Management of Rectal Cancer Without Radical Resection

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Abstract

The basis of the current treatment of rectal cancer is a radical total mesorectal excision of the rectum, and although this provides excellent oncological control, it is associated with morbidity and functional problems in cancer survivors. Organ-preservation alternatives are local excision alone for very early tumors, chemoradiation followed by either local excision of a small tumor remnant or, when there is a complete clinical response, a nonoperative watch-and-wait approach. The functional advantage of these alternatives is clear, but there is some concern about the oncological risk. Although the available studies suggest that with adequate selection and follow-up this risk is small, the evidence is still weak. Because of patients' high interest in preserving quality of life, clinicians should cautiously move ahead and offer the option of organ preservation to patients in a controlled setting while awaiting further evidence.

INTRODUCTION

TME: total mesorectal resection

Local recurrence used to be the Achilles heel of the surgical treatment of rectal cancer, with incidence figures up to 20–30%. Patients suffered from debilitating symptoms, and treatment was difficult. With optimal staging by magnetic resonance imaging (MRI), neoadjuvant (chemo)radiation in high-risk patients, and optimal surgical technique, local recurrence rates are now down to 5%. The improved oncological outcome, however, comes at a cost. Especially in elderly patients and in those with comorbidities, rectal resections are major procedures with substantial risk of perioperative morbidity and mortality. Whereas the overall mortality of rectal cancer surgery is 2–3%, 30-day mortality rates in patients over 80 years of age are in the range of 10–15%, with a 6-month mortality as high as 15–25% (1). There is also an increasing interest in the long-term quality of life in cancer survivors. Up to 50% of patients after a low anterior resection develop some degree of bowel dysfunction including elements of fecal incontinence, urgency, and frequent bowel movements, the so-called low anterior resection syndrome (2). Many patients with low tumors have difficulty accepting a permanent stoma and are asking for alternatives. Very low anastomoses can avoid a permanent stoma in some of these patients, but the functional outcomes are often not very good. The increased awareness of both the short- and long-term morbidity of radical rectal surgery is the basis for an increasing interest in organ-preservation alternatives to total mesorectal excision (TME).

ORGAN-PRESERVATION APPROACHES

The basis of the standard treatment of rectal cancer is radical TME surgery. This procedure is based on the surgical principle to remove both the tumor-bearing organ and the draining lymph nodes. For rectal cancer, this means removing the embryologically defined unit of rectum and mesorectum. The concept of organ preservation relies on a different treatment of the tumor and the lymph nodes, with three types of approaches:

1. transanal local excision of a very early tumor, with no treatment of the mesorectum because the risk of lymph node metastases is very low or nonexistent;
2. transanal local excision of early tumor with added (neo)adjuvant radiotherapy to eradicate potential small mesorectal lymph node metastases;
3. upfront chemoradiation for mostly larger tumors, with omission of TME surgery only when reassessment shows a clinical complete response.

All organ-preservation approaches inherently accept a higher incidence of residual disease in the bowel wall or lymph nodes than after TME surgery, and all rely on active surveillance to detect and treat residual disease when still amenable to salvage TME. Because in organ-preservation series salvage TME surgery for residual disease is generally not more difficult than primary TME surgery, with a good oncological outcome, the label "regrowth" rather than "local recurrence" was proposed for these events (3). The real oncological risks of organ preservation are that not all regrowths are easily amenable to salvage surgery and that some regrowths could be the source of metastases. Although the available studies described below suggest that with adequate selection and follow-up this risk is small, the exact risk is not yet well established, because the majority of the studies are relatively small retrospective and prospective cohort studies. This should be communicated clearly to patients who are considered candidates for organ preservation, and should be balanced against the possible benefits of the approach. These benefits are the avoidance of the operative morbidity and mortality of a TME procedure, and an improved quality of life with less anorectal and urogenital dysfunction and fewer colostomies.

