

Do Patients Consider Preoperative Chemoradiation for Primary Rectal Cancer Worthwhile?

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BACKGROUND: The objective of this study was to elicit future patients' preferences for preoperative chemoradiation (pre-CRT) for rectal cancer to determine whether patients' preferences are consistent with current treatment guidelines. **METHODS:** During a standardized interview, the treatment protocol, risks, benefits, and long-term outcomes associated with 1) surgery alone (SA) and 2) pre-CRT followed by surgery (CR + S) were described to healthy individuals, and a threshold task was performed. Each participant was asked which treatment option they would prefer when the risk of local recurrence was set initially at 15% for both options. If the participant indicated SA (which was expected), then the risk of local recurrence for CR + S was lowered systematically until the participant's preference changed from SA to CR + S. This threshold point represented the risk of local recurrence for pre-CRT that the participant would require before they would choose treatment with pre-CRT. **RESULTS:** Fifty individuals participated in the study, and the majority were well educated. Twenty-seven of 50 participants (54%) required a risk of local recurrence with CR + S of $\leq 5\%$ (ie, equivalent to an absolute risk reduction $\geq 10\%$) before they would choose treatment with pre-CRT. Regression analysis did not identify any variables that were predictive of the participants' preferences. **CONCLUSIONS:** Participants seemed to highly value functional outcomes and seemed willing to accept a higher risk of local recurrence to achieve this. Therefore, developers of future guidelines may need to downgrade the use of pre-CRT for all patients with stage II/III tumors from a guideline to an option. *Cancer* 2011;117:2853-62. © 2011 American Cancer Society.

KEYWORDS: rectal cancer, preoperative chemoradiation, patient preferences, threshold technique, clinical policy.

Although it has been demonstrated that preoperative radiation therapy (pre-RT) and preoperative chemoradiotherapy (pre-CRT) significantly decrease the risk of local recurrence after surgery for rectal cancer, these treatment protocols do not affect survival and lead to poorer functional outcomes (ie, bowel and sexual function) compared with surgery alone¹⁻⁷ (Table 1). Therefore, treatment decision making for pre-RT and pre-CRT is challenging because of the inherent tradeoffs between oncologic outcome in terms of local recurrence and functional outcomes in terms of bowel and sexual function.

More recently, studies from North America and Europe have reported improved outcomes for patients with intermediate-risk tumors.^{8,9} On the basis of this evidence, experts in North America have suggested that a more selective approach to the use of pre-CRT likely is indicated.¹⁰⁻¹² Gunderson et al pooled the results from 5 North American randomized controlled trials (n = 3971 patients) and observed that the 5-year disease-free survival and local recurrence rates for patients who had T2N1 and T3N0 or intermediate-risk tumors were not only similar but had improved outcomes relative to patients who had T2N2 and T3N1 or higher risk tumors⁹ (Table 2). Merkel et al analyzed the data from

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Table 1. Local Recurrence Rates and Bowel Function Results From the Dutch and Polish Rectal Trials

Variable	Dutch Trial Results ^a		Polish Trial Results ^b	
	Nonirradiated	Irradiated	Pre-RT	Pre-CRT
Risk of local recurrence, %	13.7 ^c	3.7	9.0 ^d	14.2
Bowel movements/d	Mean, 3.02	Mean, 3.69	Median, 4	Median, 5
Poor control over bowel movements, %	5 ^e	14	7	6
Use of pads, %	33	56	39	41
Activities outside the home, %	40	52	—	—
Daily activities, work and household, %	22	34	—	—

Pre-RT indicates preoperative radiation therapy; Pre-CRT, preoperative chemoradiotherapy.

^aSee Kapiteijn 2001,¹ Peeters 2007,² and Peeters 2005.³

^bSee Bujki 2006⁶ and Pietrzak 2007.⁷

^cThe local recurrence rate at 5 years for tumors located 5.1 cm to 10 cm from the anal verge.

^dThe local recurrence rate at 4 years.

^eIncontinence was reported OS at least once daily after anterior resection.

Table 2. Five-Year Outcomes Associated With Intermediate and High-Risk Rectal Cancers

Disease Stage	OS	DFS	LR	DM
Intermediate (%)				
T3N0	75	65	9	20
T1-T2N1	79	73	7	15
High risk (%)				
T1-T2N2	67	58	8	31
T3N1	60	48	12	37
T3N2	44	36	14	47

OS indicates overall survival; DFS, disease-free survival; LR, local recurrence; DM, distant metastases; T, tumor classification; N, lymph node status

^aThis table was adapted from Gunderson 2004.⁹

Table 3. Five-Year Outcomes Associated With T3 Tumors Based on the Extramural Depth of Invasion^a

Outcome	pT2	pT3a ^b	pT3b-pT3d ^c	pT4
Local recurrence (%)				
Any pN	9	10.4	26.3	33.4
pN0	7.8	5.5	15.4	10
pN1-pN2	13.4	17.1	34	55.9
Cancer-related survival (%)				
Any pN	91.2	85.4	54.1	48.7
pN0	93.6	91.2	77.2	80.4
pN1-pN2	82.8	77.8	40.3	21

pT indicates pathologic tumor classification; pN, pathologic lymph node status.

