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Treatment of clinical T1 rectal cancer in the Netherlands; a population-based overview of clinical practice

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ABSTRACT

Introduction: Local excision is increasingly used as an alternative treatment for radical surgery in patients with early stage clinical T1 (cT1) rectal cancer. This study provides an overview of incidence, staging accuracy and treatment strategies in patients with cT1 rectal cancer in the Netherlands.
Materials and methods: Patients with cT1 rectal cancer diagnosed between 2005 and 2018 were included from the Netherlands Cancer Registry. An overview per time period (2005-2009, 2010-2014 and 2015-2018) of the incidence and various treatment strategies used, e.g. local excision (LE) or major resection, with/without neoadjuvant treatment (NAT), were given and trends over time were analysed using the Chi Square for Trend test. In addition, accuracy of tumour staging was described, compared and analysed over time.
Results: In total, 3033 patients with cT1 rectal cancer were diagnosed. The incidence of cT1 increased from 540 patients in 2005–2009 to 1643 patients in 2015–2018. There was a significant increased use of LE. In cT1N0/X patients, 9.2% received NAT, 25.5% were treated by total mesorectal excision (TME) and 11.4% received a completion TME (cTME) following prior LE. Overall accuracy in tumour staging (cT1 = pT1) was 77.3%, yet significantly worse in cN1/2 patients, as compared to cN0 patients (44.8% vs 77.9%, respectively, $p < 0.001$).
Conclusion: Over time, there was an increase in the incidence of cT1 tumours. Both the use of neo-adjuvant therapy and TME surgery in clinically node negative patients decreased significantly. Clinical accuracy in T1 tumour staging improved over time, but remained significantly worse in clinical node positive patients.

1. Introduction

In the treatment of rectal cancer, surgery according to the principle of total mesorectal excision (TME) remains the cornerstone of curative treatment. However, TME has substantial morbidity and mortality [1–3]. In selected patients with low risk early-stage rectal cancer, local excision (LE) is an attractive and increasingly applied alternative to primary TME [4–6]. In terms of preserving anorectal function, lower morbidity and improved quality of life, LE is superior compared to TME [7]. LE seems oncologically safe in patients with clinical node negative pT1 rectal tumours in the absence of prognostic unfavourable histological factors, including poor differentiation grade, lymphatic or vascular invasion, tumour budding and positive resection margins. Consequently, LE is nowadays considered as the preferred treatment of choice for these patients [4–6,8–12].

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If a cT1 rectal cancer proves to be high risk pT1 or more after LE, completion TME (cTME) is recommended in order to achieve optimal oncological outcome. Although cTME has similar oncological results as primary TME, the necessity of cTME after LE indicates that the patient has unnecessarily been exposed to LE and its risks [13]. When cTME is omitted and a local recurrence occurs during follow-up, salvage surgery is mandatory with often disappointing results [14,15]. This emphasizes the need for accurate staging and diagnosis of pT1 cancers [16].

In view of the increasing incidence and the changes in management of pT1 rectal cancer over the years, we evaluated the trends in incidence and treatment strategies for patients diagnosed with cT1 rectal cancer in the Netherlands between 2005 and 2018. In addition, we analysed the accuracy of clinical staging for pT1 tumours.

2. Materials and methods

2.1. Patient selection

All data were extracted from the Netherlands Cancer Registry (NCR), a nationwide population-based registry including all newly diagnosed malignancies in the Netherlands. NCR data on patient characteristics, tumour characteristics and treatment are collected from hospital patient files and coded according to a national manual, e.g. to the International Classification of Diseases for Oncology (ICD-O) and stage according to the TNM classification [11]. Patients with a clinical T1 (any N) stage rectal and rectosigmoidal carcinoma (C19 and C20) aged $\geq$18 years old diagnosed between 2005 and 2018 were included in this retrospective study. All treatment methods were included, either with or without the application of (neo)adjuvant therapy. Patients with cT1M1 and those who did not receive (surgical) treatment were described but excluded from further analysis.