EVIDENCE IN LITERATURE

Local Excision for Very Early Tumors

TEM: transanal endoscopic microsurgery

Endoscopic polypectomy or transanal full thickness local excision for favorable T1 tumors is the most accepted form of organ preservation and is considered the preferred treatment in many guidelines (4, 5). The tumor can be an incidental finding after excision of a presumed benign polyp or can be diagnosed as an early invasive cancer before the procedure. The preferred surgical technique is transanal endoscopic microsurgery (TEM). A recent review of the literature on TEM for rectal cancer included 72 papers and provides grading of the evidence and recommendations (6). When at histology of the resection specimen the tumor has clear margins, is well/moderately differentiated, has no lymphatic or vascular invasion, and has only superficial invasion of submucosa (sm1–2), the risk of lymph node metastases and local recurrence is below 5%. In the presence of one or more adverse risk factors and when the tumor is larger than 3–4 cm, this risk increases to 20–30%, and completion radical rectal surgery is advised (6, 7). In patients who have a high operative risk or who refuse surgery, two alternatives can be considered: careful follow-up including MRI, with the option of salvage surgery when the residual disease becomes evident, or adjuvant chemoradiation. A recent review of 10 series with postoperative (chemo)radiation after local excision of T1/2 lesions reports a median local failure rate of 10%, with local failure rates of T2 in the range of 10–25% (8). The exact role of adjuvant chemoradiation as an alternative to radical resection for control of residual subclinical disease in the setting of unfavorable features after local excision is not yet clear and is the subject of an ongoing clinical trial (NCT02371304).

Chemoradiation and Full Thickness Local Excision

The approach of neoadjuvant chemoradiation and full thickness local excision of the scar or tumor remnant also uses radiotherapy to control subclinical disease in the mesorectum. Chemoradiation for rectal cancer has been shown to have higher efficacy when given preoperatively rather than postoperatively, with the added advantage of downsizing the primary tumor (9). This can be exploited to expand the indication for organ preservation to tumors that are traditionally considered unsuitable for a local excision because of a higher risk of lymph node metastases. The majority of studies still exclude large tumors and tumors with evident nodal metastases on imaging, with the idea that chemoradiation is better in controlling subclinical than clinical mesorectal disease.

Table 1 summarizes the older series in the 2008 review by Borschitz et al., as well as more recent series (10–19). In the review by Borschitz et al., the local failure rate of ypT0 and ypT1 tumors was 0–6%, whereas for ypT2 remnant this failure rate was 6–20% (10). This is generally considered too high a risk, and completion TME is often recommended for patients with a positive margin or a ypT2 tumor. Overall the local failure rate is low, below 10%, with most of the series reporting easy salvage of any regrowth. The overall survival and rate of distant metastases in the small randomized trial comparing TEM with TME after chemoradiation was not different in the two arms (12). The overall survival in these series tends to be lower than in series of "watch and wait" (W&W) for clinical complete responders. W&W series generally include only complete responders, with an inherently very good prognosis, whereas the local excision series also include ypT1 and ypT2 tumors, which are biologically less favorable with an inherently worse prognosis (20). The overall impression is that survival does not seem to be compromised by TEM compared to standard TME surgery, although level-1 evidence is lacking.

The rate of successful organ preservation is difficult to estimate from the studies because of different study methodology, intention-to-treat principles, and recommendations for immediate completion surgery. The overall rate is well over 50%, and in the most recent well-designed

Table 1 Series on chemoradiation and local excision

References	Number of patients	Height (cm)[a]	Treatment	ypT0/ypT1 (%)	Unfavorable path features[b]	Complications of TEM	Follow-up (months)	Local failure	Salvaged after local failure	Systemic recurrence	DFS[c]	OS[c]	Stoma-free survival[c]
10	237	Unknown	45-52Gy + 5FU	25/21	Unknown	Unknown	24–55	7%	Unknown	7%	Unknown	Unknown	Unknown
11	44	<8	50Gy + 5FU	Unknown	Unknown	Unknown	64	9%	Unknown	11%	92% 5yr	81% 5yr	Unknown
12	50	<6	50Gy + 5FU	28/24	48%	14%	115	8%	Unknown	4%	89%	72%	Unknown
13	63	<11	45-56Gy + 5FU	67/2	27%	27%	36	2%	2/2	5%	91% 3yr	91% 3yr	90% 3yr
14	15	<10	50Gy + 5FU	27/20	53%	Unknown	38	0	Unknown	7%	91% 3yr	73% 3yr	Unknown
15	53	<7	50-54Gy + 5FU	17/17	68%	Unknown	36	8%	8/9	Unknown	Unknown	Unknown	Unknown
16	79	<8	50-54Gy + Cap (+ Oxaliplatin)	49/14	35%	26%	56	4%	2	6%	88% 3yr	95% 3yr	94%
17	47	<10	50Gy + Cap	45/19	36%	28%	17	9%	3/4	Unknown	Unknown	Unknown	Unknown
18	14	<12	5x5Gy	Unknown	Unknown	50%	10	7%	Unknown	Unknown	Unknown	Unknown	Unknown
19	15	<10	50Gy + Cap	60/7	Unknown	Unknown	41	20%	3/3	13%	Unknown	Unknown	87%