^aThis table was reproduced from Merkel 2001.⁸

^bpT3a tumors had <5 mm extramural depth of invasion.

^cpT3b-pT3d tumors had >5 mm extramural depth of invasion.

853 patients with rectal cancer from a population-based cancer registry and demonstrated that the survival and local recurrence rates were similar for T2 tumors and T3a tumors (ie, <5 mm extramural depth of invasion). In addition, the outcomes for these patients with T2 and T3a tumors were better relative to the outcomes of patients with T3b, T3c, T3d (ie, >5 mm extramural depth of invasion), and T4 tumors⁸ (Table 3). Based on these studies, a more selective approach to the choice of pre-CRT is used in the United Kingdom in which patients who have T3 tumors with <5 mm of extramural depth of invasion with either N0 or N1 lymph node status proceed directly to surgery provided the circumferential resection margin is not threatened.¹³⁻¹⁶

Furthermore, it seems that physicians are not the only group supportive of a more selective approach to the use of pre-CRT. In a recent survey of 152 lay individuals, 86% (range, 73%-93%) chose not to receive neoadjuvant therapy when they were provided with the specific outcomes from each of 5 randomized controlled trials that

assessed the effectiveness of pre-CRT and pre-RT.^{1,5,17-20} Furthermore, although the participants were aware of the 10% survival difference demonstrated in the Swedish trial, only 24% chose to receive pre-RT.

Despite these issues, guidelines published in both the United States and Canada recommend pre-CRT for *all* patients with stage II and stage III rectal cancer and fail to incorporate the patients' treatment preferences into the final treatment recommendation.^{21,22} Therefore, the objectives of the current study were 1) to elicit future patients' preferences for pre-CRT based on the best available evidence and 2) to identify the demographic and clinical variables that predict patients' preferences for pre-CRT.

MATERIALS AND METHODS

Before the study started, ethics approval was obtained from the research ethics board at each of the participating centers.

Setting and Patient Sample

Healthy individuals who were at average risk for colorectal cancer and who attended outpatient screening colonoscopy clinics at 2 academic teaching centers in a large city were contacted by telephone and invited to participate in the study. Patients were excluded from the study if they were younger age 50 years, if they had received previous treatment for colorectal cancer, if they were not able to speak or understand English, or if they did not give informed consent.

Study Design

In this study, a cross-sectional survey was administered as a standardized, 30-minute, personal interview. Each interview consisted of 3 parts, including 1) preinterview questionnaires, 2) the threshold task to elicit participants' preferences toward pre-CRT, and 3) a debriefing questionnaire. The preinterview questionnaire collected information about clinical and socioeconomic characteristics (ie, work status, education, annual household income) and the Medical Outcomes Study 36-item short form (SF-36), a validated quality-of-life instrument that is used for the general population.^{23,24} The debriefing questionnaire consisted of a participant evaluation of the interview format and consisted of 3 questions rated on a 5-point Likert scale.

The Threshold Task

The threshold technique is a reliable and valid preference assessment method that closely mirrors the patient-physician encounter by presenting the risks, benefits, and outcomes associated with the available treatment options.²⁵⁻³² For the purpose of this study, the 2 treatment options were 1) pre-CRT followed by surgery with total mesorectal excision (TME) 8 weeks after the completion of pre-CRT (CR + S) and 2) TME surgery alone (SA). For both of these options, the surgery protocol was identical to ensure that only the patients' preferences for pre-CRT were elicited. The pre-CRT protocol (45 Gray [Gy] in 25 fractions at 1.8 Gy per fraction over 5 weeks with continuous-infusion 5-fluorouracil at 225 mg/m² daily for 5 weeks) was selected for this study, because this is the preferred protocol at our center. Furthermore, at our center, patients are counseled that there is a significant improvement in local recurrence but not survival with pre-CRT based on data from the Dutch, German, and Polish rectal cancer trials. Although the Swedish trial did demonstrate a significant improvement in both local recurrence and survival, the 5-year local recurrence rate of 27% suggests

that not all patients underwent TME surgery; therefore, it is likely that the radiation therapy compensated for non-optimal surgery, thus leading to a survival benefit.²⁰ Therefore, for the current study, the primary outcome was local recurrence, and the base-case scenario represented a stage II or stage III midrectal cancer that measured between 5 cm and 10 cm from the anal verge. This scenario was selected because pre-CRT was considered the most effective for this subgroup of patients; and, at this level, a restorative procedure would be performed. On the basis of results from the Dutch and Polish rectal cancer trials, the estimated risk of local recurrence 5 years after undergoing anterior resection alone for a stage II or stage III tumor that measured 5 cm to 10 cm above the anal verge was set at 15% (Table 1).^{3,4,33} Bowel function data were taken directly from the Dutch trial and also are provided in Table 1.² Sexual function data were taken from the study by Hendren et al, in which 180 patients with rectal cancer were surveyed using the Female Sexual Function Index and the International Index of Erectile Function, both of which are validated scales that evaluate sexual dysfunction in women and men, respectively.^{34,35} In this study, the median follow-up was 5 years, and 60% of both men and women reported significant sexual dysfunction after treatment for rectal cancer. Furthermore, patients who received pelvic radiation were 5.6 times more likely (95% confidence interval [CI], 2.8-11.3 times more likely; $P < .05$) to report that surgery made their sexual life worse. On the basis of these data, the baseline estimate for a noticeable change in sexual function for CR + S was estimated as 60%, and the corresponding baseline estimate for SA was estimated at 30% based on the lower limit of the 95% CI for pelvic radiation.

