



Review Article

Functional outcome and quality of life following treatment for rectal cancer[☆]



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ABSTRACT

Introduction: Over the last decades, treatment for rectal cancer has substantially improved with development of new surgical options and treatment modalities. With the improvement of survival, functional outcome and quality of life are getting more attention.

Study objective: To provide an overview of current modalities in rectal cancer treatment, with particular emphasis on functional outcomes and quality of life.

Results: Functional outcomes after rectal cancer treatment are influenced by patient and tumor characteristics, surgical technique, the use of preoperative radiotherapy and the method and level of anastomosis. Sphincter preserving surgery for low rectal cancer often results in poor functional outcomes that impair quality of life, referred to as low anterior resection syndrome. Abdominoperineal resection imposes the need for a permanent stoma but avoids the risk of this syndrome. Contrary to general belief, long-term quality of life in patients with a permanent stoma is similar to those after sphincter preserving surgery for low rectal cancer.

Conclusion: All patients should be informed about the risks of treatment modalities. Decision on rectal cancer treatment should be individualized since not all patients may benefit from a sphincter preserving surgery “at any price”. Non-resection treatment should be the future focus to avoid the need of a permanent stoma and bowel dysfunction.

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Resultados funcionais e qualidade de vida após tratamento do câncer retal

R E S U M O

Palavras-chave:

Câncer do reto
Qualidade de vida
Resultado funcional
Preservação de esfíncter
Estratégia watch and wait

Introdução: Ao longo das últimas décadas, o tratamento do câncer retal melhorou substancialmente com o desenvolvimento de novas opções terapêuticas. Com a melhoria da sobrevida, os resultados funcionais e a qualidade de vida são cada vez mais tidos em consideração.

Objetivos do estudo: Rever as modalidades atuais de tratamento do câncer retal, com ênfase nos resultados funcionais e qualidade de vida.

Resultados: Os resultados funcionais após tratamento para o câncer retal é influenciado pelas características do doente, do tumor, da técnica cirúrgica, do uso de radioterapia pré-cirúrgica e do método e nível da anastomose. A cirurgia poupadora de esfíncter do câncer retal baixo resulta frequentemente em maus resultados funcionais que prejudicam a qualidade de vida, denominados síndrome da ressecção anterior baixa. A amputação abdominoperitoneal impõe a necessidade de uma colostomia definitiva mas evita os riscos de resultados funcionais deficitários. Contrariamente à crença geral, a qualidade de vida a longo-prazo em doentes com colostomia definitiva é semelhante à qualidade de vida após cirurgia poupadora de esfíncter do câncer retal baixo.

Conclusão: Todos os doentes devem ser informados sobre o risco das opções terapêuticas. A decisão do tratamento do câncer retal deve ser individualizada uma vez que nem todos os doentes beneficiarão de uma cirurgia poupadora de esfíncter “a qualquer preço”. A possibilidade de tratamento sem ressecção devem ser o foco futuro para evitar a necessidade de uma colostomia definitiva e disfunção gastrointestinal.

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Introduction

Colorectal cancer is the third most commonly diagnosed cancer worldwide. Almost 1.4 million new cases were diagnosed and 693,900 deaths were estimated to occur in 2012, with about 55% of cases occurring in developed countries. In Europe, it counts as the second most frequent malignancy and cause of cancer death, with an estimated 447,000 new cases diagnosed and 215,000 deaths occurring in 2012.¹

Approximately 30% of colorectal cancer are diagnosed in the rectum and around one third of rectal cancer (RC) are located on its third distal part.^{2,3}

Improvements in earlier detection of RC from screening programs, reduction of risk factors and enhanced treatment modalities resulted in increased survival rates over the last decades.^{4,5}

Treatment of RC had been primarily focused on oncologic outcome, with detailed assessment of survival and local recurrence.⁶ Less attention has been given to functional outcomes and quality of life (QoL). QoL is the personal perception of the impact of illness or treatments on physical, psychological and social well-being.⁷ Functional and QoL impairments are frequent among patients treated for RC, predominantly in patients with low RC.⁸ With the increasing number of patients living with treatment effects,⁹ these factors get a more significant role in decision making for RC treatment.

The purpose of this study is to review current modalities in RC treatment, particularly its impact on functional outcomes and QoL. Therefore, a review of the medical literature

was performed regarding these outcomes after operative and non-operative management of RC.