Abbreviations: 5FU, 5-fluorouracil; Cap, capecitabine; DFS, disease-free survival; OS, overall survival.

[a]Distance from anal verge to lower edge of tumor.

[b]≥ypT2, poor differentiation (≥G3), lymphovascular/perineural invasion.

[c]3yr or 5yr actuarial survival as noted.

American College of Surgeons Oncology Group (ACOSOG) trial, organ preservation was possible in 91% of patients (16). One of the criticisms of organ preservation in patients with relatively small tumors who could be treated with radical surgery without chemoradiation is that the group of patients who still require radical surgery may be disadvantaged because they have worse anorectal function than those who had TME surgery alone.

The exact role of completion surgery is not yet established. Some centers are very cautious and recommend completion surgery for ypT2 tumors because of the increased risk of local failure. However, in the ACOSOG trial, only one of 24 patients with ypT2 tumors experienced a local recurrence (16). Additionally, there are patients who refuse completion surgery, and although the risk for local failure for ypT2 is higher than for ypT1, still 70–90% of patients remain free of disease with a preserved rectum (13, 17). The benefits and risks of completion surgery should be discussed with each patient on an individual basis. Clear indications for completion surgery are incomplete resection specimens and ypT3 tumors. Completion TME surgery can be difficult because of the inflammation around the TEM area, and usually a waiting period of six weeks is advised.

When compared to nonirradiated patients, patients who undergo local excision after chemoradiation have an increased rate of complications, with more wound dehiscence, pain, and readmissions, sometimes even requiring a colostomy (21). There is also some anecdotal evidence that the functional results are worse. With the increasing experience of W&W in clinical complete responders, it can therefore be reasonable to omit the local excision when there is a clinical complete response in order to avoid these complications.

Watch and Wait After Clinical Complete Response to Chemoradiation

The most paradigm-changing approach in organ preservation is to "watch and wait" when a tumor shows a complete clinical response after chemoradiation. After the pioneering paper by Angelita Habr-Gama from São Paulo (22), other positive reports were published (23, 24). The oncological and surgical community initially responded with skepticism, but recently several well-designed studies were accompanied by cautiously positive commentaries (16, 19, 25–29). The main findings of these reports are summarized in **Table 2** (19, 22–25, 28, 30–35). There is a large variation in treatment protocols: radiation dose, number of fractions, inclusion of boost, concomitant chemotherapy combinations, and consolidation chemotherapy. Some of the papers describe the complete population that received chemoradiation, whereas other papers only describe the complete responders, and it is therefore difficult to estimate the exact percentage of patients that might benefit from a W&W policy. A recent report describes a 23% incidence of pathological complete response (pCR) in the TME specimen after chemoradiation in a very large US population database, suggesting that a substantial number of patients can be treated with W&W (36).

Most of the centers offering W&W have selected this approach for distal rectal tumors, within 7 cm of the anal verge. The majority of current guidelines favor neoadjuvant therapy for distal tumors as the standard approach because of the inherently higher chance for a close or involved circumferential resection margin (CRM) after primary TME. In this setting, patients with a very good clinical response can be identified at restaging with endoscopy and MRI, and the option of organ preservation can be discussed (3). Patients with distal tumors are generally very interested in organ preservation, because with radical TME surgery they are facing a rectal amputation or a very low anastomosis with the risk of poor function (37).