Procedural Steps in the Threshold Task

Each participant received a series of six 8.5 × 11-inch flash cards with the headings 1) *Diagnosis and Goals of Treatment*, 2) *Before Surgery*, 3) *Surgery*, 4) *After Surgery*, 5) *Local Recurrence*, and 6) *Long-Term Outcomes and Summary* using a standardized script. The interview began with the interviewer reading aloud the Diagnosis and Goals of Treatment card to the participant. This card described an individual who had just been diagnosed with a midrectal cancer (5-10 cm from the anal verge) and now was considering his or her options for treatment. Participants were told that they would be making a treatment decision based on the information given about the 2 treatment options—CR + S and SA—and that they were to answer as though they actually were in the situation

LONG TERM OUTCOMES	
SURGERY ALONE	CHEMORADIATION & SURGERY
LENGTH OF TREATMENT	
• 3-4 months	• 8-9 months
BOWEL FUNCTION	
• 2-3 bowel movements per day • 5% chance of poor control over bowel movements • 25% chance of wearing a pad • 40% chance of effecting activities outside the home • 10% chance of restricted social activities • Will need to get to the toilet within 10 minutes	• 3-4 bowel movements per day • 15% chance of poor control over bowel movements • 50% chance of wearing a pad • 50% chance of effecting activities outside the home • 30% chance of restricted social activities • Will need to get to the toilet within 5 minutes
FEMALE SEXUAL FUNCTION	
30% chance of change in sexual function • decreased libido • concerns about body image • vaginal dryness • vaginal pain during intercourse	60% chance of change in sexual function • decreased libido • concerns about body image • vaginal dryness • vaginal pain during intercourse
MALE SEXUAL FUNCTION	
30% chance of change in sexual function • decreased libido • concerns about body image • changes in initiating and maintaining an erection	60% chance of change in sexual function • decreased libido • concerns about body image • changes in initiating and maintaining an erection

Figure 1. This Long-Term Outcomes and Summary card was read aloud to participants to inform them of the long-term outcomes associated with each treatment.

faced by the patient described. After this, the Before Surgery, Surgery, After Surgery, Local Recurrence, and Long-Term Outcomes and Summary cards were read aloud to the participant and presented the treatment protocol, risks, benefits, and long-term outcomes associated with each treatment (Fig. 1) (Summary Card only). The Local Recurrence card was used to define and review the implications of local recurrence with the participants and is shown in Figure 2. The purpose of the Local Recurrence card was to provide a clear overview about local recurrence (not an extensive discussion), and we believed it was representative of the issues that would be discussed with a patient who had primary rectal cancer during their initial assessment and treatment planning. In addition to the flash cards, probabilistic sliding scales were used to visually illustrate the risk of developing a local recurrence 5 years after surgery (Fig. 3).

After this information was given to the participant, the threshold task was performed. At the start of the threshold task, the risk of local recurrence was set at 15% for both CR + S and SA. This represented a clinically realistic risk of local recurrence after SA and a hypothetical risk of local recurrence after CR + S. The participant was then asked which of the 2 treatment options they would prefer initially when the risk of local recurrence was 15% for both options. It was expected that the majority of participants initially would choose SA, because the risk of local recurrence was the same for both options and SA was associated with fewer inconveniences and better functional outcomes relative to CR + S.

If the participant indicated an initial preference for SA (as expected), then the risk of local recurrence with SA remained at 15%, whereas the risk of local recurrence after CR + S was lowered systematically by 1% intervals (ie, to

LOCAL RECURRENCE

- Cancer has returned in the same part of the bowel where it started
- Most often where the bowel was joined together during surgery
- Involves the rectum, bladder, prostate and a portion of the tailbone

SYMPTOMS CAUSED BY LOCALLY RECURRENT RECTAL CANCER

Most People:

- Chronic pelvic pain from the tumor pressing on nerves and bones in the pelvis

Some People:

- Bowel blockage
- Bleeding
- Difficulty controlling bowel movements

Figure 2. This Local Recurrence card was used to define and review the implications of local recurrence with participants.

14%, 13%, 12%, and down to a minimum of 0%), making CR + S more and more appealing until the participant's preference switched from SA to CR + S. This threshold point represented the absolute risk of local recurrence with pre-CRT that would be required before the participant would choose treatment with pre-CRT. For example, if the threshold point was 5%, then this meant that the risk of local recurrence with pre-CRT would have to be $\leq 5\%$ (ie, equivalent to at least a 10% absolute risk reduction [ARR]) before the participant would choose treatment with pre-CRT.