Historical background

Although main enhancements in treatment modalities of RC were achieved over the last decades, surgery remains the privileged form of treatment.^{3,10} Abdominoperineal resection (APR), primarily described by Miles in 1908, was the first step given in modern era of RC surgery. This procedure consisted of an en bloc rectal dissection with its lymphovascular supply in order to obtain a cylindrical specimen.¹¹ The anterior resection of the rectum, popularized by Dixon 40 years later, proved to be successful in cancers of the middle and upper rectum and was the first surgical procedure to avoid a definitive stoma. However, the creation of a safety 5 cm resection margin from the dentate line did not allow resection of the lower rectum, where APR remained the only available option.¹²

Several works began to re-evaluate the effect of distal resection margins (DRM) on oncologic outcome. Many studies reported that a DRM of 1 cm or even smaller had no negative impact on oncologic outcome.¹³ In fact, distal intramural dissemination of RC is rarely observed and probably linked to high grade tumors, where survival is mostly due to metastatic spread rather than local recurrence.^{14,15} On the other side, the importance of circumferential resection margin (CRM) was confirmed in multiple works, with positive CRM negatively influencing local recurrence and survival.¹⁶ Its surgical approach was achieved by the introduction of total

mesorectal excision (TME), a surgical technique in which RC is removed with intact mesorectum, containing vasculature and lymphatic draining, en block. The mesorectum concept was defined by Heald et al. in 1980.⁶ TME adoption decreased CRM positivity and local recurrence, improving survival rates for RC patients.^{17,18} Nowadays, TME is the primary form of treatment for RC, with an overall 5-year survival up to 80%.¹⁹

Anterior resection of the rectum became a reality in low RC; tolerance for smaller DRM, implementation of TME and availability of circular stapling devices was followed by a significant decrease of APR rates.²⁰⁻²² Aside from oncologic outcome, sphincter preservation is now considered a sign of surgical quality for RC patients.¹¹

Abdominoperineal resection and anterior resection of the rectum

Several changes in indications for APR were observed after its first description. Progresses in APR technique since it was originally introduced and application of TME led to a decrease in local recurrence and mortality rates.²³ Nevertheless, recent articles established that when comparing to low anterior resection of the rectum (LAR), APR displayed worse oncological outcomes. A 2009 pooled analysis of 5 European randomized clinical trials²⁴ reported that APR had significantly higher CRM positivity (10 vs 5%), higher recurrence rates (20 vs 11%), and worse 5 years survival (59 vs 70%). Similar results were consistently found in other works.^{25,26} These reports have led to the suggestion that outcomes after APR were inherently worse compared to LAR. However, these poorest outcomes following APR could be due to tumor characteristics. Rectal tumors in patients who undergo APR appear to be less differentiated, more locally advanced and with a lower response to neoadjuvant chemoradiotherapy (CRT).^{27,28} Chen et al.²⁰ reported higher rates of CRM positivity following APR, nonetheless, after adjustment for other covariates, survival rates were not influenced by the type of surgery as an independent risk factor. A recent study in Netherlands reported no differences in CRM positivity between APR and LAR.²⁹ Therefore, similar outcomes could be obtained with both surgical techniques, even for locally advanced tumors.³⁰

Selection of surgical procedure depends fundamentally of the surgeon preference, individual characteristics and tumor specifics. If radical resection is required in low rectum tumors, the two main treatment options are LAR and APR. Although sphincter preservation is currently an important goal, APR still remains the first choice in cases of very low tumors with sphincter complex invasion or impaired preoperative state, with approximately 24% of patients requiring APR for primary tumoral resection.³¹

Low anterior resection syndrome

Bowel function is a major issue after a sphincter preserving surgery for low RC. Bowel dysfunction occurs in 30-70% of patients after LAR and may reach up to 90% in some series.³²⁻³⁴

Most common symptoms include abdominal pain, urgency, fecal incontinence, frequent bowel movements, incomplete

evacuation, dolorous, irregular and/or obstructed defecation, and clustering.^{8,33,35} When low anastomoses are performed, patients become more predispose to develop these unpleasant symptoms.⁸ This group of complaints constitutes a medical condition entitled "low anterior resection syndrome" (LARS).³⁶ Patients with previously damaged sphincters, compromised continence or chronic diarrheal pathologies are more prone to develop this syndrome.³⁷ Frequently, LARS develops shortly after surgery, decreasing in a few months, with stability been reached in the first 2 years.^{32,35,38}