The incidence of reported regrowths varies between 5% and 34% (**Table 2**), a range that probably reflects the difference in selection criteria. The vast majority of reported regrowths

Table 2 Series evaluating the watch-and-wait strategy

Reference	Number of patients	Height (<7cm)[b]	Primary T-stage ≥T3	Primary N-stage N+	Treatment	cCR N (%)	Follow-up (months)	Local failure	Salvaged after local failure	Systemic recurrence	DFS[c]	OS[c]	Stoma-free survival[c]
22[a]	265	100%	80%	22%	50Gy + 5FU	71 (27%)	57	3%	100%	4%	92%	100%	
30	361	100%	82%	28%	50Gy + 5FU	122 (34%)	60	24%	100%	6%	85% 5yr	93% 5yr	
31	70	100%	71%	39%	54Gy+5FU	47 (68%)	56	26%	92%	17%	72% 3yr	90% 3yr	88%
32	183	100%	70%	18%	50-54Gy + 5FU	90 (49%)	60	31%	78%	13–18%	68% 5yr	91% 5yr CSS	78%
23	195	95%	90%	Unknown	50Gy + Cap	21 (11%)	25	5%	100%	Unknown	89% 2yr	100% 2yr	
33	Unknown	Unknown	Unknown	Unknown	50Gy + 5FU+MMC	23	72	30%	Unknown	Unknown	Unknown	Unknown	87%
24[a]		Unknown	Unknown	Unknown	50Gy + Cap or 5FU	32	28	19%	100%	9%	88% 2yr	96% 2yr	
25	51	100%	47%	45%	60Gy + Tegafur	40 (78%)	24	26%	100%	8%	58% 2yr	100% 2yr	78% 2y
34[a]	900	100%	73%	53%	50Gy + Cap	122 (14%)	60	7%	100%	3%	90% 5yr	100% 5yr	
35[a]	Unknown	Unknown	89%	39%	Unknown	18	68	6%	100%	6%	89% 5yr	100% 5yr	
28[a]	Unknown	Unknown	76%	65%	45Gy + Cap or 5FU	129	33	34%	88%	5.5%	Unknown	96% 3yr	74% 3y
19	Unknown	Unknown	74%	76%	50Gy + Cap	85	41	15%	100%	3.5%	81% 3yr	97% 3yr	92%

Abbreviations: 5FU, 5-fluorouracil; Cap, capecitabine; MMC, mitomycin C; cCR, complete clinical response; DFS, disease-free survival; OS, overall survival; CSS, cancer-specific survival; N, number.

[a]Series where there was a surgical arm as a comparator.

[b]Percentage of patients with a distance between anal verge and lower edge of the tumor of less than 7 cm.

[c]2-year, 3-year, or 5-year actuarial survival as noted.

occur within the first two years. The reported incidence of systemic recurrence in the series is low (5–18%), in agreement with the finding that patients with a pCR after TME have a more favorable outcome than nonresponders (20). The series that compare the outcome of W&W with standard TME surgery all show comparable cancer-specific and overall survival (22–24, 28, 34, 35). The available evidence therefore suggests that, when carefully selected and followed in a dedicated program, a W&W strategy does not subject patients to an excess risk of dying when compared to standard surgery. This, however, cannot be considered proof because the series are relatively small, and there are no randomized trials.

ASSESSMENT OF RESPONSE

The traditional six-week interval between the end of chemoradiation and surgery was more or less arbitrarily chosen, and with the recent interest in organ preservation and response assessment, many centers now advocate longer intervals. A number of retrospective series show a clinically relevant higher pCR rate with a longer interval, suggesting that an interval of 8–12 weeks is better (38, 39). To select patients for organ preservation, valid diagnostic methods are required to detect residual tumor both in the bowel wall and in lymph nodes. If residual tumor is overlooked and a false diagnosis of (near) complete response is made, patients are at risk for local regrowth. Restaging modalities have therefore been a subject of investigation, and at present the best modality for selection of complete responders is a combination of digital rectal examination, flexible sigmoidoscopy, and MRI, including diffusion-weighted imaging (DWI) (40). Standard T2-weighted MRI is good at showing the degree of fibrosis, and an MRI tumor-regression grading system has been proposed that roughly corresponds with the degree of response (41). The difficulty for all imaging methods—MRI, FDG-PET (fluorodeoxyglucose positron emission tomography), and endorectal ultrasound—is to distinguish fibrotic thickening from viable tumor cells (42). Adding DWI to standard T2-weighted MRI improves the accuracy, but there still is a tendency to err on the safe side and overestimate the presence of residual tumor (43). For the luminal component of the tumor, endoscopy and digital rectal examination are highly accurate, with some additional improvement in accuracy by modern magnetic resonance techniques (40). For the lymph nodes, T2-weighted MRI is currently the best imaging method. When the primary MRI is suggestive of lymph node metastasis, organ preservation can only be considered when the nodes have been sterilized. When the lymph nodes have disappeared completely on MRI, there is a high likelihood that they are free of tumor. When the nodes have become smaller, it is more difficult to rule out remaining nodal metastases. Lymph node–specific contrast agents could offer some help, but this is still investigational (44).

