

Treatment of Rectal Cancer

Subjects: Surgery

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Rectal cancer poses a substantial healthcare challenge, emphasizing the critical need for effective treatment strategies. Among the various approaches available, surgical intervention, notably total mesorectal excision (TME), stands as the gold standard for rectal cancer management, consistently delivering exceptional oncological results. In certain instances of early-stage disease, endoscopic treatments and transanal resection techniques may be viable options, offering a more conservative approach. Additionally, for cases characterized by locally advanced tumors, radiotherapy has demonstrated significant benefits in augmenting the overall treatment efficacy.

Keywords: TME ; TaTME ; TEM ; radiotherapy ; Rectal cancer ; Risk Factors

1. Introduction

Rectal cancer is a significant global health issue, targeting the rectum and comprising approximately ten percent of all identified cancer cases ^[1]. Its incidence, complex management, and resource utilization contribute to the substantial healthcare challenge to healthcare systems worldwide. As rectal cancer is becoming more common, it implies the need for effective procedures and sufficient resources to meet the needs of people who are afflicted. Rectal cancer can represent a challenge for existing curative treatment options due to its location within the bony pelvis and proximity to important organs including the uterus, bladder, and prostate ^[2]. It also often manifests at an advanced stage, making care more difficult and decreasing the likelihood of a favorable course of therapy ^[3]. Late-stage diagnosis can occur due to various factors, including the absence of early symptoms or delayed medical attention. Consequently, rectal cancer may progress, necessitating more aggressive treatment approaches and potentially affecting patient outcomes. In addition to the impact caused by the disease, rectal cancer significantly affects both the well-being and chances of survival for individuals affected by it. Rectal bleeding, altered bladder habits, stomach discomfort, and unintentional weight loss are only a few symptoms that may seriously affect everyday life and general wellbeing ^[4]. This further intensifies the challenging experience for individuals undergoing cancer treatment. In the management of rectal cancer, several main treatment modalities are commonly employed. Surgical treatment plays a pivotal role, and the most frequently performed surgeries for rectal cancer include TME ^[5]. TME is a meticulous surgical technique that involves the complete removal of the rectum along with the surrounding lymph nodes, ensuring clear margins and minimizing the risk of local recurrence. Ultimately, radiation plays a crucial role in the management of rectal cancer, frequently employed alongside surgical intervention to improve local disease management and reduce the likelihood of relapse ^[6].

Surgery, radiation therapy, and chemotherapy are the presently used conventional treatments for rectal cancer, with surgery as the cornerstone of treatment. The recommended standard surgical technique is TME, which consists in the removal of the entire rectum along with the surrounding lymph nodes and fatty tissue to achieve clear margins ^{[7][8]}. Another treatment modality is endoscopic treatment, which involves the use of specialized instruments to remove or treat early-stage rectal tumors. Transanal resection is a procedure specifically designed for the management of rectal tumors located close to the anus. Transanal resection techniques are becoming increasingly popular for treating rectal conditions. These include TaTME (transanal total mesorectal excision), TME (total mesorectal excision), and TEM (transanal endoscopic microsurgery). They provide several potential benefits. TaTME provides enhanced visualization and access to the rectal area through the anus, allowing for precise dissection and removal of tumors ^[9]. It aims to achieve complete mesorectal excision. Additionally, the minimally invasive nature of TaTME reduces surgical trauma, leading to less postoperative pain, reduced hospital stays, and improved recovery ^[10]. TME improves oncological outcomes and reduces the risk of local recurrence ^[11]. This approach has demonstrated lower morbidity and mortality rates compared to older surgical techniques, improving long-term survival for rectal cancer patients. TEM offers a minimally invasive approach for the removal of rectal tumors. Using specialized instruments and an endoscope, TEM allows for precise tumor excision through the anus ^[12]. TEM is commonly employed for early-stage rectal tumors confined to the rectal wall, offering a less invasive alternative to extensive surgeries like TME ^[12].

Rectal cancer can be influenced by various determinants. It tends to favor patients with earlier-stage diagnoses as opposed to those who present an advanced-stage diagnosis during screening ^[13]. As per recent advancements within healthcare fields, supporting early-detection measures and introducing more effective procedures, such as treatment methods, has led to a marked increase in survival rates for rectal cancer cases over time. Several factors can impact one's chances of recovery from rectal cancer. The factors affecting cancer prognosis are varied and intricate. Tumor stage, response to therapy, genetic mutations, and the patient's overall health all contribute to outcome prediction.