Etiology of LARS is multifactorial. Causes may include injury of pelvic floor muscles, reduced rectal capacity and compliance, diminished internal anal sphincter tone and lack of inhibitory recto-anal reflex. Posteriorly to LAR, lesion of sphincters with impairment of anal pressures and low recovery of recto-anal reflex is frequently observed.³⁹

While some patients may recover almost normal bowel function, others experience these disabilities permanently, conditioning long-term QoL. In fact, LARS is tightly associated with QoL, with major effect in global health status, social function and role function.³²

Living with a stoma

It is generally assumed by many surgeons and patients that a permanent colostomy results in worse long-term QoL when compared to a sphincter preserving surgery that can avoid the adverse impact of living with a permanent stoma. This belief was a major reason to adopt LAR as the first choice of treatment for low RC.^{40,41}

Due to this assumption, there is a lack of randomized clinical trials comparing the impact in QoL of a colostomy after APR or after a sphincter-preserving technique. Nevertheless, the most recent reviews challenge that conviction.⁴²⁻⁴⁵

In a 2005 Cochrane review⁴² of 2412 patients from 25 studies, no differences were found in QoL between patients undergoing APR or LAR. The authors referred that prospective studies with larger samples and better designed were required to clarify this question.

In 2007, a meta-analysis by Cornish et al.⁴³ of 1443 patients also stated that, concerning QoL, no significant global differences were identified between APR and LAR groups, with patients having similar perception of general health. These findings were consistently reported in larger, higher quality and with self-administered questionnaires studies. This review also did not find significant differences regarding impaired body image.

These data were supported by more recent studies using reliable and validated instruments for QoL assessment.^{44,46-48}

Patients undergoing sphincter-saving ultra-low AR have significantly more complications than APR. Fisher et al.⁴⁹ reported that 20% of patients had to deal with a permanent stoma due to failure of the sphincter preserving technique, leading to a negative impact in QoL. This occurred more commonly in older patients.

Frequently impaired gastrointestinal function following a sphincter-preserving surgery could equalize the need of permanent stoma.⁵⁰ Bowel dysfunction frequently experienced by patients undergoing a sphincter preserving surgery affects

QoL, even when patients were well advised by their surgeons. These patients may have raised preoperative expectations, which ultimately results in a great frustration if they have to live with such disabilities. Oppositely, patients undergoing APR typically have lower outcome prospects. However, when they realize that a fairly normal life is possible despite living with a stoma, these patients may become more satisfied.³⁸ This may be the reason why patients undergoing AR or APR have similar overall QoL.

A possible explanation to the fact that patients with markedly impaired bowel function report a good QoL may be due to the "response-shift phenomenon": the gratefulness for living without a stoma allegedly shifts patient's global QoL expectations.⁵¹

APR should be viewed as a possibility to consider and not only an end-of-line treatment option in behalf of QoL alone. This seems to be particularly true in older patients, patients with low life expectancy or with major anorectal dysfunction.^{49,52}

Urogenital function

In RC treatment, pelvic organs and nerves are very close to the neoplasm. Damage to these structures can result not only in bowel, but also sexual and urinary impairment. The lesion severity on pelvic autonomic nerves may vary depending on the surgical approach.^{53,54} Post-operative urogenital function were improved by the introduction of TME technique and the increasing knowledge of pelvic autonomic nerve pathways.^{6,18} Currently, less than 40% of patients present urinary malfunction, while 10–70% of patients display sexual impairment.^{53,55}

Stress and overflow incontinence, urgency, incomplete emptying of the bladder, increased frequency of voiding and lack of bladder fullness perception are the most frequent complaints of patients. Male sexual dysfunction frequently involves impaired ejaculation (20–60%) and impotence (20–46%). Inability to ejaculate is often not reversible.^{54,55} In women, information regarding sexual function is rare; however, patients may complain of worsened sexual function, including problems with lubrication and dyspareunia.^{56,57}

Sexual dysfunction may not only be due to physical factors like nerve injury after surgery or radiation therapy.^{54,57,58} In fact, other factors like poor body image, depression, fatigue and loss of independence may also play an important role in sexual dysfunction.⁵⁷

Restorative methods

In order to overcome LARS symptoms, different strategies for restorative methods focusing on the proximal aspect of the anastomosis have been developed to improve rectal volume and compliance.³⁶

