Oncology
and Radiotherapy©
18(9) 2024: 001-009 • REVIEW ARTICLE

Overview of the current standards in rectal carcinoma treatment

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ABSTRACT

Rectal carcinoma is a significant global health burden. Continue advancement in the diagnosis, staging and treatment is accounting for improve patient outcome. This paper provides an in-depth review of current standards in rectal carcinoma management. It covers epidemiology, diagnostic approaches, staging, multi-modal treatment approaches, surgical techniques, chemoradiotherapy and emerging therapeutic options. Furthermore, it includes role of personalized medicine, advances in surgical techniques and the importance of multidisciplinary team in improving the outcomes. The review concludes by emphasizing the need for continuing research to refine treatment protocols to increase patient survival and quality of life.

Keywords: rectal carcinomas , mesorectal fascia (MRF), Tumor, Node, and Metastasis (TNM), positron emission tomography (PET), Global Cancer Observatory (GLOBOCAN), submucous invasion (SMI)

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Word count: 8284 **Tables:** 00 **Figures:** 00 **References:** 101

Received: 19 September, 2024, Manuscript No. OAR-24-148357
Editor Assigned: 21 September, 2024, Pre-QC No. OAR-24-148357(PQ)
Reviewed: 04 October, 2024, QC No. OAR-24-148357(Q)
Revised: 11 October, 2024, Manuscript No. OAR-24-148357(R)
Published: 18 October, 2024, Invoice No. J-148357

INTRODUCTION

Rectal carcinoma is a malignant lesion in the rectum, which lies between an imaginary line at the level of sacral promontory to the upper border of anal canal. Colorectal Carcinoma (CRC) in broader terms accounts for significant part of global cancer-related morbidity and mortality. According to the Global Cancer Observatory (GLOBOCAN) 2020 figures, colorectal carcinoma ranks third in terms of incidence and second in cancer-related mortality, with rectal carcinoma alone accounts for one-third of cases [1, 2]. Rectal carcinoma management has undergone marked evolution over the last few decades, due to advancements in imaging, surgical techniques and adjuvant therapies. This results in improvement in CRC incidence and mortality [3]. The treatment goal is simply to achieve local control and prevent distant metastases, ensuring patient's overall quality of life.

LITERATURE REVIEW

Epidemiology and risk factors

There is global variation in the incidence of rectal carcinoma, with higher rates being observed in developed countries [4]. CRC incidence is rising among younger adults (15 years-49 years), while it is decreasing among older adults (50 years-74 years) in the United States [5]. The mortality from CRC reduced by about 35% from 1990 to 2007, and the current figures is about 50% low from the peak mortality rates [6, 7]. The causative risk factors include age, gender, genetic predisposition, and lifestyle factors like diet, smoking and lack of physical activity. Hereditary conditions like Familial Adenomatous Polyposis (FAP) and Lynch syndrome, as well as chronic inflammatory conditions like ulcerative colitis and Crohn's disease significantly increases the risk of developing rectal carcinoma.

Rectal carcinoma shows a characteristic natural history, with benign lesions such as rectal polyps acting as precursor of rectal carcinoma [8]. An increase in polyp size is associated with malignant potential, reported up to 40% in polyps>2 cm in size [9]. Most of these lesions are resectable endoscopically. If R0 resection is achieved, only endoscopic surveillance is required. If there is evidence of Submucous Invasion (SMI), surgical resection is recommended, because of the risk of lymph node involvement [10].

Diagnostic strategies

The early diagnosis of rectal cancer is critical for successful

management. Diagnostic evaluation typically begins with a thorough history and physical examination, followed by colonoscopy, which remains the gold standard for diagnosing rectal cancer. Total colonoscopy is important to evaluate for synchronous lesions or other pathologies of colorectum [3]. Early endoscopic finding of high-risk features for SMI (like poor differentiation, >1 mm of SMI, tumor budding, lymphovascular invasion, large size >2 cm) is critical for best management strategy [8].

Computed Tomography (CT) and Positron Emission Tomography (PET) are increasingly used in the assessment of distant metastases and recurrent disease. Advancements in molecular diagnostic tools including Circulating Tumor DNA (ctDNA) and Microsatellite Instability (MSI) testing have further refined the diagnostic workup, allowing for more personalized treatment strategies [11, 12].