2. Pathology

Rectal cancer develops in the rectum. The disease occurs when malignant cells grow uncontrollably from the tissue lining the inside of this area ^[12]. Initially, normal cells in the rectal lining undergo mutations, forming polyps that can eventually turn into malignant tumors over time ^[14]. Key genes responsible for regulating cell division, such as APC, KRAS, and TP53, are often mutated during this process ^[14]. If left untreated, rectal cancer can progress locally, invading nearby tissues and structures, and can also spread to regional lymph nodes and distant organs through the bloodstream or lymphatic system.

3. Epidemiology of Rectal Cancer

The incidence of rectal cancer shows significant geographic and demographic disparities. Western countries generally have a higher incidence than Asian countries ^[15]. Possible factors contributing to this disparity could be the existing differences in diet and lifestyle ^[15]. The number of new instances of colon cancer is expected to rise up to 106,970 by 2023, with rectal cancer accounting for around 46,050 of those new diagnoses in the United States. This surprising statistic underscores colo-rectal cancer as the third most prevalent cancer worldwide ^[13], emphasizing its significant impact on global health. Rectal cancer affects 15 to 25 people per 100,000 individuals yearly within the European Union. Unfortunately, a third of those affected pass away due to this disease annually ^[16]. Rectal cancer often affects people over 70 years, but this threshold is projected to rise. The estimated yearly death rate is 4–10 individuals per a hundred thousand people. However, significant variance persists among five-year survival statistics depending on the distinctiveness observed across underlying conditions. For localized cancer (confined to the rectum), it may be around 90% ^[13]. But if it spreads to lymph nodes or other organs, these rates decrease significantly for localized rectal cancer. Over the last two decades, stages II–III rectal cancer has had a five-year OS rate of 65% ^[17]. For stage IV of rectal cancer, the 5-year relative survival rate is approximately 17%, according to the American Cancer Society ^[18]. Although the prevalence of rectal cancer has decreased due to widespread screening measures facilitating the detection and management of premalignant lesions ^[19], recent studies have indicated a rise in its occurrence among younger individuals. Furthermore, it is projected that the incidence of rectal cancer specifically will rise by 124.2% for patients aged 20–34 years by 2030 ^[20]. In regions like Hong Kong, colon and rectal cancers show distinguishing patterns in incidence. This implies that these two cancer forms have different underlying causes ^[21]. A gap exists among individuals under 50 years due to the rising prevalence of rectal cancer in younger people ^[6]. In addition, compared to Caucasians, Black people have a higher incidence of rectal cancer ^[2]. Survival outcomes among younger patients with locally advanced rectal cancer also demonstrate racial disparities favoring the Caucasians ^[22]. Additionally, rectal cancer incidence shows temporal trends characterized by a general decline but an increase in young adult population countries such as Australia, Canada, and the United States ^[23].

4. Risk Factors

Rectal cancer can stem from various risk factors, out of which the advanced age is a significant one. Colorectal cancer risk is significantly associated with dietary habits characterized by excessive consumption of processed foods and red meats, inadequate fiber intake, and a deficiency in fruits and vegetables ^[24]. A hazard may also come from a sedentary lifestyle or harmful habits like obesity, smoking, or binge drinking ^{[25][26]}. Research uncovered a dose–response connection which suggested that moderate alcohol intake reduces the overall risk, while excessive consumption of alcohol raises the risk for colorectal cancer ^[15].

5. Diagnosis

The diagnosis involves multiple steps. Initially, methods like barium enema or CT colonography may be employed, but a colonoscopy is ultimately necessary to obtain a tissue sample for biopsy ^[14]. While flexible sigmoidoscopy can help reduce CRC mortality, it cannot fully replace a complete diagnostic colonoscopy ^[14]. In cases where colonoscopy is incomplete, capsule endoscopy has been approved by the FDA (Food and Drug Administration) as an alternative ^[14].

Although routine laboratory tests are useful, they do not provide a definitive diagnosis [14]. CT scans can assess the tumor and lymph node stages and detect distant metastases with good sensitivity [14]. While PET scanning is not commonly used in preoperative staging, a biopsy of suspicious metastatic sites is still necessary to confirm the diagnosis [14].

6. Factors Influencing the Choice of Treatment Modality

When considering the choice of treatment modality, several factors come into play. Patient characteristics, such as age, overall health status, and individual preferences, must be taken into account. For instance, younger patients without significant comorbidities may tolerate more invasive surgical interventions, whereas older patients with underlying health issues may benefit from less invasive approaches like endoscopic procedures or transanal resections [27].

