Organ preservation in rectal cancer: a synopsis of current guidelines

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Abstract

Aim The high morbidity associated with radical resection for rectal cancer is an incentive for surgeons to adopt strategies aimed at organ preservation, particularly for early disease. There are a number of different approaches to achieve this. In this study we have collated current national and international guidelines to produce a synopsis to support this changing practice.

Method The PubMed, Embase, Trip, National Guideline Clearinghouse and BMJ Best Practice databases were interrogated. Guidelines published before 2010 were excluded. The AGREE-II tool was used for quality assessment.

Results Twenty-four guidelines were drawn from 2278 potential publications. A consensus exists for local excision for 'low-risk' T1 rectal cancer but there is no agreement on how to stratify the risk of treatment failure. There is a low level of agreement for rectal preservation for more advanced disease, but when mentioned

it is recommended for unfit patients or in the context of a clinical trial. Guidelines are inconsistent with respect to surveillance in node-negative disease and after complete response to chemoradiotherapy.

Conclusion According to current guidelines and consensus statements, organ preservation for rectal cancer beyond low-risk T1 is still considered experimental and only indicated in patients who are unsuitable for radical surgery. Follow-up strategies and cN0 staging deserve attention, highlighting the need for high-quality clinical trials.

Keywords Rectal cancer, organ preservation, local excision, radiotherapy, guideline

What does this paper add to the literature?

This systematic review of national and international guidelines and consensus statements for rectal-preserving treatment strategies identifies gaps in our knowledge and highlights areas for future research.

Background

A blanket approach to rectal cancer treatment is shifting to tailor-made treatments which take into account functional outcome and quality of life as well as oncological control. This has occurred as encouraging results have been reported after either local excision, primary chemoradiotherapy or a combination of both. In addition, national screening programmes have led to rectal cancer being picked up at an early stage when rectal preservation is oncologically safer with a lower risk of nodal and distal spread.

It remains uncertain exactly when to carry out organ preservation, even in some T1 lesions. There is an urgent need to define standardized treatment strategies at an international level to help us balance oncological control with functional outcome and quality of life [1].

It is now 13 years since Habr Gama and colleagues presented data which showed that a 'watch and wait' (W&W) policy could be safely applied to patients who had achieved a clinical complete response after neoadjuvant chemoradiotherapy for rectal cancer. Since then other centres have selectively adopted this approach, but rectal preservation after complete remission or excision remains controversial as the standard of care [2].

Key to this dilemma is the stratification of risk of local and regional nodal recurrence for intermediate-

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and high-risk early rectal cancers since this is increased after local excision even with neoadjuvant radiotherapy. In providing a tailored approach this has to be weighed against the morbidity associated with (completion) total mesorectal excision (TME) [3].

The aim of this study was to systematically review national and international guidelines to provide an overview on the consensus and controversies concerning rectal preservation strategies in the treatment of rectal cancer.

Method

Search strategy

We performed a systematic search for regional, national and international guidelines and consensus documents which had provided guidance for rectal cancer treatment. This search was carried out between November 2015 and June 2016 by interrogating Medline (via Pubmed), Embase, Trip, National Guideline Clearinghouse and BMJ Best Practice databases as well as the websites of the ministries of health of several Western countries.

Selection process

Search criteria insisted that guidelines had to have been published in 2010 to the current date and written in English, Dutch, German, Scandinavian or Latin languages. These could be regional or national. We also included consensus statements issued by international organizations such as the European Society of Medical Oncology and the European Association of Endoscopic Surgery.

After extraction of duplicates, references were independently screened by two reviewers (WAB, SO) on title and abstract using the online Covidence review manager (Covidence online review manager 2015, <https://www.covidence.org/>). If there was any disagreement consensus was achieved by discussion. After this second round of screening, an additional check on duplicates, updates, addendums and withdrawn status was performed. Full-text assessment of the remaining documents was performed independently by two reviewers (WAB, SO).