When compared to straight colorectal or coloanal anastomosis, colonic j-pouch, colonic side-to-end anastomosis and coloplasty are associated with lower stool frequency, incontinence, urgency, and fragmented stool pattern. These data are supported by a recent meta-analysis⁵⁹ reporting colonic j pouch, side-to-end coloanal or transverse coloplasty to have

similar functional outcomes, that are superior when compared to straight anastomosis in the first post operative year. However, there appears to be no significant differences beyond 2 years. This long-term improvement could be explained by the continued increase in neorectal volume and recovery of anorectal reflexes and sphincter function following straight anastomosis, that probably allows continued improvement of compliance and function.⁶⁰

Better functional results are obtained shortly after RC surgery when a pouch is used if the anastomosis is within 3 and 5 cm from the anal verge. If a pouch is created in an upper level, evacuation problems are more likely to occur.^{36,61} When it is located higher than 7 cm from the anal verge, a straight anastomosis should be performed from a functional perspective.³⁶ Since urgency, frequency and incontinence are harder to manage than evacuation difficulties, the pouch should also not be too small.^{36,61}

The few works that addressed post-operative QoL between restorative methods did not report significant differences between these techniques.⁵⁹

Approach techniques

Laparoscopic surgery

Laparoscopic technique has been recently applied to TME for RC. Recent randomized clinical trials indicated that, when compared to open surgery, this technique has no compromise in oncologic outcomes, has similar complication rates and advantages in earlier postoperative recovery with less blood loss, rapid intestinal recovery, shorter hospital stay and lower postoperative pain.^{62–66}

With laparoscopic surgery allowing a better visualization of the operative field, this could contribute to a better preservation of pelvic autonomic nerves, therefore reducing genitourinary dysfunction following RC surgery.⁶²

The United Kingdom Medical Research Council CLASSIC trial^{67,68} is the only randomized clinical trial that compared genitourinary functions between open and laparoscopic surgery for RC. While no difference was found in terms of bladder function, male patients had a tendency for worse sexual functions after laparoscopic surgery. This would have a stronger impact in sexually active male patients with large or low RC, and could have implications when deciding the best operative approach.^{67,68}

However, more recent prospective studies stated that neither laparoscopic nor open surgery appears to have superior results regarding preservation of urinary or sexual function, although available data is limited.⁶⁹ These results could be explained by the continued increase in experience with laparoscopic surgery.

It is unclear whether laparoscopic approach could offer better QoL. When comparing different surgical approaches, studies evaluating QoL have obvious disagreements. While some studies reported a better QoL in both short and long-term after laparoscopic surgery,^{66,70} others did not find any benefits in long-term QoL following this surgical approach.^{71–73} In a multicenter randomized clinical trial (COLOR II),⁷⁴ there were no significant differences in QoL

between these surgical approaches at 1, 6 or 12 months. Both laparoscopic and open surgery impaired postoperative QoL, recovering gradually to preoperative levels overtime.

Since laparoscopic or open surgery might not present differences in QoL, the previously described benefits of laparoscopic surgery like less blood loss, rapid intestinal recovery, shorter hospital stay and lower postoperative pain, could be taken more into account when selecting surgical approach for RC treatment.

Robotic surgery

Robotic surgery has emerged during the last decade with several studies reporting comparable safety and feasibility to laparoscopic surgery in RC surgery.⁷⁵ When compared to laparoscopic surgery, robotic surgery has the advantages of providing high-resolution 3D view, physiologic tremor reduction and articulating instruments.⁷⁶

Despite being rarely evaluated, some studies have suggested that robotic surgery could achieve better functional outcomes, however, this is still unclear, as more international multicenter randomized clinical trials are needed to determine these possible advantages.⁷⁵

New sphincter preserving techniques

Intersphincteric resection (ISR)

ISR was described in 1994 by Schiessel et al.⁷⁷ A transanal division of the rectum, with removal of entire or part of the internal anal sphincter, is performed after TME. This was only possible due to acceptable reduction of distal safety margins to 1 cm.¹³

This extreme sphincter preserving surgery has been used over the last decades for patients with very low RC, who otherwise had indication for APR with permanent colostomy.^{77,78}

In T1-3 tumors located between 3 and 3.5 cm from the anal verge, oncologic outcomes (both overall survival and 5-year disease-free survival) does not appear to be adversely affected by ISR, when compared to LAR or APR.⁷⁹⁻⁸¹