Conversely, if the participant initially preferred CR + S when the risk of local recurrence was 15% for both options, then this choice was confirmed with the participant by reviewing the finding that CR + S was not any more effective than SA and was associated with more inconveniences and poorer functional results. Once CR + S was confirmed as the participant's treatment choice, the participant's reasons for this choice were obtained to determine whether or not they understood the task and the specific reason for this choice. In all cases, if CR + S was preferred initially over SA, then the threshold point was recorded as 15%, which meant that the participant

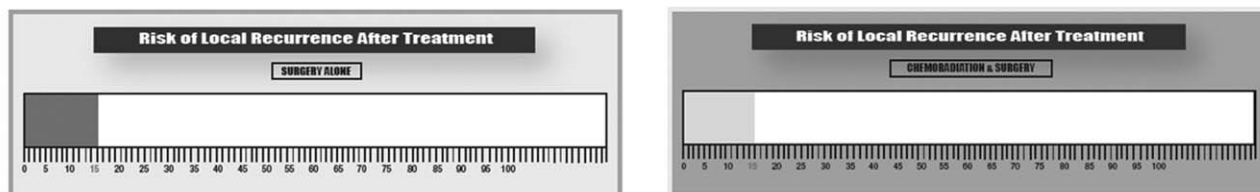
would choose pre-CRT even when the risk of local recurrence was the same as that for SA (ie, equivalent to an ARR of 0%). Before starting the study, the threshold task was pilot tested on 5 healthy individuals and on 10 patients with rectal cancer who had received previous CRT to ensure good comprehension and face validity.

Sample Size and Data Analysis

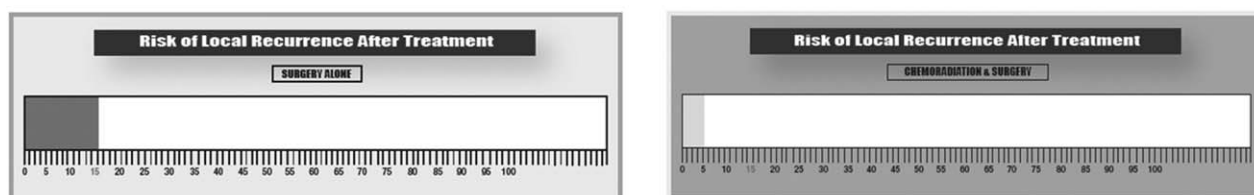
Because this study was descriptive, the sample size was estimated to ensure a 95% CI around a threshold estimate. A sample size of 50 was required to ensure a 95% CI with a precision of at least 0.15 for any given proportion of participants.³⁶ Statistical testing was performed using SAS software (version 9.2; SAS Institute, Cary, NC). Continuation-ratio ordinal regression models were constructed to determine demographic or clinical predictors of the participants' threshold points. For these models, threshold points were grouped based on the natural distribution of responses and were categorized as from 15% to 14%, from 13% to 6%, from 5% to 1%, and 0% or not willing to switch. This ordinal outcome was regressed onto each putative predictor in simple regressions and subsequently into 1 multivariate regression that

THRESHOLD TASK

- Initially, the participants were asked which treatment they preferred when the risk of local recurrence was 15% for both options
- In this situation, it was expected that the majority of the participants would prefer SA



- After the participant indicated they preferred SA, the risk of local recurrence stayed at 15% for SA AND
- The risk of local recurrence for CR + S was lowered by 1% intervals until the participant's preference switched to CR + S



- In this example, the threshold point is 5%
- This participant would require the risk of local recurrence to be 5% or less before they would choose CR + S

Figure 3. For the threshold task, probabilistic sliding scales were used to visually illustrate the risk of developing a local recurrence 5 years after surgery. SA indicates surgery alone; CR, chemoradiation; S, surgery.

included all predictors. Beta coefficients from the models were exponentiated to provide continuation odds ratios (ORs). Although similar in concept to a traditional OR, these ratios denote the likelihood of an individual choosing the next threshold given the current threshold level.³⁷

RESULTS

Participant Characteristics

Sixty-six eligible individuals were invited to take part in the study, and 50 (76%) completed the interview. Most individuals declined to participate because of time constraints or prior commitments. The average age of the study participants was 61 years, and the majority of participants were well educated, worked either full or part time, earned >50% of the total household income, and indi-

cated that they would prefer an active role in treatment decision making (Table 4).