The AGREE-II instrument was used for quality-assessment of the included guidelines [4]. This instrument incorporates 23 items which were scored independently by the two reviewers from 1 to 7, with 7 being the maximum score. A mean score was calculated for each paper, and if a paper scored 3 or less it was excluded.

Data extraction

Data extraction, categorization and establishment of consensus were carried out by two of the authors

(WAB and SO). Selected topics of interest included rectal preservation strategies applied to clinical and pathological stage, preoperative imaging for early rectal cancer, local excision techniques, W&W after neoadjuvant chemoradiotherapy as well as follow-up regimes.

Consensus and level of evidence

In order to reach consensus, at least two-thirds of the guidelines that made a relevant statement on a specific topic needed to have a similar recommendation. For the conclusion statements, the highest level of evidence, as classified according to the Oxford Centre for Evidence-based Medicine Levels of Evidence 2009, was retrieved from the included guidelines (<http://www.cebm.net/oxford-centre-evidence-based-medicine-levels-evidence-march-2009/>). If the included guidelines did not report their recommendations according to the Oxford classification, the level of evidence was manually reassigned.

Results

Literature search

The search resulted in a total of 2278 articles. After extraction of duplicates, 1894 titles were evaluated. Of these, 1857 were further excluded based on title or abstract. An additional 26 guidelines were retrieved by searching websites of ministries of health and national surgical or oncological societies and by cross-checking references. Ultimately, 54 guidelines were assessed by full text for inclusion. Out of these, 28 guidelines were excluded based on criteria as provided in Fig. 1 (flowchart) leaving 26 papers to be included for quality assessment.

The remaining 26 guidelines consisted of 16 national guidelines (e01–e04, e06–e09, e11, e14, e17–e19, e24, e25, e27), eight consensus statements (e10, e12, e13, e15, e16, e20–e22) and two chapters (e05, e26) (the key to guideline numbering is given in Table 1). The mean score of the guidelines was 4.70. The Cuban (e04) and Danish (e05) guidelines were excluded due to mean scores of 2.21 and 2.67, respectively (Table 2). Eventually, a total of 24 guidelines were included (Fig. 2).

Synopsis

1. Staging modalities: magnetic resonance imaging (MRI) and endorectal ultrasound (ERUS)

Since local excision is only recommended for early node-negative rectal cancer, it is imperative to assess the

Figure 1 Inclusion flow chart.

depth of invasion and node status. Two modalities are available: MRI is accessible in most institutions, in contrast to ERUS which is operator dependent and less commonly performed.

ERUS is better at assessing the depth of invasion for small rectal cancers and can differentiate T1 and T2 lesions. MRI is better when the tumour is more locally advanced in terms of assessing mesorectal fat

Table 1 Included guidelines.

No.	Guideline	Country	Year
e01	Colorectal carcinoma	Netherlands	2014
e02	Cancer colorectal en la Argentina	Argentina	2011
e03	Guía de práctica clínica para la detección temprana, diagnóstico, tratamiento, seguimiento y rehabilitación de pacientes con diagnóstico de cáncer de colon y recto	Colombia	2013
e04	Consensus nacional de cáncer de recto [excluded]	Cuba	2013
e05	Danish Colorectal Cancer Group retningslinier lokal tumorresktion i rectum [excluded]	Denmark	2014
e06	Nasjonalt handlingsprogram med retningslinjer for diagnostikk, behandling og oppfølging av kreft i tykktarm og endetarm	Norway	2015
e07	Thésaurus national de cancérologie digestive, ch 5 cancer du rectum	France	2013
e08	Evidence based guideline for colorectal cancer	Germany	2014
e09	Protocolos clínicos e diretrizes terapêuticas em oncologia	Brazil	2014
e10	Early rectal cancer: the European Association for Endoscopic Surgery (EAES) clinical consensus conference	EAES	2015
e11	European guidelines for quality assurance in colorectal cancer screening and diagnosis	European Commission	2010
e12	Management of patients with colorectal cancer: a personalized approach to clinical decision making	European Society of Medical Oncology	2012
e13	Rectal cancer: ESMO clinical practice guidelines for diagnosis, treatment and follow-up	European Society for Medical Oncology	2013
e14	Consensus document for management of colorectal cancer	India	2014
e15	Review of current best practice and priorities for research in radiation oncology for elderly patients with cancer: the International Society of Geriatric Oncology (SIOG) taskforce	International	2014
e16	Practice parameters for early rectal cancer management: Italian Society Of Colorectal Surgery guidelines	Italy	2015
e17	Management of early colorectal cancer	New Zealand	2011
e18	National Institute for Health and Care Excellence	UK	2011/14
e19	SIGN Colorectal	Scotland	2015
e20	ACR Appropriateness Criteria® local excision in early stage rectal cancer	USA	2015
e21	Practice parameters for the management of rectal cancer (ASCRS)	USA	2013
e22	EURECCA colorectal: Multidisciplinary management: European consensus conference colon and rectum	Europe	2014
e24	NCCN clinical practice guidelines in oncology: rectal cancer	USA	2015
e25	JSCCR guidelines 2014 for the treatment of colorectal cancer	Japan	2014
e26	Early stage rectal cancer	Canada (Alberta)	2013
e27	Cancer colorectal adénocarcinome	France	2012