For the primary tumor, a typical complete response often presents as a white scar in the rectal mucosa, with or without telangiectasia and no palpable lesions, and can easily be distinguished from a residual mass (**Figure 1**). However, the endoscopic findings are sometimes less clear, and small, residual flat ulcers can be seen, or some residual redness of the mucosa, with or without subtle soft lesions on digital rectal examination. These lesions can be complete responses where the mucosa has not yet healed and are sometimes called “near complete responses.” Biopsies unfortunately have a limited clinical value for ruling out residual cancer due to sampling errors (45).

A local excision of the remaining scar offers two main advantages: It provides histological proof of a complete response, and it clears the bowel wall of any small tumor remnant. The main disadvantage is that there is a higher complication rate than in nonirradiated patients, with a painful, slowly healing ulcer as one of the more troubling complications. Patients with a true complete response have therefore no benefit from a local excision. An alternative is to extend the

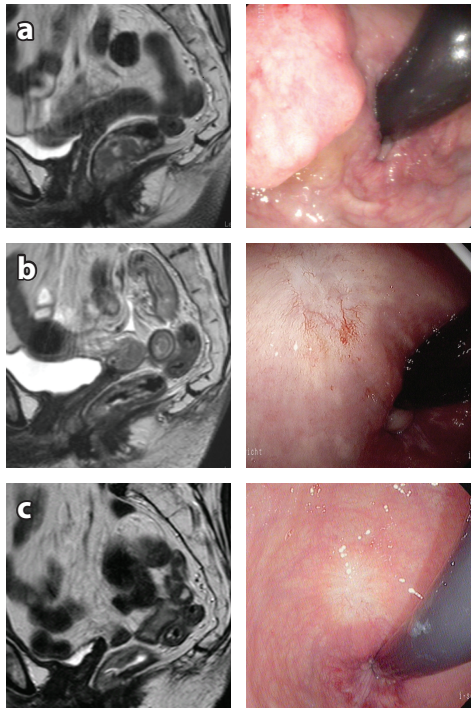

Figure 1

Typical complete response. (*a*) A cT2N1 rectal cancer at the anorectal verge, prior to chemoradiation. (*b*) A typical complete response after chemoradiation. (*c*) Follow-up after 3.5 years. Note the typical black scar on sagittal T2 weighted magnetic resonance image.

observation interval for an additional 1–2 months in patients with a very good response, as it can take several months before the full effect of the chemoradiation becomes evident (46).

FOLLOW-UP: DETECTION AND TREATMENT OF REGROWTH

The acceptance of a 10–30% incidence of regrowths due to residual disease is an inherent part of an organ-preservation approach. In addition to the standard follow-up after treatment of rectal cancer, aimed at detection of metastases, follow-up after organ preservation is aimed at early detection of local regrowth. The vast majority of local regrowths after W&W are intraluminal and occur within 12–18 months (**Figure 2**). Frequent examination by DRE and endoscopy during the first two years is therefore the backbone of the local follow up. This should be supplemented by MRI to detect the less frequently occurring regrowths deeper in the bowel wall or lymph nodes (47). After a local excision of a ypT0 scar the risk of regrowth is low, but when there is a ypT1 and especially a ypT2 remnant, the risk for regrowth is 20% or more. Follow-up imaging is essential for early detection and treatment of residual tumor in lymph nodes. Although some centers use endorectal ultrasound, MRI is generally considered to be better with a higher resolution, a larger field of view, and it is less operator dependent.