Tumor characteristics, including stage, location, and histological type, also play a pivotal role in selecting the appropriate treatment modality. Early-stage tumors confined to the mucosa or submucosa may be amenable to endoscopic treatment or transanal resection, while locally advanced tumors often necessitate a multimodal approach involving surgical resection, radiation therapy, and chemotherapy [28]. Multidisciplinary discussions involving surgeons, gastroenterologists, oncologists, and radiologists are paramount to determining the most suitable treatment strategy based on tumor characteristics. Rectal cancer treatments have progressed, yielding improved results for patients. Despite this, there are an array of limitations. One prevalent limitation is the invasiveness of surgical interventions like TME. It also yields potential complications such as urinary or sexual dysfunction or worsened bowel obstruction [25]. In addition, certain individuals cannot have surgery due to health complications or poor overall wellbeing. Another point worth mentioning is how radioactive and chemotherapeutic elements can lead to toxicity affecting various body parts, leading to several side effects. Such effects may include stomach disorders like nausea, vomiting, diarrhea, blisters followed by skin irritations, and blood abnormalities [26].

Healthcare system factors further influence the choice of treatment modality for rectal cancer. The availability of resources, expertise, and multidisciplinary teams can impact the range of treatment options. Specialized centers with experienced surgeons may offer a broader array of surgical techniques and superior outcomes. Access to advanced imaging modalities and radiation oncology services also plays a role in the consideration of radiotherapy. Geographical location and the overall healthcare infrastructure can affect patient access to specific treatments. Collaborative efforts among healthcare providers, regional networks, and referral centers are crucial to ensure that patients receive the most appropriate and optimal treatment considering the available healthcare system factors. Each treatment modality comes with its own advantages, limitations, and applications based on cancer stage (Table 1). Surgical resection is considered the standard but can impact quality of life. Endoscopic techniques are less invasive, except they but have higher recurrence risks. Transanal resection is advantageous for organ preservation, but is inefficient for larger tumors. Radiotherapy improves outcomes for advanced cases. Nevertheless, it carries long-term toxicity risks. Overall, treatment decisions require balancing all constituents, such as tumor factors, patient characteristics, and available resources.

Table 1. Rectal cancer treatment modalities: a literature matrix synthesis.

Procedure	Efficacy	Side Effects	Applicability (Stages)	Quality of Life Impact
TEM (total endoscopic microsurgery)	Effective for early-stage tumors and rectal adenomas, with good local control and low recurrence rates [29][30][31].	Low rates of clinically relevant postoperative morbidity [32].	Most effective for early-stage rectal cancer, particularly Tis and T1 N0 M0 tumors [33][34]. Used for higher-stage cancers after neoadjuvant therapy has been explored [35].	Reduced surgical trauma, fewer complications, and rapid postoperative recovery [36].
taTME (transanal total mesorectal excision)	Offers better visualization of the distal rectum and ability to perform deep pelvic dissection [37][38]. Lower conversion rate compared to laparoscopic TME [9].	Associated with a significant rate of intraoperative complications during the learning curve [39].	Primarily indicated for mid- and low-rectal cancer.	Initially decreases quality of life scores, but most scores return to baseline values after 6 months [40].
TME (total mesorectal excision)	High efficacy in providing improved local control and survival in early-stage and locally advanced rectal cancer (LARC) [41].	Significant morbidity, bowel dysfunction, sexual and urinary dysfunction [42][43][44].	Most effective in LARC [42].	Major long-term side effects include major low-anterior resection syndrome (LARS), which can significantly impact the quality of life [45].

Procedure	Efficacy	Side Effects	Applicability (Stages)	Quality of Life Impact
Radiotherapy	Effective as a palliative treatment for symptomatic rectal cancer ^[46] . Improves outcomes when combined with chemotherapy for locally advanced rectal cancer ^{[47][48][49]} .	Anal and urinary dysfunction, cardiovascular morbidity, and radiation proctopathy ^{[50][51]} .	Standard of care for locally advanced rectal cancer. Short-term preoperative radiotherapy reduces toxicity and prevents local relapse ^{[52][53]} . Adjuvant radiotherapy improves cause-specific survival in certain stages ^[54] .	Long-term effects on anorectal function, leading to bowel frequency, fecal incontinence, and other functional problems ^{[55][56]} .

LARC—locally advanced rectal cancer.

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