involvement and any breach of the mesorectal fascia. Fourteen guidelines supported the use of MRI in assessing larger lesions (e06–e08, e10, e12–e14, e16, e17, e20–e22, e26, e27).

MRI is the investigation of choice for assessing lymph node involvement. Seven guidelines provided MRI criteria for lymph node involvement: irregular border, signal heterogeneity and round morphology (e01, e10, e12, e13, e16, e21, e22). Two guidelines mentioned a size of > 8 mm as a risk factor (e12,

e22), and the Dutch guideline mentioned a size of > 5 mm as a risk factor when concomitant suspicious morphological features were observed (e1).

In six guidelines MRI was the recommended staging investigation, with ERUS being reserved for expert centres or when local excision was planned (e1, e3, e8, e11, e18, e19). The NCCN guidelines (USA) did not differentiate between MRI or ERUS and suggested that clinicians should use whatever staging imaging was available (e24). Four

Figure 2 Level of evidence per topic, 1a being the highest and 5 the lowest.

guidelines did not mention imaging at all (e2, e9, e15, e25).

MRI and ERUS are complementary in the staging of rectal cancer. ERUS is better at assessing depth of invasion in small early cancers whilst MRI is superior at assessing lymph node status, mesorectal involvement and any breach in the mesorectal fascia.

Consensus: level of evidence 2b.

2. Treatment based on clinical stage (cTNM)

cT1N0M0

Thirteen guidelines advised local excision for cT1N0M0 rectal cancer (e01, e03, e06, e07, e10, e12, e14, e17, e20–e22, e24, e25). Eight mentioned neoadjuvant treatment for Stage cT1–2 before any local excision but that this should only take place within the setting of a clinical trial (e01, e03, e06, e8, e10, e11, e20, e21). The European Society of Medical Oncology (ESMO) guidelines also approved the use of contact radiotherapy or brachytherapy for frail patients (e12).

Guidelines from Canada and the UK advised TME for cT1N0M0. The Canadian guideline was supportive of local excision with the proviso that the consent process included information that there may be a higher risk of recurrent disease. The UK NICE guideline stated that TME should be considered standard therapy for early rectal cancer as the evidence for all other treatment strategies was of inadequate quality (e13, e18, e26). The European Union guideline refrained from any

recommendation based on cT1N0M0 stage (e11). Six guidelines did not make a distinction between clinically and pathologically staged rectal cancer and were not included in this analysis (e02, e16, e09, e15, e19, e27).

Local excision is a safe approach for cT1N0M0 rectal cancer.