For both endoscopy and MRI, it is essential that all previous images are stored for comparison and that the MRI images contain the same sequences, preferentially from the same machine. Comparing the serial images provides a powerful tool for early detection of a regrowth. The

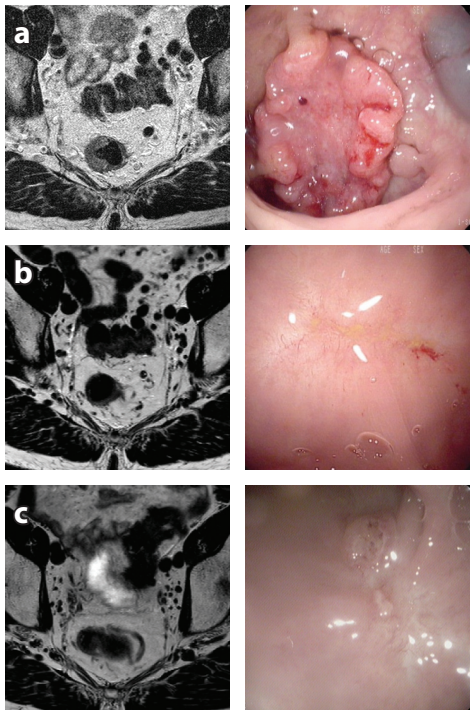

Figure 2

Luminal regrowth. (*a*) A cT3N0 rectal cancer located 4.5 cm from the anorectal verge, prior to chemoradiation. (*b*) A clinical complete response after chemoradiation. (*c*) Small regrowth detected only by endoscopy at nine months follow-up. Salvage surgery revealed a ypT2N0 tumor.

endoscopic picture as well as the MRI images can be more difficult to interpret in the first six months after a local excision because of the initial inflammation and scar tissue.

The follow-up schedule should take into account the risk for regrowth and the higher incidence of regrowth in the first 1–2 years. After local excision of a very early lesion with minimal or no risk for recurrence, endoscopic surveillance without MRI is usually enough. For patients with a larger tumor, both endoscopy and MRI are recommended. Our current schedule entails a flexible sigmoidoscopy every 3–4 months, with MRI in the first year and every 6 months thereafter until the fifth year.

The standard treatment of a regrowth with the best oncological outcome is TME. Alternative treatment options can sometimes be considered, such as a local excision of an isolated luminal regrowth in a patient with a high operative risk or a patient who chooses to avoid major surgery with a poor functional outcome or a definitive colostomy. In patients with a very high operative risk, external reirradiation or endoluminal radiotherapy are also treatment options.

Organ-preservation series show that with adequate follow-up and early detection, local regrowths are mostly amenable to salvage treatment with good outcome. The salvage rate in **Tables 1** and **2** varies between 78% and 100%, also including patients who refuse surgery or who are medically inoperable. Regrowths are usually detected when small and only rarely extend to the mesorectal fascia. TME surgery after W&W is generally not more difficult than it would have been initially, although one report describes more fibrosis with a longer interval without an increased risk for complications (48). Salvage TME for a regrowth after TEM can be difficult

because scar tissue and fibrosis can extend into the mesorectal fascia and sometimes even beyond that (6). The difficulty depends on the location and depth of the local excision, as well as on the postoperative degree of inflammation. A report from the São Paulo group describes a high CRM+ rate of salvage TME, with a high repeated local recurrence rate, and on this basis immediate completion surgery is recommended when unfavorable features are found upon histology of the TEM resection specimen (15).

FUNCTIONAL OUTCOME AND QUALITY OF LIFE

Preservation of function and quality of life is one of the main reasons for the interest in organ-preservation strategies. After low anterior resection, deterioration of bowel function is common, especially after neoadjuvant chemoradiation. Reportedly up to 75% of patients experience severe long-term dysfunction, most commonly a combination of urgency, frequency, incontinence, and clustering of bowel movements (2). With organ-preservation approaches, many patients can avoid a permanent colostomy, with colostomy-free survival rates of 70–90% (**Tables 1–2**). Although functional problems can also occur after organ preservation because of long-term radiotherapy effects, the few available data suggest that patients receiving organ-preservation therapy report significantly fewer changes in bowel habits, less incontinence, and a lower defecation frequency than do patients receiving low anterior resection (23). The most common functional complaints after W&W are clustering of bowel movements and some urge incontinence, but major incontinence is rare. Patients who undergo local excision or TEM after chemoradiation have a higher rate of postoperative complications than do nonirradiated patients, but it is not yet clear if this has a negative impact on the functional results. In general, there is a need for better data on the functional outcome of organ-preservation strategies.