Functional outcome is a major concern in ISR. LARS is frequently observed after this technique; a 2012 meta-analysis of 8 studies stated that 11-63% of patients reported fecal incontinence and 30-86% reported total continence. However, authors stated that functional outcomes are incompletely reported and, when available, demonstrate wide variability.⁸¹

When compared to LAR, fecal continence is more frequently impaired after ISR. This is probably explained by a significant decrease of the postoperative sphincter resting pressure.⁸² An estimated 40-85% of anal resting pressure is contributed by internal anal sphincter, playing a major role in maintaining continence.⁸³ However, both techniques appear to result in comparable urgency and stool frequency.⁸⁴

Performing only a partial excision⁸² and the construction of a colonic j-pouch^{85,86} improves functional results, predominantly in the first year after surgery. Preoperative CRT significantly impairs functional outcomes.⁸⁷

Few works have addressed post-operative QoL after ISR and data is contradictory.⁸¹ Young patients with early stages

RC (T1-2), who do not require preoperative radiotherapy (PRT) and have good preoperative sphincter pressures, are the best candidates for ISR.^{37,78} Patients should be informed about the possible impairment of functional outcomes after ISR, particularly stool incontinence, and decide if dealing with such conditions is preferable to live with a permanent stoma.

Anterior Perineal PlanE For ultra low Anterior Resection of the rectum (APPEAR)

Williams et al.⁸⁸ initially described APPEAR technique in 2008 as an alternative method for very low rectal resection. It is indicated for RC within 2-5 cm from the anal verge.⁸⁹ This technique uses an abdominal and a perineal approach, in which a crescent shaped incision is made in the perineum, between the vagina or the scrotum and the anal verge. This allows a better access to the distal rectum for mobilization when compared to the ultra-low AR and a better preservation of the sphincter muscle when compared to ISR.³⁷

The pilot study⁸⁸ included 14 patients, 7 with rectal neoplasia. No local recurrences were reported, but one patient developed systemic disease. Seven patients (50%) presented anastomotic perineal fistulae and, at 1-year follow-up, 5 (36%) patients were not considered for ileostomy reversal. Three patients (21%) developed transient sexual dysfunction but no urological impairment was found. The authors also reported that after perineal dissection, patients with RC had a median Wexner continence score of 5 following ileostomy closure. No significant difference was observed in anorectal physiologic testing or QOL.

In a more recent study,⁹⁰ no local recurrence was reported and, after ostomy closure, the median Wexner score documented was 5.5.

More studies are needed for evaluation of this recent technique, since there is a lack of studies on oncologic and functional outcomes and QOL.

Transanal Total Mesorectal Excision (TaTME)

TaTME is a rectal natural orifice transluminal endoscopic surgery (NOTES). It consists of a transanal approach, usually with transabdominal assistance. TaTME allows a better mobilization of the distal rectum and sphincter preservation for difficult to reach distal RC, particularly in male patients with a narrow pelvis and/or obesity where the abdominal approach is challenging.^{91,92} Contrary to APPER technique, there is no need to create a separate perineal wound.

Evidence suggests that TaTME is feasible and safe. A recent systematic review of 26 studies reported adequate and reproducible oncologic outcomes, with CRM positivity being equal to those achieved in low AR and inferior to those achieved in APR.⁹³ A more recent multicenter prospective study of 56 patients⁹⁴ reported an average DRM of 10 mm and an average CRM of 8 mm, with R0 resection achieved in 53 patients (94.6%). Twenty six per cent of patients had postoperative complications. Functional outcome was only accessed by this study, with 28% (13) of patients reporting a fragmented stool pattern and evacuation difficulty. The reported median Wexner score for incontinence was 4 (3-12).

The transanal approach can be performed with either transanal endoscopic microsurgery (TEM) or transanal minimally invasive microsurgery (TAMIS). It appears that both techniques offer similar resection quality.^{95,96}

TaTME technique may be a promising alternative to conventional low AR, but there is a necessity of further studies to better evaluate oncological and functional outcomes, as well as the impact on QoL.

Local excision

In recent years, with improvements of screening programs leading to early diagnosis of RC, more attention is being paid to local excision as an attractive alternative to radical transabdominal resection. Local excision can be performed using conventional transanal excision, TEM or the more recently described TAMIS.

