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ORIGINAL RESEARCH

How Is Rectal Cancer Managed: a Survey Exploring Current Practice Patterns in Canada

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Abstract

Introduction Locally advanced rectal cancers are most often treated with neoadjuvant chemoradiation followed by surgical resection. However, there are differing opinions surrounding management of rectal cancer, including a lack of consensus on the optimal time interval between chemoradiation and surgery, and the management of patients with complete clinical response following neoadjuvant therapy. This study seeks to summarize management trends for rectal cancer among a sample of Canadian surgeons.

Methods A 14-question survey was distributed to surgeons across Canada managing rectal cancer. Surgeons were identified from the membership lists of the Canadian Association of General Surgeons and the Canadian Society of Colon and Rectal Surgeons. Web-based questionnaires were distributed by email.

Results A total of 115 surgeons were emailed the survey with a response rate of 38.4%. Approximately 50% of surgeon responders had been in practice for more than 10 years, with the majority practicing in academic centers. Half were considered high-volume rectal cancer surgeons with more than 20 cases per year. All surgeons used magnetic resonance imaging for staging of rectal cancer, but only 50% presented all rectal cancer cases at multidisciplinary cancer conferences. The majority of surgeons applied minimally invasive techniques for surgical resection, including the utilization of transanal endoscopic microsurgery (TEMs) and transanal minimally invasive surgery (TAMIS); however, only a small fraction performed high-volume transanal total mesorectal excision (taTME). Regarding the management of complete clinical response (cCR) following neoadjuvant chemoradiation, less than 5% chose the watch and wait management strategy for all patients and 40% did not use it at all. The majority of surgeons reported waiting between eight and 10 weeks between chemoradiation and surgery, and 40% made that decision regardless of patient or tumor factors.

Conclusion The majority of surveyed surgeons use MRI for pelvic staging and discuss rectal cancer cases at multidisciplinary cancer conference. Many are using minimally invasive techniques; however, the use of taTME is not yet widespread. Surgeons currently favor longer intervals from neoadjuvant chemoradiation to surgery, and the management strategy for patients with complete clinical response remains controversial. Great variability exists in rectal cancer management, thus presenting an opportunity for improvements by adopting standardization and centralization of rectal cancer management.

Keywords Rectal cancer · Neoadjuvant therapy · Chemoradiation · Time interval · Surgery · Complete clinical response · Current practices

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Introduction

Colorectal cancer is the second most diagnosed cancer in Canada, and is the second leading cause of cancer-related death for men, and third for women [1]. Approximately 25% of all colorectal cancer corresponds to rectal cancer, which has notable differences from colon cancer in terms of presentation, demographics, metabolic and genetic pathways, and prognosis [2].

Rectal cancer surgery has evolved dramatically during the last few decades, from the conventional blunt dissection, to the more precise sharp dissection known as total mesorectal excision (TME). This was originally described by professor Heald et al. [3] and has significantly impacted on both oncologic and functional outcomes [4]. Most recently, less invasive transanal techniques have evolved. These include transanal endoscopic microsurgery (TEMS) and transanal minimally invasive surgery (TAMIS), which provide resection for complex polyps and early rectal cancers without requiring formal oncologic resection, but at the cost of foregoing regional lymph node staging. These techniques are also being used to assess for complete pathologic response (pCR) in patients with complete clinical response (cCR) after neoadjuvant chemoradiation for locally advanced rectal cancers. Some surgeons are employing the 'watch and wait' strategy for patients with cCR, where surgical resection is avoided and close surveillance is employed. However, radical resection remains the gold standard for all patients following neoadjuvant therapy [5, 6]. The novel technique of transanal total mesorectal excision (taTME) has emerged most recently but has proven to be challenging to learn and implement [7, 8]. The available evidence suggests improved visualization compared to laparoscopy and comparable oncologic outcomes, in spite of it being in its early phase [9]. Significant interest to learn the technique has been demonstrated by surgeons globally [10].