FUTURE TRENDS

Providing More Evidence

Despite the increasing interest in organ-preservation strategies, especially from the patient community, there are still many unanswered questions regarding long-term functional and oncological outcomes, long-term toxicity of radiotherapy, optimal radiation dose and fields, etc. (49). Randomized trials will provide the best answers for a number of clinical questions, such as whether to deliver a radiotherapy boost or whether to choose chemoradiation and organ preservation versus a low anterior resection in small rectal tumors. Patients who already have received chemoradiation and who show a very good response, and patients who are facing a rectal amputation, are unlikely to find randomized trials attractive. Many of these patients express a strong preference to avoid major surgery and/or a definitive colostomy. The next best level of evidence consists of large well-documented prospective cohort studies. Combining data of centers that practice watch-and-wait into a large registry database such as the International Watch and Wait Database provides an opportunity to study and compare real word differences in assessment, follow up, and outcome (50).

Increasing Response Rates

Large database studies show a pCR rate in TME after chemoradiation of ~20% (36). The response rates are even higher when smaller tumors are treated with chemoradiation. In addition to increasing the interval between chemoradiation and local excision, there are two main ways to

increase the response rates: intensifying the radiotherapy and adding systemic therapy. In rectal cancer, as in many other tumors, there is a dose–response relationship, and a significant increase in response rate is expected with doses higher than the currently used 45–50.4 Gy (51). This increased dose is usually delivered as a local boost to the tumor, either via external radiotherapy or endocavitary techniques. Studies with a total dose of 55–60 Gy show organ-preservation rates of >50% (25, 31, 52). Adding oxaliplatin to fluorouracil (5FU) during chemoradiation resulted in more toxicity but little or no increase in pCR rate (49). Another approach is to add systemic therapy either before or after (chemo)radiation (53). One study convincingly showed pCR rates increased from 18% to 38% with increased cycles of FOLFOX after chemoradiation (48). Whereas all of the above approaches have the potential to increase the rate of organ preservation, they also have the potential to increase toxicity and should be considered investigational.

Predicting Response

Many studies have reported baseline clinical variables that are associated with a higher incidence of complete response, such as lower T stage, lower N stage, and small tumor volume. The baseline prediction is of little value for patients who have a more advanced tumor with an established indication for neoadjuvant therapy. The prediction at primary presentation can, however, be valuable for patients with smaller tumors, who can be treated with surgery alone but who also have a higher chance of a complete response to chemoradiation. With the combination of variables obtained from clinical data, tumor biopsies, and radiological images, a good predictive model could support a more rational treatment choice that maximizes oncological and functional outcome and minimizes the futile use of radiotherapy. At present there is not yet such a validated predictive model, although there have been promising reports on a limited number of variables, as summarized in a recent review (54).

CONCLUSION

Organ preservation is not simply a new treatment option in rectal cancer, it is a paradigm shift with a change in basic treatment concepts: willingness to adapt the surgical plan according to the response, extension of the observation time in good responders, the role of TME as salvage surgery, and the expanded role of patients in treatment choices. There is at present no high-level evidence that organ preservation is as safe as standard TME surgery. Because of the high interest of patients in preserving quality of life and function, the surgical community should cautiously move ahead and offer the option of organ preservation to patients in a controlled setting, while at the same time providing more evidence on the benefits and risks of the organ-preservation approach. We encourage surgeons to set up a prospective organ-preservation protocol with standardized assessment and follow-up and add their data to a large multicenter database (50). At least initially, it seems wise to concentrate organ preservation in a limited number of centers, in order to gain sufficient expertise more quickly. This will provide high-quality information on the benefits and risks while offering an improved quality of life for our patients.

DISCLOSURE STATEMENT

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