Staging

Accurate staging is essential in guiding the appropriate management of rectal carcinoma. The Tumor Node and Metastasis (TNM) staging system, established by the American Joint Committee on Cancer (AJCC), are universally used to classify the extent of disease. Staging involves assessing the depth of Tumor invasion (T), regional lymph Node involvement (N), and the presence of distant Metastases (M).

High-resolution Endorectal Ultrasonography (ERUS) and pelvic Magnetic Resonance Imaging (MRI) are integral in the local staging of the disease, providing detailed information about tumor invasion and involvement of adjacent structures [8, 13]. ERUS is superior to MRI in defining the depth of invasion of muscularis mucosa and differentiating T1 from T2 tumors (specificity 86% vs. 69%, p=0.02) [14]. However, ERUS can't identify mesorectal fascia and Circumferential Resection Margin (CRM), which are required to in assessing the need for neoadjuvant chemotherapy [15]. Endo-Rectal Ultrasound (ERUS) is particularly useful for staging early-stage tumors, while CT scans of the chest, abdomen, and pelvis are necessary to detect distant metastases. Lung metastases reported in about 4%-9% patients, whereas liver metastases reported in 20%-34% patients [16, 17].

Magnetic Resonance Imaging (MRI) is the preferred imaging modality for local staging, offering superior soft tissue contrast and enabling precise assessment of the Circumferential Resection Margin (CRM) and Mesorectal Fascia (MRF) involvement. MRI gives adequate information of local staging (T stage and CRM) and clear delineation of anatomic location as regard to sphincter involvement [13, 18-23]. CRM by MRI measured the closest distance from mesorectal fascia; a clear CRM is defined as >1 mm from mesorectal fascia and levator muscles, whereas involved CRM is within 1 mm of mesorectal fascia or levator muscle [24]. Nodal staging is more challenging, as size alone does not give information of the presence of malignant cells [25, 26]. A meta-analysis found that both ERUS and MRI have similar sensitivities and specifities for lymph node evalutation (ERUS 67% and 78%; MRI 66% and 76%) [27]. However, ERUS is operator dependent and should only be used to evaluate pelvis if MRI is contraindicated like in patients with pacemaker. Pelvic CT is not recommended for staging, as it has lower sensitivity for both CRM status and lymph node involvement [27].

MULTIMODAL TREATMENT APPROACHES

The management of rectal cancer is essentially multidisciplinary, involving a combination of surgery, chemotherapy, and radiation therapy. The choice of treatment is influenced by the stage of the disease, the patient's overall health, and the goal of treatment, whether curative or palliative [28]. Further, if rectal excision is feasible, early consultation with an enterostomal therapist is recommended for preoperative site marking and educating patients [3].

Surgical techniques

Surgery forms the main modality of curative rectal carcinoma treatment. Different operative choices are available (endo-anal, open, laparoscopic and robotic), determined by tumor's location, stage, patient's anatomy and surgeon's ability [3, 29, 30]. The gold standard surgical procedure for mid and low rectal carcinomas is Total Meso-Rectal Excision (TME), which aims to achieve clear resection margin with removal of entire mesorectum, which is considered critical to minimize local recurrence [3, 13]. Surgery should aim not only to curative resection, but also to preserve autonomic plexus and anal sphincter [29].

For early rectal carcinomas (T1-T2, N0), local excision or Trans-Anal Endoscopic Microsurgery (TEMS) is an option especially in patients who are not fit for more extensive surgery. However, there is higher risk of local recurrence as compared to TME.

Minimally invasive surgery, such as laparoscopic and robotic TME, are increasingly favored due to the potential benefits in reducing postoperative morbidity and enhancing recovery. Evidence from COLOR II trial and ROLARR trial confirms the oncological safety and efficacy of these minimally invasive procedures, with outcomes comparable to that of open surgery in terms of Disease-Free Survival (DFS) and Overall Survival (OS) [31, 32].

Endoscopic approaches

Endoscopic Mucosal Resection (EMR) is an option for lesions confined to the mucosal layer Tumor in-situ (TIS). It involves lifting of the lesion by local injection of physiological saline into underlying mucosa. The lesion is then dealt with a snare and resected with electrocautery. Lesions <2 cm can be removed en-bloc, whereas larger lesions in piecemeal. A variation of the technique uses cold EMR instead of electrocautery [33].