Consensus: highest level of evidence 1b.

cT2N0M0

None of the 17 guidelines which considered this clinical stage recommended local excision alone (e1, e3, e6–e16, e21, e22, e24, e25). One consensus statement advised neoadjuvant treatment followed by local excision (e20). Ten guidelines mentioned neoadjuvant therapy followed by local excision as an option in a trial setting, in frail patients or in those who adamantly refused a TME (e01, e03, e06, e07, e10–e12, e15, e16, e21). Six guidelines did not consider this specific stage (e02, e17, e18, e19, e26, e27).

For cT2N0M0 rectal cancer, TME should be considered standard of care.

Consensus: highest level of evidence 2b.

Local excision following neoadjuvant therapy can be offered in trial setting, or for patients who are not fit for or those refusing major surgery.

Consensus: level of evidence 2b.

3. Pathological staging: definition of high-risk pT1

Six guidelines did not categorize T1 rectal cancer as high- or low-risk pT1 using pathological criteria (pT1) (e9, e14, e15, e17–e19).

Thirteen guidelines defined a pT1 tumour as high risk if the tumour was poorly differentiated, there was lymphatic or venous-invasion or if the resection margin was less than 1 mm (e01, e02, e06, e07, e08, e10–e12, e16, e21, e22, e24, e25). The Argentinean guideline suggested that the resection margin should be < 3 mm (e02). Size > 3 cm was a high risk factor in six guidelines (e1, e2, e7, e8, e17, e21).

Four guidelines based the classification of pT1 as high or low risk on SM classification alone (e3, e13, e26, e27). Eight guidelines mentioned SM classification as a factor in addition to those of poor differentiation, lymphatic and venous invasion and margin involvement (e6, e7, e10, e12, e16, e22, e24, e25). Whilst SM3 was defined as high risk in four guidelines (e12, e22, e24, e25), others also included SM2 (e6, e7, e10, e16). The German and EURECCA guidelines stated that current evidence was of inadequate quality to include SM classification in the definition of low- or high-risk pT1 rectal cancer (e8, e22). In conclusion, 12 out of 18 guidelines mentioned SM3 as indicator for high-risk pT1.

Tumour budding refers to the number of individual cells or cell clusters which infiltrate the interstitium at the resection margin. This was mentioned as a high risk factor in four guidelines (e7, e11, e25, e27). One guideline mentioned a three-tier grading system: Grade 1 (fewer than four tumour cells within the microscopic field) was considered as low risk whilst Grade 2 (five to nine cells) and grade 3 (more than 10 cells) were considered to be high risk [e25].

A pT1 rectal cancer is defined as high risk if any of the following characteristics is mentioned in the pathology report: poor differentiation, lymphatic or venous invasion, a clear resection margin of less than 1 mm and SM3.

Consensus: level of evidence 2b.

4. Treatment based on pathological stage (pT)

4a. pT1 Low risk (well to moderately differentiated, no venous invasion, no lymphatic invasion, < 3–4 cm, SM1–2)

Following local excision or polypectomy of a low-risk T1 rectal cancer satisfying the above pathological stage criteria, 19 papers recommended that no adjuvant therapy (completion surgery or (chemo)radiotherapy) was

indicated (e01–e03, e06–e14, e16, e19, e20, e22, e24, e25, e27). Five guidelines did not explore the risk of recurrence for pT1 or the place of adjuvant treatment after local excision (e15, e17, e18, e21, e26).

For pT1 low risk, local excision is deemed sufficient.

Consensus: highest level of evidence 1b.

4b. pT1 high risk (poor differentiation, or venous invasion, or lymphatic invasion, or R1, or > 3–4 cm, or SM3)

Eighteen guidelines recommended completion TME for high-risk pT1 rectal cancer with the above characteristics (e01–e03, e06–e08, e10–e14, e16, e19, e20, e22, e24, e25, e27). The guideline from Brazil (e09) advised adjuvant (chemo)radiotherapy. Nine other guidelines mentioned this as an option within a clinical trial or for patients not fit for surgery or those who declined surgery (e07, e8, e10, e12, e13, e20, e22, e24, e27). The French Thésaurus suggested contact radiotherapy to be an option for frail patients (e07). Five guidelines did not clarify a specific treatment for this stage (e15, e17, e18, e21, e26).