Compared to the newer techniques, conventional transanal excision has a reported lower resection quality and higher local recurrence and mortality.^{96,97}

In 1980, Buess et al.⁹⁸ developed TEM, a minimally invasive technique initially described for removal of adenomas that were endoscopically unresectable, using specific instruments and a rectoscope that offered high precision for transanal local excision.

TEM can achieve rectal preservation for benign polyps and early RC. It eliminates the need for a permanent colostomy and is associated with lower morbidity and impact on functional outcome and QoL than TME.⁹⁹⁻¹⁰¹ The safety and effectiveness of this technique is well documented, with several studies reporting survival and local recurrence comparable to radical surgery in well selected cases.^{99,102-105} Nevertheless, oncologic outcomes of this technique still remain a matter of study and debate.

TEM is an option to consider in patients with adenomas not manageable through endoscopy or with favorable early stage RC who want to avoid radical resection of the rectum and are willing to accept a possible higher risk of local recurrence.^{89,106,107} It can also be recommended for patients with advanced tumor unable to undergo radical surgery, as a palliative treatment.^{89,106,107} Presently, the eligible proportion of RC that could undergo local excision is small. This proportion may increase with the combined use of CRT in carefully selected cases.¹⁰⁶

There is a concern that a prolonged use of a 40 mm diameter operating scope could overstretch the anal sphincters and cause postoperative impairment in fecal continence. In fact, resting anal pressure is frequently reduced postoperatively, however this reduction is only temporary (likely to have resolved by 3 months) and it does not appear to change continence scores.^{100,108-110}

Several studies reported that TEM has a negative impact on anorectal function and QoL, with patients complaining of fecal incontinence, increased stool frequency, pain, flatulence, sore skin and embarrassment.^{111,112} These effects are also reported to be temporary. Homps et al.¹¹² analyzed 102 patients after TEM for RC and reported that functional outcome and QoL deterioration was worse after 6 weeks but returned to normal levels at 12 weeks. Similar results were found by Lezoche

et al.,¹¹¹ with bowel function returning to normal levels at 26 weeks.

Allaix et al.¹¹³ analyzed 93 patients who underwent TEM after 5 years follow-up and reported that anorectal function declined in the first 3 months, returning to preoperative levels 12 months after surgery. There was no difference in long-term continence and QoL scores before and after surgery.

In a 41 patients prospective study by Cataldo et al.,¹⁰⁸ no differences were found in FISI (fecal incontinence severity index) and FIOL (fecal incontinence QoL) scores, number of bowel movements per 24 h and urgency between preoperative and 6 weeks after surgery.

Doornebush et al.¹⁰⁰ and Planting et al.¹⁰¹ reported that fecal incontinence QoL was improved after surgery in patients with preoperative fecal incontinence. This could be due to improved fecal continence after tumor excision in patients that had diarrhea caused by a mucous producing tumor.

In the limited existing literature, it appears that QoL and anorectal function may be impaired after TEM surgery, with no long-term effect.

TEM has the disadvantage of a steep learning curve and elevated costs of specialized instrumentation.¹¹⁴ In 2009, TAMIS was developed as a feasible and low-cost alternative to TEM for local excision of rectal lesions. This new technique uses familiar laparoscopic instruments through a transanal multi-channel single-port, a simple and easy to use device with low equipment costs and minimal setup time.¹¹⁵

Both TEM and TAMIS have the same indications,^{95,116} however there is a lack of studies reporting functional and oncologic outcomes of TAMIS for early RC and adenomas resection. One study evaluating TAMIS functional outcome after resection of rectal polyps reported functional outcomes to be comparable to those obtained with TEM.¹¹⁷

Neoadjuvant therapy

Regardless of the increasing development of surgical techniques, it is now generally accepted as standard practice to use a multimodal approach in RC treatment in order to achieve optimal results. PRT significantly reduces local recurrence rates, improves local control and enables sphincter preservation in selected cases, however it does not appear to change overall survival.¹¹⁸⁻¹²⁰

Nevertheless, in addition to surgery, PRT is related with an increased incidence and severity of bowel dysfunction, with patients reporting more fecal incontinence, urgency, and higher stool frequency and evacuation disorders.^{56,118,121} It is also associated with a diminished resting and squeeze pressures in anorectal manometry.¹²²

Chen et al.¹²³ investigated health-related QoL in the Dutch TME trial and reported that addition of PRT to TME increases the risk of major LARS score from 35 to 56%, with major LARS being associated with reduced health related QoL. It has also been shown that PRT increases the risk of sexual and urinary dysfunction,¹²⁴ further compromising QoL.^{118,121}

When associated to local excision techniques, PRT therapy significantly increases postoperative morbidity.¹²⁵ In a Polish multicenter trial,¹²⁶ patients that undergone local excision and PRT had similar anorectal functional outcomes compared

to those observed in patients undergoing AR alone. The authors concluded that better functional outcomes achieved by local excision could be compromised by PRT.