Endoscopic full-thickness resection using a full-thickness resection device allows deep resection of lesions that are not amenable to EMR [34]. Endoscopic Submucosal Dissection (ESD) is another technique where incision is given around the lesion, followed by submucosal injection and dissection to remove the lesion en bloc. ESD has a lower recurrence rate compared to EMR (0.9-2% vs. 12.2-14%) [35, 36].

Transanal approaches

It provides an opportunity to avoid open surgery for early rectal carcinoma (T1, N0) [3]. Transanal Minimally Invasive Surgery (TAMIS) is like single-port laparoscopic surgery through the open anal sphincter complex to locally excise low- to mid-rectal tumors. However, it lacks the Total Mesorectal Excision (TME) component. This serves a good approach for tumors less than 3 cm, having well or moderately differentiated histopathology without lymphovascular or perineural invasion and minimal submucosal

invasion [37, 38]. Subsequently, if pathologic features show positive margins, lymphovascular invasion, poor differentiation or submucosal invasion, a more radical resection is recommended [39].

Transanal approach can also be combined with transabdominal approach (laparoscopic or robotic) for TME (taTME) [8, 29]. The morbidity and oncologic outcomes of taTME is similar to laparoscopic TME [40, 41]. The advantages of local procedures include minimal morbidity and mortality, as well as rapid postoperative recovery [42]. The limitation (disadvantage) is the lack of nodal clearance.

Open surgery

Traditional open surgery is still considered the standard operation for resection of rectal carcinoma. It involves a large abdominal incision to access the rectum and surrounding tissues. Total Mesorectal Excision (TME) consists of precise excision of rectum and the surrounding mesorectal fat containing lymph nodes, which is important to minimize local recurrence. Open approach gives direct visualization and access to the operative field, making it easier to manage complex anatomy and unexpected intraoperative challenges. It is technically feasible, as for surgeons in resource-limited settings, open surgery remains the only viable option, as it does not need any specialized instrument or extensive training. It provides good results in terms of oncological outcomes, with evidence from long-term data supporting its efficacy in achieving clear margins and reducing local recurrence rates. However, it is associated with higher postoperative morbidity including increased pain, longer hospital stays and slower recovery as compared to minimally invasive techniques. It needs larger incision to gain access to operative field, with consequent increased risk of wound infections and other wound-related complications.

Sphincter preserving procedures are preferable but it's not possible in all cases; however, NAT can help downstage tumor and sphincter preserving procedure may become possible [3]. For lesions in upper two-thirds of rectum, Low Anterior Resection (LAR) is recommended extending upto 4 cm, 5 cm below the distal edge of tumor, with Total Mesorectal Excision (TME), followed by colorectal anastomosis or colostomy [3, 29]. Ultra-Low Anterior Resection (ULAR) with distal resection margin of only 1 cm is recently supported by different studies; in combination with multimodality treatment, it provides a good option for sphincter preservation [43-46]. Abdominoperineal Resection (APR) with TME is recommended when tumor directly involves the anal sphincter or levator muscles. It consists of en bloc resection of rectosigmoid, rectum and anus, with TME and perianal soft tissues, followed by creation of colostomy [47, 48]. Intersphincteric Resection (ISR) consists of dissection between the internal and external sphincter to resect the rectum en bloc with internal anal sphincter and anal mucosa [46, 49]. It gives oncologically acceptable outcome for low rectal carcinoma, similar to APR [49, 50]. Partial Excision of Levator Ani Muscle (PELM) technique with ISR and coloanal anastomosis provides another option to preserve anal sphincter in low rectal carcinoma, with comparable outcomes [51, 52]. For lower two-third rectal carcinoma, Pelvic Lateral Lymph Node Dissection (PLND) is suggested to decrease the recurrence and improve survival [53, 54]. However, PLND is consider mandatory according to Japanese guideline, when lower border of tumor is located distal to peritoneal reflection and the tumor has invaded beyond muscularis propria [55].