The recommended treatment following local excision/polypectomy of a high-risk pT1 is a completion TME.

Consensus: level of evidence 2b.

Adjuvant (chemo)radiotherapy may be an alternative to completion TME within a clinical trial setting, or for patients unfit for surgery.

Controversy: highest level of evidence 3b.

4c. pT2

Seventeen guidelines (e01–e03, e06–e08, e10–e14, e16, e19, e20, e22, e24, e27) recommended a completion TME after local excision of a pT2 rectal cancer. Adjuvant radiotherapy was mentioned as an alternative for TME in the Brazilian guideline (e09). Seven guidelines also considered radiotherapy as an alternative to TME, but only in the setting of a clinical trial or in frail patients or those who declined surgery (e07–e10, e12, e13, e20). Six papers did not comment on further treatment for this pathological stage (e15, e17, e18, e21, e25, e26).

Standard care after local excision of pT2 rectal cancer should be completion TME.

Consensus: level of evidence 2b.

Adjuvant (chemo)radiotherapy following local excision for pT2 rectal cancer is an alternative for completion TME within the setting of a clinical trial, in patients unfit for surgery or in those who have declined surgery.

Controversy: level of evidence 3b.

5. Treatment strategy for complete clinical response to neoadjuvant treatment (ycCR/ycT0)

Eight guidelines referred to W&W as an option for patients with a clinical complete response (cCR) after chemoradiotherapy for a clinically advanced rectal cancer. The Dutch guideline considered TME surgery as standard care irrespective of any response after chemoradiotherapy with W&W for ycCR only in the context of a clinical trial (e01). Two guidelines considered W&W appropriate for patients unfit for surgery or for those refusing surgery (e07, e15). Five guidelines drew attention to close monitoring for ycCR but concluded that there was no high-quality evidence to support this strategy (e08, e13, e18, e21, e24). No guidelines provided an exact definition of cCR.

Should the site of the rectal cancer be excised after cCR? Four guidelines recommended this strategy (e01, e13, e15, e16). The French Thésaurus and EAES consensus statements proposed the excision of the scar in ycCR within the setting of a clinical trial (e07, e10). One guideline specified that scar excision should be carried out for ypT (postchemoradiotherapy). The Dutch guideline considered that surveillance could only be considered for ypT0–1 after local excision if recommended by a multidisciplinary team with expertise in rectal preservation but that ypT2–3 patients should undergo completion TME [e01].

W&W for ycCR with intensive surveillance by an experienced team can be considered for patients unfit for and declining surgery, but should be undertaken in the setting of a clinical trial. Local excision of the scar or small residual disease following (chemo)radiotherapy can be considered as alternative to TME surgery, with close surveillance for ypT0–1.

Controversy: highest level of evidence 3b.

6. Technique of local excision

Nine local excision techniques were reported: snare polypectomy, endoscopic mucosal resection (EMR), endoscopic submucosal dissection (ESD), transanal excision (TE), transanal endoscopic microsurgery (TEM),

transanal minimally invasive surgery (TAMIS), posterior transphincteric resection, posterior proctectomy and transcoccygeal resection. TEM was preferred in 11 guidelines (e07, e08, e11–e14, e16, e20–e22, e25). Two considered TAMIS to be equivalent to TEM (e01, e15). One guideline preferred TAMIS over TEM (e10). Transanal resection of tumour was indicated in one guideline (e09) but considered obsolete by five guidelines (e08, e11, e16, e20, e21). Endoscopic excision by snare polypectomy, ESD and EMR were also acceptable (e06, e10, e18). The European Commission guideline considered ESD inferior to TEM for rectal cancer (e11). Five guidelines did not specify which local excision technique was advised (e03, e14, e17, e26, e27).

A minimally invasive surgical approach is preferred for local excision of early stage rectal cancer, using either TEM or TAMIS.

Consensus: highest level of evidence 2b.