Improved preoperative imaging with endorectal ultrasound (ERUS) and magnetic resonance imaging (MRI) has also allowed for advances in rectal cancer care through more precise staging of patients. The MERCURY study group has been instrumental in this advancement by demonstrating that high-resolution MRI accurately predicts the presence of threatened or compromised circumferential margins, therefore providing improved selection of candidates for neoadjuvant therapy [11].

The role for chemoradiation in the management of rectal cancer has been clearly proven in the literature. The benefits of preoperative radiation combined with TME were demonstrated with improved rates of local recurrence in the Dutch Trial [12], and both improved local recurrence and overall survival in the Swedish trial [13, 14]. The German trial established the advantages of neoadjuvant chemoradiation over adjuvant therapy [15, 16]. In France, the Lyon R90-01 study demonstrated improved clinical response and tumor downstaging when extending the interval from neoadjuvant radiation to surgery from 2 weeks to 6 to 8 weeks [17]. Subsequently, the 6 to 8-week interval became the standard management of rectal cancer. Although long-term follow-up from this group was unable to show an advantage of the 6 to 8-week waiting interval over the 2-week waiting interval for local recurrence or survival [18], surgeons have continuously challenged the 6 to 8-week dogma, and different intervals have been studied without reaching a conclusion on the optimal timing for surgery after neoadjuvant chemoradiation [19].

Currently, there are no specific recommendations in guidelines regarding the time interval between neoadjuvant chemoradiation and surgery. For instance, the American Society of Clinical Oncology (ASCO) has not established any specific guidance on the subject. The National Comprehensive Cancer Network (NCCN) addresses the issue broadly, providing a time range of five to 12 weeks for surgery after neoadjuvant therapy [6]. As such, the topic remains controversial, and currently there are many different intervals applied by surgeons globally.

The purpose of this study was to assess and understand the current trends in practice patterns for rectal cancer management among a representative sample of Canadian surgeons. The main questions included the optimal time interval between neoadjuvant chemoradiation and surgery, the role of transanal approaches for rectal cancer, management of clinical complete response, and the use of laparoscopy versus laparotomy in rectal cancer cases.

Methods

A 14-question survey was distributed to the surgeon members of the Canadian Society of Colon and Rectal Surgeons (CSCRS) (http://cscrs.ca/colon-and-rectal-surgeons-directory/). Surgeons were excluded if they were no longer practicing. A web-based questionnaire was generated using SurveyMonkey™ (SurveyMonkey, Palo Alto, California, USA) and distributed by email. Survey reminders were sent bi-weekly for 60 days. The survey was designed to require less than 10 min to complete, and included questions regarding timing for surgery following neoadjuvant chemoradiation and the reasoning for timing, surgeon experience, volumes and practice settings, use of MRI and ERUS, and surgical approach. Average response rates were calculated.

High-volume surgeons were considered those that performed more than 20 of a certain type of surgery per year. This number was selected based on publications defining high-volume surgeons for rectal cancer surgery ranging from 10 to 40 cases for TME [20–25], TEMS/TAMIS [26], and taTME [27, 28]. The survey design did not allow for the identification of responders' practice locations.

Ethics approval for the study was obtained through the University of Liverpool Ethics committee. All responses were anonymous. No participant or patient integrity, or disclosure of sensitive information, was deemed to be at risk. Permission was obtained from the CSCRS to distribute the survey using their membership list.

Results

A total of 115 surgeons were emailed the survey. Forty-four (38.3%) completed surveys were returned. An additional three (2.6%) responded indicating that they were no longer practicing, resulting in a total response rate of 40.9%. The majority of the participants had significant surgical experience, with over 80% reporting practicing for at least 5 years (Table 1). 86.4% of the participants worked at academic institutions, and 52.3% performed more than 20 mesorectal dissections per year.

The majority of surgeon responders (75.0%) performed TEMs or TAMIS, with 22.7% being considered high-volume surgeons for these cases (Fig. 1). A significant proportion of surgeons claimed to perform taTME (47.7%), but only four surgeons (9.1%) qualified as high-volume surgeons (> 20 cases per year).