Laparoscopic surgery

It involves creation of multiple small ports (via small incisions) through which camera and specialized instruments are inserted to perform the resection. It aims to reduce the operative trauma associated with large wound of open surgery, while maintaining the oncological principles of TME. It is associated with reduced postoperative pain, shorter hospital stays, faster recuperation as compared to open surgery [13]. The laparoscopic camera provides magnified view of the operative field, thus enhancing visualization of pelvic anatomy with more precise dissection of tissues [29]. There is also less intraoperative blood loss as compared to open surgery [13]. It offers comparable oncological outcomes to open surgery in terms of Disease-Free Survival (DFS) and Overall Survival (OS) as reported in large randomized controlled trials, such as COLOR II trial, CLASICC trial and COREAN trial [13, 56-58]. Local recurrence rates are also comparable, suggesting that laparoscopic TME is oncologically safe.

However, there are also some disadvantages. Laparoscopic instrument manipulation and tissue dissection is technically more challenging in the confined space of the pelvis. This accounts for longer operative times and a steep learning curve for surgeons [30]. Another concern is the risk of conversion to open surgery, especially in cases of large tumors, obesity or significant adhesions/infiltrations. In case of conversion, the benefits of laparoscopic surgery are practically lost, with potentially higher morbidity and mortality. Significant training and experience are required in order to perform successful laparoscopic colo-rectal surgery. Surgeons must be equipped with advanced laparoscopic techniques, which may not be available in the low-resource settings.

Robotic-assisted surgery

It offered the latest advancement in minimally invasive rectal cancer surgery. It provides the surgeon with a high-resolution, three-dimensional view of the operative field and wristed instruments that gives greater dexterity and precision than traditional laparoscopic instruments [29]. The surgeon controls the robotic arms from a console, in a relax sitting without suffering undue fatigue, and perform necessary instrument handling and tissue dissection with precise movements within the confined pelvic space. The articulated instruments of robotic system differ from laparoscopic instrument as it can rotate and bend like a hyperactive wrist, thus allowing more precise dissection, especially in the narrow pelvis. The ergonomic design of the robotic console decreases surgeon's fatigue, which is important during long and complex procedures [30]. There are lower conversion rates of robotic-assisted surgery to open surgery as compared to laparoscopic, which is of value in challenging cases like obese patients or bulky tumors [13]. The oncological outcomes are similar to both open and laparoscopic approaches in terms of resection margin status, lymph node harvest and local recurrence rates [59-61]. The Robotic vs. Laparoscopic Resection for Rectal Cancer (ROLARR) trial, a multicenter RCT, found no significant differences in DFS and OS between robotic and laparoscopic surgery, though the robotic surgery had lower conversion rates [31].

The drawback of robotic surgery is that the installation of robotic system and its maintenance is associated with a high cost, which is

difficult in low-resource settings. The high cost includes the initial investment in the robotic platform, disposable instruments and the longer operative time, thus increasing the overall healthcare costs. Hence, robotic surgery is limited to institutions in high- and middle-income countries, limiting widespread adoption of this technology. Although the robotic system design is intuitive, there is still a learning curve to master robotic surgery techniques, especially for surgeons transitioning from open or laparoscopic surgery.

Comparative outcomes and considerations

Oncological outcomes:

- All three approaches (open, laparoscopic, and robotic) have shown comparable outcomes in terms of achieving negative margins and adequate lymph node harvest, which are critical for oncological success. Studies such as the COLOR II and ROLARR trials have provided evidence that minimally invasive approaches do not compromise oncological principles [31, 56].

Patient recovery and quality of life:

- Surgical innovations and availability of anastomotic stapler devices have lowered the anastomotic leak rates. Use of Indocyanine Green (ICG) fluorescence angiography quickly evaluate blood supply at anastomotic site. Further, inspecting stapled rings like doughnuts and air leak test with intraoperative colonoscopy can confirm the integrity of anastomosis [29, 30].
- Both laparoscopic and robotic-assisted surgeries are associated with improved short-term recovery outcomes compared to open surgery, including less postoperative pain, faster return of bowel function, and shorter hospital stays. These benefits can translate into an earlier return to normal activities and work, which is a significant consideration for patient quality of life.
- Laparoscopic and robotic approaches may also offer long-term functional outcomes, especially in terms of bowel and urinary functions. However, these advantages need to be weighed against the technical difficulties and the availability of surgical expertise.