7. Surveillance protocol following rectal preservation

Five out of 24 guidelines suggested a surveillance protocol (e01, e03, e11, e12, e22). None mentioned a follow-up protocol for W&W. The Dutch guidelines recommended endoscopic inspection of the scar and a pelvic MRI every 3–6 months over the first 2–3 years after local excision. Other guidelines recommended digital rectal examination and rigid sigmoidoscopy up to 5 years. Fourteen guidelines recommended similar surveillance protocols after curative treatment of rectal cancer, irrespective of the type of surgery or tumour stage (e01–e03, e07–e09, e11–e13, e19, e22, e24, e25, e27). Six stated that imaging modalities and carcinoembryonic antigen (CEA) testing were of no proven value for pT1N0 and R0 resections (e01, e11–e14, e16).

There was no single surveillance protocol after rectal preservation for rectal cancer. However, there was consensus that endoscopic surveillance of the scar after local excision was appropriate.

Controversy: highest level of evidence 5.

Discussion

This article is a synopsis of 24 national and international guidelines or consensus documents on rectal-preserving therapies for rectal cancer. Despite the growing attention and expanding application of this treatment strategy, the only consensus is for local excision of low-risk T1 rectal cancer, although even here there is no

agreement about how to stratify what is low risk. Conversely, TME surgery is generally regarded as the standard of care for all other stages with rectal-preserving alternatives only applicable to those patients who are unfit for radical surgery or when the technique is employed in the context of a clinical trial setting. How unfit patients have to be to be 'unfit for surgery' is never defined.

There was a low level of agreement between guidelines on the following: MRI-based lymph node assessment, W&W after complete response following neoadjuvant therapy, the definition and assessment of ycCR, and surveillance protocols.

Emerging evidence and future research topics

Despite there being general agreement for pretreatment imaging for rectal cancer, the guidelines did not achieve consensus for defining the image-derived status of local lymph nodes. We think this has been hampered by the low sensitivity of 72–91% for endo-ultrasonography and 65–76% for MRI [5–8]. Diffusion-weighted-MRI has been shown to offer better sensitivity and specificity for lymph node detection, but prospective studies and uniformity in definitions are needed to fully evaluate its role in preoperative staging (Topic 1) [9,10].

Consensus was observed on the appropriateness of organ-preserving local excision for cT1N0M0 and pT1 low-risk carcinomas (Topic 2). Some pathological features (differentiation grade, lymphatic or venous invasion, resection margins and SM classification) were accepted as markers for tumour recurrence (i.e. high-risk pT1). A recent retrospective study and systematic review showed tumour budding to be an independent predictor for increased cancer recurrence [11,12]. Tumour size and budding were not embedded in the majority of guidelines. With reference to tumour budding, we think this may be due to a lack of standardization of assessment (Topic 3).

In the case of cT1–3N0M0, neoadjuvant radiotherapy should only be used within the setting of a clinical trial. Whilst this treatment is associated with complications in the short and long terms this should be balanced with potential long-term oncological success and preservation of the rectum. Whilst the CARTS study reported that organ preservation could be achieved with neoadjuvant chemoradiotherapy followed by TEM in half of patients with a cT1–3N0M0, this was at the cost of a 3.6% mortality rate related to the chemoradiotherapy. In addition there is substantial overtreatment of poor responders [13]. Two trials are either being evaluated or are in progress. In the UK, the TREC trial randomized patients with cT1–2N0M0 to either TME or

short-course radiotherapy followed by TEM. The GRECCAR-2 trial successfully randomized patients with cT2–3 with a good response to neoadjuvant radiotherapy to local excision or TME [14]. These trials at the very least have demonstrated that it is possible to randomize patients with early rectal cancer to standard surgery or to rectal preservation. We hope that the multinational STAR-TREC trial will provide further evidence for rectal preservation based on clinical stage (Topic 4).

Up to 40% of locally excised benign rectal lesions may harbour malignant cells [15]. The risk of local

Table 2 Quality assessment of included guidelines.