Distribution of the Participants' Threshold Points

The distribution of the participants' threshold points varied widely across the entire spectrum of available scalar values (Fig. 4). Overall, 23 of 50 participants (46%) said that they would choose pre-CRT if the risk of local recurrence with pre-CRT was >5% (ie, equivalent to an ARR between 0% and 9%). Conversely, 27 of 50 participants (54%) said that they would choose pre-CRT only if the risk of local recurrence with pre-CRT was ≤5% (ie, equivalent to an ARR ≥10%). It is noteworthy that 8 of 50 participants (16%) said that they would prefer pre-CRT even when there was no benefit over SA (ie, equivalent to an ARR of 0%), and 4 of 50 participants (8%) said

Table 4. Participant Characteristics

Characteristic	No. of Patients (%)
Age: Mean±SD, y	60.8±8.0
Sex, n=50	
Men	23 (46)
Women	27 (54)
Education, n=50	
≤High school	9 (18)
University or college	41 (82)
Marital status, n=50	
Single	16 (32)
Married/long-term relationship	34 (68)
Employment status, n=50	
Not working outside of the home	4 (8)
Part time	19 (38)
Full time	18 (36)
Retired	9 (18)
Preferred role in decision making, n=50	
Active	27 (54)
Collaborative	21 (42)
Passive	4 (2)
Financial role, n=49	
>50% of household income	31 (64)
≤50% of household income	12 (24)
Retired/pension	6 (12)
SF-36 score: Mean±SD	
Physical Component Score	49.2±9.4
Mental Component Score	48.1±8.3

SD indicates standard deviation; SF-36, the Medical Outcomes Survey 36-item short-form health survey.

that they would not agree to pre-CRT even if the risk of local recurrence with pre-CRT was 0% (ie, equivalent to an ARR of 15%). The 8 patients who preferred pre-CRT when it did not include any benefit indicated that they understood that CR + S was not any more effective than SA; however, they believed that, psychologically, they would feel better knowing that they had done everything possible to cure their rectal cancer.

Variables Predictive of Participants' Preferences

Univariate analysis for the independent variables (age, sex, education, marital status, preferred role, financial role, and SF-36 score) indicated that participants who had completed university (OR, 4.56; 95% CI, 1.61-12.67; $P = .004$) or who had a higher score on the SF-36 Physical Component Scale (PCS) (OR, 1.03; 95% CI, 1.01-1.08; $P = .03$) were significantly more likely to demand a lower risk of local recurrence with pre-CRT. However, none of

these variables reached significance in the multivariate analysis.

Participant Evaluation of the Interview Format

Although the interview involved a considerable amount of detailed information, it was our experience that, in real time, the interviews ran smoothly; and, on average, the interview was completed within 30 minutes. Although 66% of participants felt that they received the right amount of information, 22% reported that they would have preferred a little more information. Overall, 90% of participants felt that the interview and the threshold task were easy to understand; and 90% believed that that, if they actually were faced with the treatment decision outlined in the clinical scenario, the interview would be helpful for making a treatment decision.

DISCUSSION

The results from this study demonstrated that participants' preferences for pre-CRT were distributed widely, and there were no clinical or demographic variables associated with the participants' treatment preferences. The finding that 54% of participants would not choose pre-CRT until it offered a risk of local recurrence ≤5% (ie, equivalent to an ARR ≥10% or a 67% relative risk reduction) suggests that a significant proportion of patients may be willing to accept a higher risk of local recurrence to avoid pre-CRT.

The current results are important, because they validate and add to the generalizability of 2 previous studies in this area by Couture et al and Harrison et al.^{38,39} Taken together, these 3 studies have demonstrated that both future patients and patients who currently have colorectal cancer seem to highly value functional outcomes and may be willing to accept a higher risk of local recurrence (ie, forego pre-CRT) to achieve these outcomes. Couture et al reported that 31 of 47 patients with colorectal cancer (65%) would not accept postoperative CRT (post-CRT) until the 10% baseline risk of local recurrence was reduced to ≤5% (ie, equivalent to an ARR <5% or a 50% relative risk reduction).³⁸ In this study, 11 of 47 participants (23%) were unwilling to accept post-CRT even when the risk of local recurrence was 0% (ie, equivalent to an ARR of 10%). In a second study by Harrison et al, 52 of 100 patients with colorectal cancer (52%) were willing to trade, on average, 24% of their remaining life expectancy to avoid pre-CRT relative to anterior resection alone.³⁹