Technical and economic considerations:

- The choice between these three approaches often depends on the availability of resources and surgeon's expertise. Surgeons well experienced in a particular approach are likely to achieve best outcomes with that approach.
- A significant barrier to widespread adoption of robotic-assisted surgery remains the higher cost. Though there are clear advantages of reduced conversion rates and improved ergonomics, the economic burden must be carefully considered by the healthcare systems.

CHEMORADIOTHERAPY

It plays an important role in the management of rectal carcinoma, especially in the neo adjuvant and adjuvant settings. The main objective is to reduce tumor size and eradicate micro-metastases, thereby enhancing the likelihood of a complete surgical resection with clear margins.

Neoadjuvant Chemoradiotherapy (NaCRT)

Neo adjuvant therapy administered before surgical resection, has become a cornerstone in the management of locally advanced rectal cancer (stages II and III, T3-T4 or N+). Its concurrent use has demonstrated an increased rate of tumor down staging, improved chances of achieving a Pathological Complete Response (pCR) and reduced risk of local recurrence [62]. The most commonly used chemotherapeutic regimen include 5-Fluorouracil (5-FU) or capecitabine.

Long-Course Chemoradiotherapy (LCRT) consist of radiotherapy (45 cGy to 50.4 cGy) over a 5 weeks–6 weeks period with simultaneous chemotherapy, and a 6 weeks–10 weeks period of rest before TME. This strategy offers tumor-free surgical margins and higher rates of colorectal anastomosis in low rectal tumors [63]. Short-Course Radiotherapy (SCRT) consisting of 25 Gy in 5 fractions with TME in the following 7 days, has shown significant reduction in local relapse [13, 64-66]. Both NaCRT strategies have shown similar oncological results in terms of overall survival, local recurrence and surgical complications [67-69]. However, radiotherapy is associated with radiation-induced injury and hematologic toxicities [70].

However, systemic recurrence still happens with 25% patients developing distant metastasis during follow up [71-73]. Addition of systemic chemotherapy as a part of NaCRT can diminish systemic recurrence rates [13]. Total Neoadjuvant Therapy (TNT) consists of either SCRT or LCRT with full adjuvant dose of chemotherapy is promising [74-76]. Systemic chemotherapy has been shown to improve Pathological Complete Response (pCR) to NaCRT [77]. The CAO/ARO/AIO-04 German trial showed higher rates of pCR in locally advanced rectal carcinoma when oxaliplatin was added to fluorouracil-based chemotherapy [78, 79]. OPRA trial randomized patients to induction or consolidation TNT, followed by surgery or WW depending on response; higher rates of organ preservation was found in the consolidation arm (58% vs. 43%; p=0.01), with no difference in disease-free survival or distant-metastasis-free survival [80].

Several studies, including the German CAO/ARO/AIO-94 trial, have demonstrated the superiority of neo adjuvant chemoradiotherapy over postoperative adjuvant therapy, with lower local recurrence rates and improved sphincter functions [78, 81]. However, its impact on overall survival remains unclear, as distant metastasis accounts for a significant cause of mortality in these patients.

The optimal timing of surgery following neo adjuvant therapy is also an area of active research. Traditionally, surgery is performed 6 weeks-8 weeks after the completion of chemoradiotherapy; however, recent studies suggest that extending the interval may lead to higher rates of Pathological Complete Response (pCR) and potentially better outcomes [82]. The total duration of perioperative therapy (including NAT and adjuvant) should not exceed 6 months [3].

Following NaCRT, about 50%-60% patients are down-staged, with approximately 20% showing Pathological Complete Response (pCR) [83, 84]. The response after NaCRT is assessed using Digital Rectal Exam (DRE), MRI and endoscopy, with a combined accuracy of 98% to predict absence of tumor [3, 85]. Digital Rectal Exam (DRE) of a Clinical Complete Response

(cCR) should either be normal or minor mucosal abnormalities such as soft scar. Endoscopic features of Clinical Complete Response (cCR) include a flat white scar, telangiectasia and absence of ulcer and nodularity [86]. MRI features of Clinical Complete Response (cCR) include a scar not thicker than rectal wall, no visible lymph nodes and lack of apparent diffusion coefficient map [86]. FDG-PET/CT can also be used to determine response to NaCRT [87].