Pelvic MRI was used by all surgeons for staging of rectal cancer (Table 2). Some surgeons (18.6%) used both ERUS and MRI routinely, but no surgeons used ERUS exclusively. Exactly half of participant surgeons presented all of their rectal cancer patients at multidisciplinary cancer conference (MCC), and the other half presented a select number of cases. The vast majority of surgeons (59.1%) primarily used laparoscopic surgery, whereas only 29.6% used laparotomy. Interestingly, 73.2% felt that there was literature that suggested that minimally invasive surgery was not equivalent to open surgery. Many responders commented that their opinions were based on the ACOSOG Z6051 randomized control trial by Fleshman et al., which reported that for patients with stage II/III rectal cancers, laparoscopic resection compared to open was not non-inferior for pathologic outcomes [29], and the ALACART randomized control trial by Stevenson et al., which reported that for patients with T1-T3 rectal cancers, laparoscopic surgery was not non-inferior to open surgery [30].

There was wide variation in the answers regarding common practice for patients with clinical complete response (cCR) (Fig. 2). 4.6% reported that they always used the 'watch and wait' strategy, whereas 40.9% reported that they never use it. The most common response (43.2%) indicated that the highest proportion of surgeons were being selective while using the watch and wait strategy for patients believed to have cCR.

Over half of surgeons (56.8%) were waiting between eight to 10 weeks from neoadjuvant chemoradiation to surgery, with 22.7% waiting a shorter and more traditional interval of 6 to 8 weeks, and 18.2% waiting over 10 weeks (Fig. 3). 41.9% commented that they always wait the same amount of time before operating, with 25.6% reporting that they consider the size of the tumor when choosing a time interval. Only 11.6% based their decision on previous teaching, suggesting that there is no current gold standard.

Table 1 Surgeon demographics ($N = 44$)

Characteristics	Response, *n* (%)
Years of practice	
> 15	11 (25.0)
10–15	9 (20.4)
5–10	16 (36.4)
1–5	7 (15.7)
In-training	1 (2.3)
Practice type	
Academic	32 (72.7)
Community	6 (13.6)
Both	6 (13.6)
Yearly volume of advance rectal cancer	
> 20	23 (52.3)
10–20	13 (29.6)
5–10	4 (9.1)
< 5	4 (9.1)

Discussion

The majority of surgeons included in this study worked at academic centers, thus greatly under representing practices in community hospitals. Only surgeons registered on the Canadian Society of Colon and Rectal Surgeons Directory were sent this survey, which explains the small number of surgeons included in the study. The strong representation of academic colorectal surgeons is likely explained by the limited distribution of colon and rectal surgeons across Canada, as specialist colon and rectal surgeons almost exclusively practice in a few large cities per province, and the remainder of colon and rectal surgery is performed by community general surgeons (not included in this survey). Our geographical characteristics and vast landmass represent an immense challenge for patient access to specialist care. It has been previously mentioned that training, experience, type of center, and volume significantly influence outcomes in rectal cancer care [22–25]. Most of the responders had significant experience; however, only half were considered high-volume rectal cancer surgeons.

All survey participants were using MRI as their main modality for pelvic staging, with a significant minority using both MRI and ERUS as part of routine staging. Rectal cancer staging is often performed with a combination of techniques including carcinoembryonic antigen (CEA), computerized tomography (CT) scan of the chest, abdomen, and pelvis, MRI of the pelvis, and ERUS. Our results demonstrated that all surveyed surgeons were using MRI for pelvic staging, but there was more variability and less use of ERUS. The American Society of Colon and Rectal Surgeons (ASCRS)