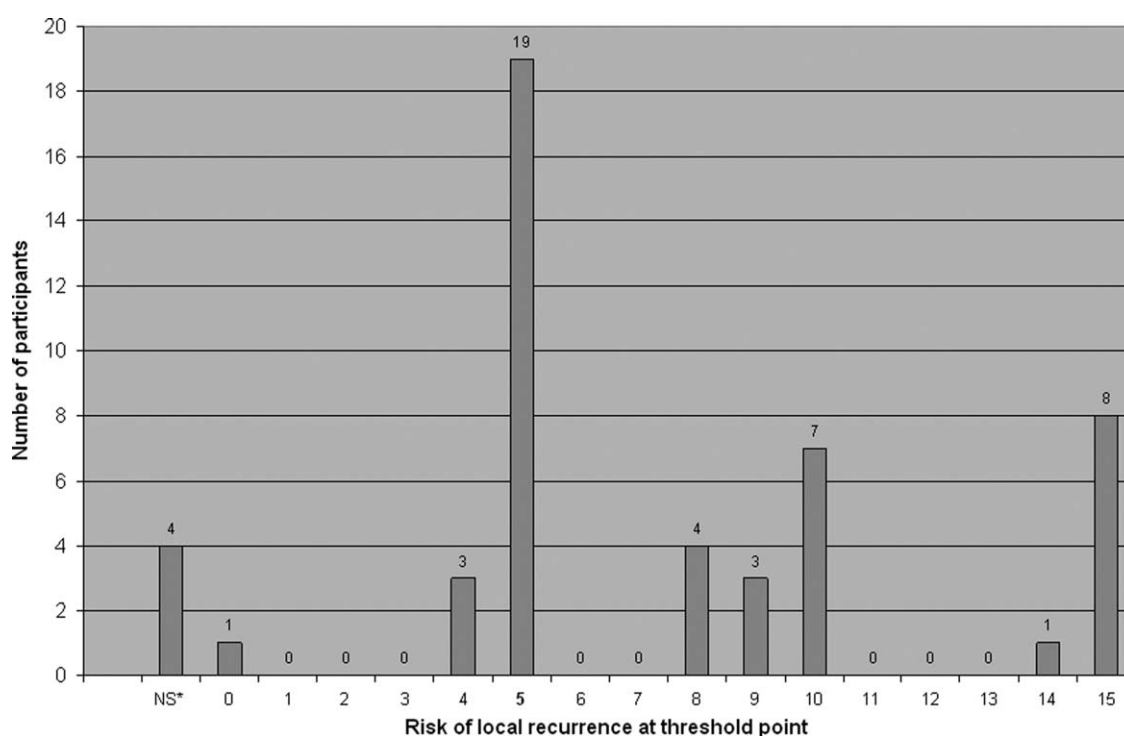


Figure 4. This chart illustrates the distribution of participants' threshold points for preoperative chemoradiation (pre-CRT). Note that patients did not switch to pre-CRT even when the risk of local recurrence with pre-CRT was 0%.

Furthermore, it is not only patients who seem willing to accept a less effective treatment option to achieve improved functional results. Solomon et al elicited the attitudes of patients with colorectal cancer and of physicians toward local excision versus abdominal perineal resection (ie, colostomy) for rectal cancer.⁴⁰ In their study, although 50 of 97 patients (52%) were willing to trade life expectancy to avoid a colostomy and would choose to undergo transanal excision, significantly more colorectal surgeons (38 of 43; 88%) and oncologists (93 of 103; 90%) were willing to trade, on average, 12% to 14% of their remaining life expectancy to avoid a colostomy and would choose undergo transanal excision. Eddy has classified clinical treatment policies as standards, guidelines, and options based on the strength of evidence for the treatment outcomes and the distribution of patients' preferences for these outcomes.⁴¹ In this classification, standards apply when patients unanimously agree on the overall desirability of the known outcomes, guidelines apply when the majority agrees on the overall desirability of the known outcomes, and options apply when patients are split evenly on the overall desirability of the known outcomes. On the basis of this classification, it seems rea-

sonable that the use of pre-CRT should be considered as a treatment option rather than a guideline.

Because it has been demonstrated that being a woman, younger age, and higher education are independent predictors of a preferred active role in the treatment decision-making process, a regression analysis was conducted to determine whether there were any independent demographic or clinical predictors for the actual choice of treatment. Although there were no independent predictors of treatment choice identified in the current study, 2 other studies in patients with breast cancer that used individually tailored decision-support tools demonstrated that younger age, higher income, and treatment by university-based physician were independent predictors of a treatment choice for adjuvant chemotherapy.^{42,43} It is noteworthy that, to our knowledge, there has been no investigation into the risks and benefits of physician awareness of these demographic and clinical predictors on the patient-physician interaction, the preferred role in treatment decision making, or the actual treatment choice.

The participants' positive evaluation of the interview format suggests that patients wanted to be involved in the

decision-making process, were able to understand the issues, and believed that the information provided in this study would be helpful in arriving at a treatment decision for pre-CRT. Therefore, the interview format used in this study easily could be developed into a formal decision board and used to assist both patients and physicians with treatment decision making regarding pre-CRT.

For this study, healthy patients who were at average risk for developing colorectal cancer were interviewed rather than patients with colorectal cancer. Although the scenario was hypothetical for this group, it did represent a group of individuals who actually could be faced with this treatment decision in the future (ie, future patients). Patients with colorectal cancer were not selected for this study because we believed that their responses may have been biased by their previous treatment. Furthermore, patients who actually had faced a decision about pre-CRT were not included because we did not believe that their inclusion would be ethically appropriate or feasible given the sample size required. However, it is worth noting that our results are similar to those from the studies by Couture et al and Harrison et al, who interviewed patients with colorectal cancer. A common criticism of patient preference studies is that participants do not comprehend the clinical issues, such as local recurrence, as fully as treating physicians. However, in the studies by Harrison et al and Solomon et al, physicians were even more willing to trade life expectancy (and to accept higher rates of local recurrence) than patients, and those findings serve to support the results from our current study.