Guideline/country	Year of publication	Agree overall score*	Agree score (mean)†
Netherlands (e01)	2014	6.5	6.1
Argentina (e02)	2011	4	3.5
Colombia (e03)	2013	4.5	4.6
Norway (e06)	2015	6.5	5.6
France (Thésaurus) (e07)	2013	5	4.7
Germany (e08)	2014	7	5.8
Brazil (e09)	2014	5	4.7
EAES (e10)	2015	6	4.9
European guidelines for quality assurance in colorectal cancer screening and diagnosis (e11)	2010	7	6.3
ESMO: personalized approach (e12)	2012	6	4.4
ESMO: clinical practice guidelines (e13)	2013	6	3.2
India (e14)	2014	4	3.3
IOSG (e15)	2014	2.5	3.6
Italy (e16)	2015	6	4.4
New Zealand (e17)	2011	5.5	6.2
NICE (e18)	2014	7	6.7
SIGN (e19)	2015	6.5	6.4
ACR appropriateness (e20)	2015	3.5	3.4
ASCRS (e21)	2013	6	4.7
EURECCA (e22)	2014	7	6.5
NCCN (e24)	2015	7	5.4
JSCCR (Japan) (e25)	2014	5	4.3
Alberta, Canada (e26)	2013	4.5	4.2
France (e27)	2012	4.5	4.6

*Overall Agree score as based on the mean of all agree scores of the different sections together.

†The mean of the total Agree scores as provided by the two independent reviewers (WB and SO).

recurrence can vary from 15% to 42%. Current guidelines suggest that these patients should undergo completion TME when there is a high risk of recurrence (Topic 4) [15]. The role of adjuvant radiotherapy following local excision for this type of early rectal cancers is limited to small retrospective series with heterogeneous cohorts [16]. The aim of the TESAR trial (NCT02371304), which is currently recruiting, is to look in detail at this subgroup [17].

A clinical complete response (cCR) is observed in 12–30% of the patients after neoadjuvant therapy. This depends on the initial disease stage, the type of neoadjuvant treatment and the time elapsed before evaluation [18,19]. There is still a wide variation in the exact definition of a cCR. A combination of digital rectal examination, endoscopy, CEA measurement, CT and MRI seems to be most accurate in evaluating any response [20]. The exact criteria for cCR were not assessed in the guidelines examined in this study. Patients judged to be complete responders may reflect a selection bias to those with favourable tumour characteristics [21]. Using propensity score matching, Renehan *et al.* [19] have shown that 60% of the complete responders can be treated by organ preservation. Adequate surveillance is needed because up to one-third developed local recurrence at a salvageable stage. It should be emphasized that any W&W strategy following cCR needs specific expertise and results should be closely monitored as part of a clinical trial or registry. How to improve the cCR rate in early rectal cancer is one of the research questions currently being addressed. There is a need to better define how, when and for how long patients with cCR need to be assessed and followed up (Topic 5).

Few studies have compared TEM and TAMIS for local excision of early rectal cancer. Both techniques are recommended for local excision (Topic 6). One retrospective single-centre cohort study of 69 patients who had undergone local excision of early rectal cancer by TEM ($n = 40$) or TAMIS ($n = 29$) reported no significant difference in margin involvement between the two techniques [22]. Since the techniques are similar, the additional value of a randomized controlled trial is debatable.

There is little evidence on which to base any surveillance protocol after rectal preservation, and this would explain the lack of standardized follow-up protocols among the included guidelines. An intensified schedule which includes endoscopic inspection of the scar and pelvic MRI for lymph node assessment seems appropriate following rectal-preserving strategies. Frequency and duration need to be defined as well as cost-effectiveness (Topic 6).

Conclusion

Although rectal-preserving treatment strategies for rectal cancer are mentioned in the majority of national and international guidelines, we need to define the indications and contraindications. There are a number of trials currently recruiting patients in order to define the optimal treatment strategies, to improve outcomes and to determine what exactly makes a rectal cancer ‘early’. Rectal preservation should still be regarded as an experimental treatment strategy until there is agreement over lymph node imaging, surveillance protocols and risk assessment based on pathological examination.

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