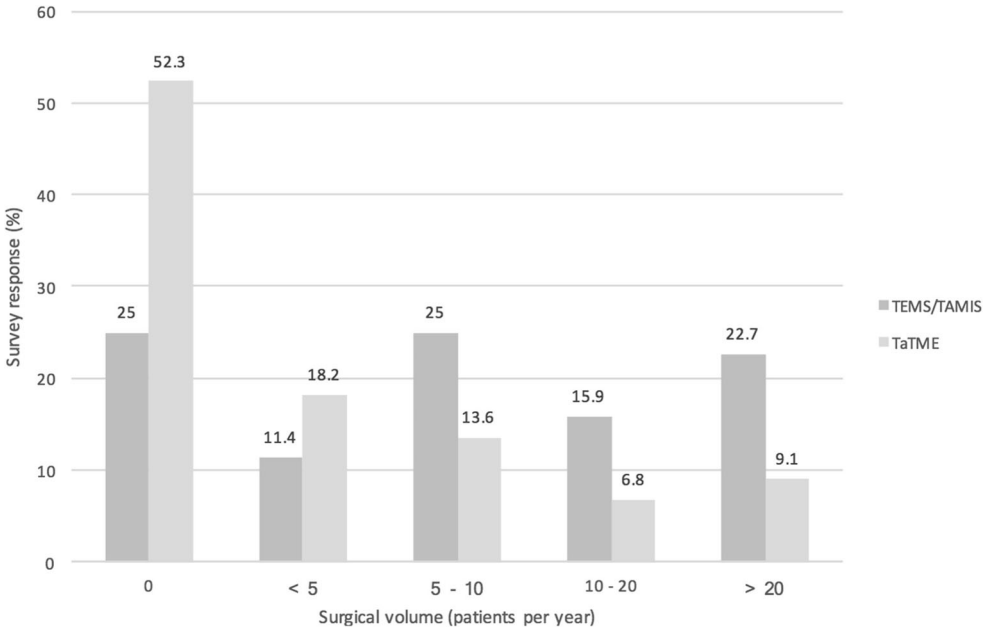

Fig. 1 Practice volumes for transanal endoscopic microsurgery (TEMS), transanal minimally invasive surgery (TAMIS), and transanal total mesorectal excision (TaTME)

gives a strong recommendation for use of dedicated MRI or ERUS for rectal cancer staging, and states that they are complementary methods of staging based on their advantages and disadvantages [5]. For instance, ERUS is more accurate at assessing T1/T2 tumors, whereas MRI is more accurate for T3/4 tumors, obstructing lesions, N stage, assessing circumferential resection margin (CRM), and response to neoadjuvant therapy [31–35]. The NCCN prefers staging with MRI over ERUS [6]. The Cancer Care Ontario (CCO) guidelines mandate the use of high-resolution MRI for staging of all rectal cancers as per the MERCURY group standards [11, 36]. Guidelines from New Zealand and Great Britain also recommend MRI for all patients with rectal cancer [37, 38]. In comparison to our results, a survey performed in New Zealand reported similar use of MRI with 86.1% of responders routinely using MRI for suspected T3 rectal cancers [39]. Also of interest, a survey from the UK reported that only 49% of responders offered preoperative MRI to all rectal cancer patients, with 51% reporting lack of access to MRI as their reason for not using it more regularly [40]. Our results are representative of a significant sample of Canadian colon and rectal surgeons, and support good use of appropriate staging with MRI and ERUS in Canada.

Table 2 Staging and treatment of rectal cancer ($N = 44$)

	Response, *n* (%)
Staging imaging	
Pelvic magnetic resonance imaging (MRI) alone	35 (81.4)
Endorectal ultrasound (ERUS) alone	0 (0.0)
MRI and ERUS in combination	8 (18.6)
Presentation at multidisciplinary cancer conference	
All patients	22 (50.0)
Select patients	22 (50.0)
No patients	0 (0.0)
Most common surgical approach	
Laparotomy	13 (29.6)
Laparoscopic	26 (59.1)
Robotic	1 (2.3)
Transanal total mesorectal excision (TaTME)	4 (9.1)
Awareness of literature against laparoscopic approach	
Aware	30 (73.2)
Unaware	11 (26.8)

All surveyed surgeons presented a proportion of their rectal cancer cases at MCCs. However, there appeared to be significant variability and subjectivity regarding the choice of patients that were presented. Currently, there is no national consensus for staging and management of rectal cancer in Canada. In the University of Toronto Surgical Oncology Manual, it is recommended to discuss patients with ≥ T3 tumors, ≥ N1 status, recurrent rectal cancers, metastatic disease, ambiguous T2/T3 staging, suspected close CRM, residual tumor, or adverse features following local excision, stage IV disease, underlying inflammatory bowel disease, familial cancer syndromes, and patients with significant co-morbidities that are unable to tolerate some forms of treatment at MCCs [41]. CCO gives strong recommendations to present all patients with rectal cancer at MCCs [36]. In both New Zealand and Great Britain, the guidelines also recommend discussing all rectal cancer patients in a multidisciplinary setting [37, 38]. A survey performed in the UK reported substantially higher rates of MCC discussion for all rectal cancer patients