Finally, the data presented to participants in the current study were based primarily on results from the Dutch TME trial, which evaluated pre-RT, and not pre-CRT. These data were used because we believed that they provided the highest quality evidence for local recurrence and bowel function. More recently, increasing evidence has indicated that local recurrence rates and functional outcomes with pre-RT and pre-CRT are similar (Table 1).^{6,7} Similarly, the description of local recurrence used for the current study reflected the description that was given to patients at our center and, thus, may or may not be as detailed as the description used at other centers. Although the use of these data may have limited our study, it is unlikely that these data would significantly change the overall “big-picture” finding that patients’ preferences for pre-CRT are widely distributed and that patients highly value functional results after treatment for rectal cancer.

In conclusion, the current report adds to a growing body of literature that both colorectal cancer patients and

their physicians seem to highly value functional outcomes and may be willing to accept a less effective treatment option to achieve better functional outcomes. Therefore, developers of future guidelines will need to strongly reconsider the use of pre-CRT for all patients with stage II and stage III rectal cancer and may need to downgrade the recommendation for pre-CRT from a guideline to an option for both midrectal and upper rectal cancers.

CONFLICT OF INTEREST DISCLOSURES

Dr. Baxter has received an Early Researcher Award from the Ontario Ministry of Health and Innovation.

REFERENCES

1. Kapiteijn E, Marijnen CA, Nagtegaal ID, et al. Preoperative radiotherapy combined with total mesorectal excision for resectable rectal cancer. *N Engl J Med*. 2001;345:638-646.
2. Peeters KC, Marijnen CA, Nagtegaal ID, et al. The TME trial after a median follow-up of 6 years: increased local control but no survival benefit in irradiated patients with resectable rectal carcinoma. *Ann Surg*. 2007;246:693-701.
3. Peeters KC, van de Velde CJ, Leer JW, et al. Late side effects of short-course preoperative radiotherapy combined with total mesorectal excision for rectal cancer: increased bowel dysfunction in irradiated patients—a Dutch Colorectal Cancer Group study. *J Clin Oncol*. 2005;23:6199-6206.
4. Marijnen CA, van de Velde CJ, Putter H, et al. Impact of short-term preoperative radiotherapy on health-related quality of life and sexual functioning in primary rectal cancer: report of a multicenter randomized trial. *J Clin Oncol*. 2005;23:1847-1858.
5. Sauer R, Becker H, Hohenberger W, et al. Preoperative versus postoperative chemoradiotherapy for rectal cancer. *N Engl J Med*. 2004;351:1731-1740.
6. Bujko K, Nowacki MP, Nasierowska-Guttmejer A, Michalski W, Bebenek M, Kryj M. Long-term results of a randomized trial comparing preoperative short-course radiotherapy with preoperative conventionally fractionated chemoradiation for rectal cancer. *Br J Surg*. 2006;93:1215-1223.
7. Pietrzak L, Bujko K, Nowacki MP, et al. Quality of life, anorectal and sexual functions after preoperative radiotherapy for rectal cancer: report of a randomised trial. *Radiother Oncol*. 2007;84:217-225.
8. Merkel S, Mansmann U, Siassi M, Papadopoulos T, Hohenberger W, Hermanek P. The prognostic inhomogeneity in pT3 rectal carcinomas. *Int J Colorectal Dis*. 2001;16:298-304.
9. Gunderson LL, Sargent DJ, Tepper JE, et al. Impact of T and N stage and treatment on survival and relapse in adjuvant rectal cancer: a pooled analysis. *J Clin Oncol*. 2004;22:1785-1796.
10. Carne PW, Nelson H. Are we overtreating rectal cancer: time for another trial? *Ann Surg Oncol*. 2004;11:124-126.
11. Mamon H, Willett CG. Is radiation therapy required for patients with intermediate-risk rectal cancer? *Clin Adv Hematol Oncol*. 2007;5:638-644, 585.

