Despite the recent advance in imaging techniques, the exact preoperative staging is not always possible. Several studies showed a high rate of misdiagnosis (up to 34.6%) with endorectal ultrasound (ERUS) examination [16, 18, 27]. Its accuracy is better for the diagnosis of early cancer (about 80-95%) [28]. Regarding the nodal status, ERUS has specificity and sensitivity 78% and 55% or 75% according to a recent meta-analysis of 35 studies [29]. One of the reasons for the lower accuracy is...
the widespread notion that metastatic lymph nodes (> 1 cm). However, Wang et al., demonstrated that most of the metastatic lymph nodes were < 5 mm and more frequently located at the side of the tumor and in the periphery of the mesorectum [30] and several another characteristic such as shape, border and hyperechogenicity should be assessed. Even though, there ERUS is associated with 20% false negative results [28]. Magnetic resonance imaging is more sensitive regarding the more advanced T stage and for assessment of the circumferential margin [31]. The accuracy and sensitivity regarding nodal status are 69% and 77% despite the use of lymph node-specific contrast solutions [28]. The accuracy of the response to radiotherapy is 77% for T0 and 65% for N0.

The facts as mentioned earlier highlight the need for searching of risk factors allowing for more precise risk stratification. Tumors of the lower third of the rectum associated with 20% false negative results [28]. Magnetic resonance imaging is more sensitive regarding the more advanced T stage and for assessment of the circumferential margin [31]. The accuracy and sensitivity regarding nodal status are 69% and 77% despite the use of lymph node-specific contrast solutions [28]. The accuracy of the response to radiotherapy is 77% for T0 and 65% for N0.

The authors declare no conflict of interest.

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Disclosure

No conflicts of interest have been declared.

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