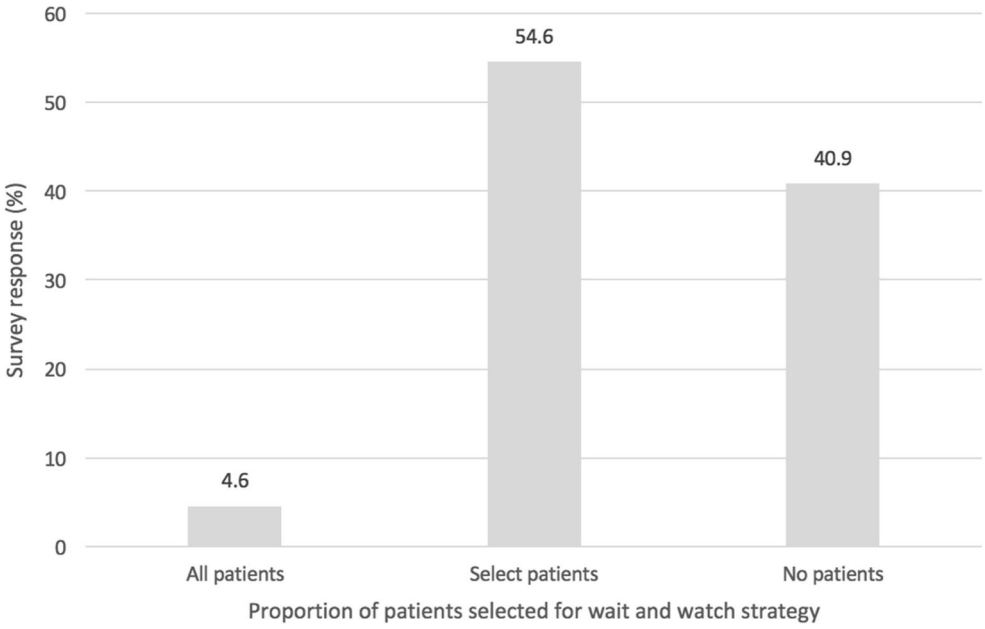

Fig. 2 Practices patterns for wait and watch management strategy for clinical complete response (cCR) following neoadjuvant chemoradiation

compared to our survey, with 95% of surgeon responders presenting all cases at MCCs [40]. Due to variability of care, there is a global movement towards standardization and centralization of the management of rectal cancer, for example in the UK [42] and by the OSTRiCh consortium in the USA [21], with the goal to improve both oncologic and functional patient outcomes. A Canadian taskforce has been assembled, and Canadian rectal cancer staging and management guidelines will soon be available.

The majority of surgeon survey responders were noted to utilize laparoscopy, although minimally invasive surgery has encountered significant resistance from many colorectal and gastrointestinal surgeons with resistance being more evident in rectal cancer surgery. Almost two-thirds of surgeon responders reported that they use laparoscopy most commonly for the treatment of rectal cancer. Those that preferred the open technique reported the lack of evidence to support a minimally invasive approach and brought up the recent results of the ACOSOG Z6051 and ALACART trials. The North American ACOSOG Z6051 trial included 240 patients that were randomized to laparoscopic resection and 222 to open resection for stage II and III rectal cancers after completing neoadjuvant chemoradiation [29]. Non-inferiority criteria were unable to be attained for the laparoscopic group with regards to pathologic outcomes including circumferential radial margin greater than 1 mm, distal margin without tumor, and completeness of total mesorectal excision. In the Australian ALACART trial, a randomized control trial with many similarities to the ACOSOG Z6051, non-inferiority was also unable to be demonstrated for surgical outcomes with