12. Kachnic LA, Hong TS, Ryan DP. Rectal cancer at the crossroads: the dilemma of clinically staged T3, N0, M0 disease. *J Clin Oncol*. 2008;26:350-351.
13. MERCURY Study Group. Extramural depth of tumor invasion at thin-section MR in patients with rectal cancer: results of the MERCURY study. *Radiology*. 2007;243:132-139.
14. Smith N, Brown G. Preoperative staging of rectal cancer. *Acta Oncol*. 2008;47:20-31.
15. Burton S, Brown G, Daniels IR, Norman AR, Mason B, Cunningham D. MRI directed multidisciplinary team preoperative treatment strategy: the way to eliminate positive circumferential margins? *Br J Cancer*. 2006;94:351-357.
16. Glynn-Jones R. *Whose guidelines are they anyway?* *Clin Oncol (R Coll Radiol)*. 2010;22:261-264.
17. Kornmann M, Henne-Bruns D, Porzolt F. Neoadjuvant treatment of rectal carcinoma: assessment of health care services by physicians and lay persons. *J Clin Oncol*. 2008;26:4866-4868.
18. Cedermark B, Johansson H, Rutqvist LE, Wilking N. The Stockholm I trial of preoperative short term radiotherapy in operable rectal carcinoma. A prospective randomized trial. Stockholm Colorectal Cancer Study Group. *Cancer*. 1995;75:2269-2275.
19. Martling A, Holm T, Johansson H, Rutqvist LE, Cedermark B. The Stockholm II trial on preoperative radiotherapy in rectal carcinoma: long-term follow-up of a population-based study. *Cancer*. 2001;92:896-902.
20. Improved survival with preoperative radiotherapy in resectable rectal cancer. Swedish Rectal Cancer Trial. *N Engl J Med*. 1997;336:980-987.
21. Tjandra JJ, Kilkenny JW, Buie WD, et al. Practice parameters for the management of rectal cancer (revised). *Dis Colon Rectum*. 2005;48:411-423.
22. Wong RK, Berry S, Spithoff K, et al. Preoperative or postoperative therapy for stage II or III rectal cancer: an updated practice guideline. *Clin Oncol (R Coll Radiol)*. 2010;22:265-271.
23. Ware JE Jr, Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Med Care*. 1992;30:473-483.
24. Stewart AL, Hays RD, Ware JE Jr. The MOS short-form general health survey. Reliability and validity in a patient population. *Med Care*. 1988;26:724-735.
25. Llewellyn-Thomas HA. Investigating patients' preferences for different treatment options. *Can J Nurs Res*. 1997;29:45-64.
26. Llewellyn-Thomas H, Thiel E, Paterson M, Naylor D. In the queue for coronary artery bypass grafting: patients' perceptions of risk and "maximal acceptable waiting time." *J Health Serv Res Policy*. 1999;4:65-72.
27. Llewellyn-Thomas HA, Williams JI, Levy L, Naylor CD. Using a trade-off technique to assess patients' treatment preferences for benign prostatic hyperplasia. *Med Decis Making*. 1996;16:262-282.
28. Dales RE, O'Connor A, Hebert P, Sullivan K, McKim D, Llewellyn-Thomas H. Intubation and mechanical ventilation for COPD: development of an instrument to elicit patient preferences. *Chest*. 1999;116:792-800.
29. Kennedy ED, To T, Steinhart AH, Detsky A, Llewellyn-Thomas HA, McLeod RS. Do patients consider postoperative maintenance therapy for Crohn's disease worthwhile? *Inflamm Bowel Dis*. 2008;14:224-235.
30. Palda VA, Llewellyn-Thomas HA, Mackenzie RG, Pritchard KI, Naylor CD. Breast cancer patients' attitudes about rationing postlumpectomy radiation therapy: applicability of trade-off methods to policy-making. *J Clin Oncol*. 1997;15:3192-3200.
31. Brundage MD, Davidson JR, Mackillop WJ. Trading treatment toxicity for survival in locally advanced non-small cell lung cancer. *J Clin Oncol*. 1997;15:330-340.
32. Brundage MD, Davidson JR, Mackillop WJ, Feldman-Stewart D, Groome P. Using a treatment-tradeoff method to elicit preferences for the treatment of locally advanced non-small-cell lung cancer. *Med Decis Making*. 1998;18:256-267.
33. Hendren SK, O'Connor BI, Liu M, et al. Prevalence of male and female sexual dysfunction is high following surgery for rectal cancer. *Ann Surg*. 2005;242:212-223.
34. Rosen R, Brown C, Heiman J, et al. The Female Sexual Function Index (FSFI): a multidimensional self-report instrument for the assessment of female sexual function. *J Sex Marital Ther*. 2000;26:191-208.
35. Harrison RC, Riley A, Wagner G, Osterloh IH, Kirkpatrick J, Mishra A. The International Index of Erectile Function (IIEF): a multidimensional scale for assessment of erectile dysfunction. *Urology*. 1997;49:822-830.
36. Rosner B. *Fundamentals of Biostatistics*. 4th ed. Boston, MA: Duxbury Press; 1995.
37. McCullagh P. Regression models for ordinal data (with discussion). *J R Stat Soc B*. 1980;42:109-142.
38. Couture J, Chan R, Bouharaoui F. Patient's preferences for adjuvant postoperative chemoradiation therapy in rectal cancer. *Dis Colon Rectum*. 2005;48:2055-2060.
39. Harrison JD, Solomon MJ, Young JM, et al. Patient and physician preferences for surgical and adjuvant treatment options for rectal cancer. *Arch Surg*. 2008;143:389-394.
40. Solomon MJ, Pager CK, Keshava A, et al. What do patients want? Patient preferences and surrogate decision making in the treatment of colorectal cancer. *Dis Colon Rectum*. 2003;46:1351-1357.
41. Eddy DM. Clinical decision making: from theory to practice. Designing a practice policy. Standards, guidelines, and options. *JAMA*. 1990;263:3077, 3081, 3084.
42. Siminoff LA, Gordon NH, Silverman P, Budd T, Ravdin PM. A decision aid to assist in adjuvant therapy choices for breast cancer. *Psychooncology*. 2006;15:1001-1013.
43. Peele PB, Siminoff LA, Xu Y, Ravdin PM. Decreased use of adjuvant breast cancer therapy in a randomized controlled trial of a decision aid with individualized risk information. *Med Decis Making*. 2005;25:301-307.