Watch and Wait (WW) is an organ preservation strategy in selected patients that experience a cCR after neo adjuvant therapy [3, 29, 46, 62]. Markers that can predict the risk of relapse may help in selection of patients who are safe candidates for WW [88]. TP53 and KRAS mutations present in about 70% and 40% rectal tumors, respectively, are associated with poor response to NaCRT [89, 90]. Conversely, mismatch repair deficiency gene is associated with good response to NaCRT [91].

Total Neoadjuvant Therapy (TNT)

It represents an emerging treatment strategy that consists of administering systemic chemotherapy before or after neoadjuvant chemoradiotherapy, but prior to surgery. The objective is to treat micro-metastasis earlier in the treatment path, thereby reducing the risk of distant metastases [46].

The RAPIDO and PRODIGE 23 trials have given sound evidence for the use of TNT in patients with high-risk locally advanced rectal carcinoma [92, 93]. These studies demonstrated improved DFS and higher Pathological Complete Response (pCR) rate with TNT as compared to standard neo adjuvant chemoradiotherapy alone. It also allows a longer interval between chemoradiotherapy and surgery, potentially leading to higher Pathological Complete Response (pCR) rates and improved outcomes.

Adjuvant Chemoradiotherapy (ACRT)

After surgical resection of stage II and stage III rectal carcinoma, adjuvant chemotherapy is recommended especially if these patients have not received neoadjuvant chemotherapy, and are found to have high-risk histopathological features postoperatively, such as positive margin, T4 tumor or extensive nodal involvement. The main objective is to reduce the risk of local recurrence and improve overall survival. Several studies, including INT 0114 trial, has evaluated its role in improving local control in high-risk patients. However, the benefits in terms of overall survival remains uncertain, and decision of its use should be individualized based on patient's risk factors and response to neo adjuvant treatment [94, 95].

It should be administered as soon as the patient is medically fit; a meta-analysis found each 4-weeks delay in chemotherapy result in 14% decrease in OS [96]. The preferred regimen usually is FOLFOX (Fluorouracil, Leucovorin and Oxaliplatin) or CAPEOX (Capecitabine and Oxaliplatin) in high-risk patients [3]. The addition of oxaliplatin has shown improved DFS, especially in high-risk patients [81, 97].

The use of adjuvant radiotherapy is limited to cases with high risk of local recurrence, such as positive margin or locally advanced carcinoma. The SEER analysis of stage III rectal carcinoma found that postoperative radiotherapy is associated with significant reduction in the risk for cancer death [98]. Postoperative chemoradiotherapy is also recommended when stage I rectal carcinoma is upstaged to stage II/III after histopathologic examination [3]. The QUASAR trial have mentioned the potential benefits of adjuvant chemoradiotherapy in improving survival, though the decision of its use must be individualized based on patient's risk profile [99].

EMERGING THERAPIES AND PERSONALIZED MEDICINE

The use of personalized medicine is a new dimension in the management of rectal carcinoma, where treatment decisions are guided by the molecular profile of tumor and patient's individual characteristics. Several molecular markers and emerging therapies are being investigated to achieve improve outcomes.

Immunotherapy

It has revolutionized the treatment of many cancers, and its role in rectal carcinoma is an area of active research. The immune checkpoint inhibitors, such as pembrolizumab and nivolumab, has shown good results in patients with Deficient Mismatch Repair (dMMR) or Microsatellite Instability-High (MSI-H) rectal carcinomas [100]. However, these patients represent only a small subset of rectal carcinoma cases.

The KEYNOTE-177 trial has shown the efficacy of pembrolizumab as a first-line treatment for MSI-H/dMMR metastatic colorectal carcinoma, with improved progression-free survival compared to standard chemotherapy [101]. However, its application in non-metastatic rectal carcinoma is still under investigation, while there is a need of future research to explore its potential role in the neo adjuvant and adjuvant settings.

Targeted therapy

These inhibit specific molecular pathways involved in cancer growth and progression, are being evaluated for rectal carcinoma treatment. Agents targeting Epidermal Growth Factor Receptor (EGFR) and Vascular Endothelial Growth Factor (VEGF) pathways, such as cetuximab, panitumumab and bevacizumab, have shown efficacy in metastatic colorectal carcinoma. However, their role in non-metastatic rectal carcinoma remains to be fully established [13].