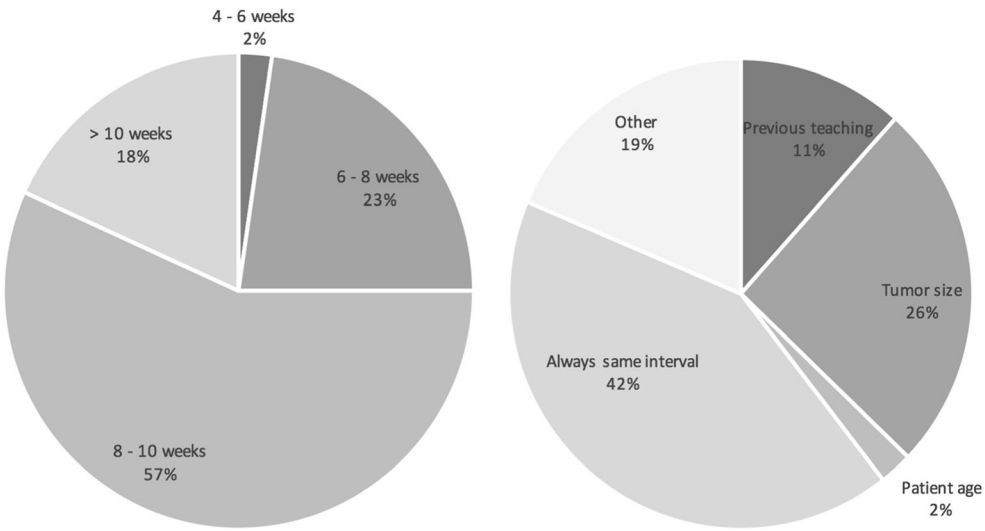

Fig. 3 Surgeon selected time intervals between neoadjuvant chemoradiation and surgery, and reason for selection

laparoscopy compared to open for T1–3 rectal cancers [30]. However, caution should be taken when applying the results of these studies to practice as their methodology has been criticized [43, 44]. Long-term outcomes have yet to be published for these two studies; however, other earlier studies have reported similar recurrence and survival outcomes for laparoscopy and laparotomy. For example, the COREAN trial randomized 340 patients with rectal cancer to either laparoscopy or laparotomy and reported similar disease-free survival for both cohorts [45]. Similarly, the 3-year outcomes for the COLOR II trial demonstrated that locoregional recurrence and disease-free and overall survival were similar for both laparoscopic and open cohorts [46]. Due to the non-inferiority demonstrated by long-term outcomes in these randomized trials, both NCCN and ASCRS state that laparoscopy can be offered to patients for resection of rectal cancer if the surgeon possesses appropriate minimally invasive training for proctectomy with TME [5, 6].

Compared to laparoscopy, there is even less use of the minimally invasive techniques of TEMs, TAMIS, and taTME for rectal cancer. This was reflected in our survey with only 22% (10 surgeons) performing high-volume TEMs and/or TAMIS, and only 9% (four surgeons) performing high-volume taTME. Despite the low number of high-volume surgeons using taTME, we were surprised at the high proportion of surgeons that reported using taTME in their practice. This may be a result of the large number of academic colorectal surgeons in our study, with the possibility of low-volume surgeons trying to incorporate the new technique into their practice, due to the recent attempt at dissemination of this challenging approach [8, 27]. Currently, there are no official guidelines on how these technologies should be safely implemented and disseminated [10, 47]. NCCN guidelines mention TEMs only briefly to state that it may be used for treatment of well to moderately differentiated T1 lesions for similar indications for transanal excision [6], and the other techniques are not discussed. Further prospective trials are required to better report on outcomes associated with these techniques for rectal cancer.