The mechanisms that could contribute to the adverse impact of radiotherapy on anorectal function are not yet completely understood. Da Silva et al.¹²⁷ observed that pelvic irradiation increases collagen deposition and causes damage to internal anal sphincter myenteric plexus. These effects could be responsible to the decrease of maximum anal resting and squeeze pressures and reduction of neorectum capacity, contributing to anorectal dysfunction.^{128,129}

Presently, there is few available data on functional outcomes after preoperative CRT for RC treatment, however it appears that both PRC and preoperative CRT have similar anorectal functional results¹³⁰ and long term QoL.¹³¹

Both potential benefits and risk of increased anorectal dysfunction after PRT should be considered when choosing the most adequate treatment option.

“Wait-and-see policy”, the next step in rectal cancer treatment?

In select patients with complete tumor regression after CRT, adoption of a non-operative strategy could avoid a mutilating surgery and its sequelae, resulting in better functional outcomes and QoL.¹³²

Approximately 15–20% of patients with locally advanced RC have a pathological complete response (pCR) after neoadjuvant CRT, with no residual tumor observed in the resected specimen.¹³³ pCR is found in a subgroup of patients with clinical complete response (CCP), in which residual tumor is not clinically detectable. However, there is a poor correlation between clinical and pathological responses, making it difficult to determine which patients with CCP also has pCR.¹³⁴

Habr-Gama et al.¹³⁵ was the first to systematically evaluate the outcomes of a non-operative strategy in patients who achieved cCR after CRT. The results obtained in this series were impressive, with no cancer-related death reported in a mean 57 months follow-up, suggesting that these patients had similar survival rates to patients who had radical surgery after CRT and had pCR confirmation. Other studies have supported these results.^{136,137}

A more recent study by Habr-Gama et al.¹³⁸ reported a sustained complete response at 1 year in 57% of patients managed non-operatively after CRT and, after a mean 56 months follow-up, 51% of patients were free of recurrence.

Despite remaining controversial and in an experimental phase, results from the Habr-Gama series suggests that a group of selected patients with complete response after CRT could be managed with the wait-and-see approach, after evaluation of risks and benefits with the patient.

Conclusion

Over the last decades treatment for RC has improved with development of new surgical options and treatment modalities. While oncologic outcome remains the primary goal in RC treatment, functional outcomes and QoL are getting more attention. If similar oncological outcomes are achieved for RC

treatment options, functional outcomes and QoL play a major part when deciding for the most adequate treatment option for each patient.

Functional outcomes after low RC treatment are influenced by multiple factors, including patient and tumor characteristics, surgical technique, the use of radio or chemotherapy and the method and level of anastomosis.

Sphincter preserving surgery remains a priority and a mark of surgical quality RC treatment, in part due the general belief by both patients and surgeons that avoiding a permanent colostomy would result in better long term QoL. However, there is enough evidence to support that long-term QoL in patients with a permanent stoma are similar to those after sphincter preserving surgery for low RC. Patients should be aware that sphincter preserving surgery for low RC often result in poor functional outcomes that impairs QoL. Therefore, depending on patient's characteristics and personal preferences, decision should be individualized since not all patients may benefit from a sphincter preserving surgery “at any price”. Postoperative bowel disabilities should always be taken into account when surgery technique is selected and patients who are not willing to live with such potential limitations should consider undergoing a non-sphincter preserving surgery.

Local excision and non-operative treatments are starting to get more attention in carefully selected patients, in which the need of a permanent stoma and bowel dysfunction could be avoided, achieving better QoL. However, the “wait-and-see policy” still remains in an experimental phase, requiring more studies to better evaluate this approach.

Patients need to be clearly informed about all the treatment options for low RC and its potential outcomes, including the possibility of a non-surgical approach, so that patients could have more realistic expectations and be involved in the decision making process.

Conflicts of interest

The authors declare no conflicts of interest.

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