Further, identification of actionable mutations, such as Kirsten Rat Sarcoma (KRAS), Neuroblastoma RAS (NRAS) and BRAF, through molecular profiling allows for the selection of targeted therapies in metastatic disease [101]. The presence of these mutations can guide treatment decisions by predicting resistance to Epidermal Growth Factor Receptor (EGFR) inhibitors. However, targeted therapies have not yet become standard in the management of localized rectal carcinoma, but nevertheless providing a direction for future research to expand their use in selected group of patients [3].

Circulating tumor DNA (ctDNA) and liquid biopsy

Analysis of circulating tumor DNA (ctDNA) (liquid biopsy) is an emerging tool in the management of rectal carcinoma. Its detection in the blood of patients with rectal carcinoma provides real-time insights into tumor biology, treatment response and minimal residual disease. Its role as a biomarker to guide treatment decisions, such as the need of adjuvant therapy or monitoring of recurrence, is an area of further research.

The potential of ctDNA in predicting recurrence and guiding

postoperative management in colorectal carcinoma is promising [88]. Its ability to help detect minimal residual disease could allow for more personalized treatment strategies, avoiding unnecessary chemotherapy in patients who are likely to be cured by surgery alone.

Multidisciplinary care

Rectal carcinoma management requires a multidisciplinary approach involving colorectal surgeons, medical oncologists, radiation oncologists, radiologists, pathologists and other healthcare professionals to ensure an effective delivery of optimum care avoiding undue morbidity and mortality [8, 30].

Establishing a multidisciplinary tumor board in high-volume center is likely to improve the planning of treatment, adherence to clinical guidelines and patient outcome. These boards facilitate discussions on complex cases, allowing integration of different perspectives and expertise in the decision-making process. Its role is especially important in the management of locally advanced and recurrent rectal carcinoma, where treatment decisions are quite challenging and require careful consideration [30].

QUALITY OF LIFE AND SURVIVORSHIP

The impact of rectal carcinoma treatment on Quality Of Life (QOL) and long-term survivorship is a critical consideration in the management. The goal of treatment is not only to achieve cure but also to preserve function and minimize the impact of treatment-related side effects.

Sphincter preservation

It is one of the top considerations in rectal cancer surgery, especially in patients with low rectal tumors. Sphincter-preserving surgery, such as Low Anterior Resection (LAR) with TME is the preferred choice if feasible, as it avoids the need for a permanent colostomy. However, the decision of sphincter preservation must be balanced against the risk of compromising oncological outcomes.

The role of neoadjuvant chemoradiotherapy in down staging tumors and facilitating sphincter preservation has been well established. In selected patients, a "watch-and-wait" approach, where surgery is deferred in favor of close surveillance following a complete clinical response to neoadjuvant therapy, is being explored as a means of avoiding surgery and preserving function.

Management of treatment-related toxicities

Treatment-related toxicities, including bowel dysfunction, urinary dysfunction, sexual dysfunction, and neuropathy, can significantly impact the Quality Of Life (QOL) of rectal carcinoma survivors. The management of these toxicities requires a multidisciplinary approach, with input from specialists such as gastroenterologists, urologists, and physical therapists.

Long-term follow-up and supportive care are essential for managing chronic side effects and addressing the psychological and social challenges faced by rectal carcinoma survivors. The development of survivorship care plans, which outline the follow-up schedule, surveillance strategies, and management of late effects, is an important aspect of post-treatment care.

CONCLUSION

The management of rectal cancer has evolved significantly over the past few decades, driven by advances in diagnostic techniques, surgical approaches, and adjuvant therapies. The current standards of care emphasize a multidisciplinary approach, incorporating neo adjuvant chemoradiotherapy, TME, and adjuvant therapy in the management of locally advanced disease. Emerging therapies, including immunotherapy and targeted therapy, hold promise for further improving outcomes, particularly in patients with advanced or high-risk disease.

Ultimately, the decision on the surgical approach should be made within the context of a multidisciplinary team, taking into account the patient's preferences, the surgeon's experience, and the resources available. Ongoing research and clinical trials will continue to refine these techniques and their application in rectal cancer treatment. The goal is not to achieve oncological control but also to preserve function and maintain Quality Of Life (QOL) for survivors.

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