The most commonly chosen survey response for time interval from neoadjuvant chemoradiation to surgery was eight to 10 weeks, with the majority always using the same interval despite patient or tumor factors. Significant controversy surrounds the optimal time interval between completion of neoadjuvant chemoradiation and surgery for locally advanced rectal cancer. The NCCN gives a wide recommendation of five to 12 weeks [6], thus leaving this decision up to surgeons' discretions. The results of the Lyon R90-01 randomized trial [17] lead to a 6 to 8-week interval becoming the paradigm for surgical management of rectal cancer. A comparison of a 2-week interval versus a 6 to 8-week interval in that study favored the longer interval with tumor response rates of 72 vs 53% ($p = 0.007$), and pathological response rates of 26 vs 10% ($p = 0.005$). Since that time, surgeons and oncologists have been lengthening time intervals in hopes of achieving improved tumor downstaging and downsizing. In our survey, only 23% of surgeons continued to wait the previously accepted 6 to 8 weeks, whereas 57% waited eight to 10 weeks, and 18% waited over 10 weeks. Currently, in the literature, there are a total of 14 publications including two RCTs [48, 49], two prospective studies [50, 51], and 10 retrospective reviews [52–61], that compare different wait time intervals from neoadjuvant chemoradiation to surgery for rectal cancer. These include intervals as short as 6 weeks [52] to as long as 12 weeks [49]. Three of these publications reported significant improvements in disease-free survival [53, 54, 59], and two reported decreased rates of local recurrence with longer intervals [55, 57]. All except four of the publications report a significantly higher number of patients obtaining pCR with longer time intervals [49, 50, 53–59, 61]. Despite the number of studies assessing time interval between neoadjuvant chemoradiation and surgery, an optimal time interval for maximal tumor response has yet to be clarified [19].

Great variability was seen in the use of the watch and wait strategy for patients with cCR on the survey. Partial and complete pathologic response following neoadjuvant chemoradiation is time-dependent outcomes that have proven difficult to predict [62]. pCR occurs in 15–27% of patients and is associated with improved disease-free survival, overall survival, and decreased local recurrence [63]. The 'watch and wait' strategy, which consists of closely scheduled surveillance for patients with cCR, and surgical resection for progression or recurrence of disease, is a current topic of debate in the surgical and oncology fields. In our survey, 40% of surgeons reported that they do not use the watch and wait strategy for any patients, with less than 5% using this strategy for all patients with cCR. Current guidelines from NCCN and ASCRS do not support the use of the watch and wait strategy for localized rectal cancer, and recommend radical resection despite the appearance of cCR [5, 6]. Concern remains regarding the inaccuracy of physical exam and imaging modalities in predicting patients with pCR [64]. A randomized trial is required to better guide recommendations.

Survey responses demonstrate that substantial variation exists in management strategies for rectal cancer despite available evidence-based guidelines. Controversy exists regarding possible better outcomes with centralization and standardization of rectal cancer care to high-volume centers [65] . This is especially relevant with the growing complexity of rectal cancer management. An interdisciplinary approach is of critical importance to ensure best oncologic and functional outcomes for patients. Further trials including long-term outcomes are required to better address many areas of rectal cancer management that were questioned in this survey, followed by updates to current guidelines.

Limitations

The main limitation of this study was the low response rate of 38.3%, which could introduce nonresponse bias and affect both reliability and validity of the survey results. Another possible limitation was response bias (also called survey bias) that is inherent in all surveys and results from survey responders giving answers that they feel are acceptable to their colleagues.

The poor generalizability of our results to non-academic centers is also a major limitation, due to the large number of survey participants practicing at academic centers and the small number of colon and rectal surgeons practicing in Canada. We were unable to ascertain the distribution of surgeon survey responders by province, and unable to include many community general surgeons practicing colon and rectal surgery. This introduces significant bias to our results with regard to the distribution of care. However, we believe that the survey results are representative of practice patterns by academic colon and rectal surgeons in Canada.

Conclusion

The majority of the surveyed colon and rectal surgeons were using MRI for pelvic staging of rectal cancer, as well as discussing selected cases at multidisciplinary cancer conference. Most were utilizing minimally invasive techniques in the management of rectal cancer, with some surgeons incorporating novel approaches such as TEMS, TAMIS, and taTME. Unanswered questions remain surrounding the management for cCR and the optimal time interval after neoadjuvant chemoradiation. Great variability in management exists, thus presenting an opportunity for improvements by adopting standardization and centralization of rectal cancer management.

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