2.2. Staging modalities

The NCR database does not contain information on specific staging modalities used throughout the study period. Nonetheless, according to Dutch guidelines, the workup for patients diagnosed with rectal cancer consist of endoscopy with biopsy, chest X-ray, an abdominal CT-scan and an MRI of the rectum. Some specialized centres use endorectal ultrasound in addition to MRI, but it is not mandatory. Nodal metastasis was defined according to established radiological criteria: >3 mm in the first version of the guideline, >5 mm in the second version and the addition of morphological features in the revised version in 2014: 1) irregular boundary; 2) heterogeneous texture; 3) round shape. Short axis diameter <5 mm, combined with all three malignant morphological features. Short axis diameter of $\geq$9 mm).

2.3. Subgroups

The population was divided into cT1 patients without nodal involvement (cN0) or unknown nodal involvement (cNx) and those with nodal involvement (cN1/2). Further subdivision was based on the applied treatment strategy: neoadjuvant therapy (NAT) versus no neoadjuvant therapy (no NAT) and subsequently into LE only, primary TME and LE + cTME. Local excision was subdivided into endoscopic resection or transanal surgical excision. To analyse incidence and treatment trends over time, the cohort was subdivided into three time periods: 2005–2009, 2010–2014 and 2015–2018. These time periods are based on relevant events in time such as the introduction of MRI in rectal cancer patients (strongly advised since 2010 and guideline required in 2011) [17] and implementation of population screening in 2014 [17].

2.4. Endoscopic and surgical procedures

Local excision includes both endoscopic resection and transanal surgical excision techniques. Endoscopic techniques include endoscopic polypectomy, endoscopic submucosal dissection (ESD), endoscopic full-thickness resection (eFTR), or endoscopic mucosal resection (EMR). Transanal surgical excision techniques include transanal excision according to Parks, and any rigid or flexible transanal excision platform such as transanal endoscopic microsurgery (TEM), transanal endoscopic operation (TEO) and transanal minimally invasive surgery (TAMIS).

The TME group includes open, laparoscopic or robot-assisted surgery including low anterior resection (LAR), abdominoperineal excision (APE), Hartmann's procedure and rectosigmoidectomy. Noteworthy, for proximal rectal cancers it might be possible that a partial mesorectal excision has been performed. Unfortunately, these specific details are lacking. Completion TME (cTME) was defined as TME surgery within 6 months after primary LE, and includes patients with inadequate resection margins of local surgery, unfavourable histological features and incomplete margins. The 6-month time interval has been previously described and is likely to include all patients who underwent 'completion surgery' [18,19].

2.5. Statistical analysis

Descriptive statistics were used to describe all variables. Continuous variables are presented as median with interquartile range (IQR). Categorical variables are presented as frequency with percentages and statistically compared using the chi-square test or Fisher-exact test, as appropriate. Trend analyses were performed using the Chi Square for Trend test. When analysing trends between the three treatment groups (LE only, primary TME and LE + cTME), one treatment group (e.g., LE) was compared to the rest (e.g., primary TME and LE + cTME).

The accuracy of clinical tumour staging was determined by the number of patients with cT1 tumours who received endoscopic/surgical treatment, in whom a pT1 stage was confirmed after pathological examination of the resection specimen. Neoadjuvant therapy included radiation therapy (RTx), chemotherapy (CTx) or chemoradiation therapy (CRTx). Considering the potential pathological response that may be induced by neoadjuvant therapy, patients treated with neoadjuvant chemoradiation therapy were excluded from the analysis on accuracy of clinical staging. In addition, patients who were treated with neoadjuvant radiation therapy but underwent "delayed" endoscopic/surgical management (i.e. time from incidence to endoscopic/surgical treatment more than 8 weeks) were also excluded for this analysis because this could also induce downstaging.

For all statistical tests, the threshold for significance was set at $P < 0.05$. Statistical Package for Social Sciences (SPSS, Chicago, IL, USA Version 20.0) was used to prepare the database and for statistical analysis.

3. Results

3.1. Patient selection and therapy

According to the NCR, a total of 45,874 Dutch patients were diagnosed with rectal and rectosigmoidal cancer between 2005 and 2018. Of those, 3095 patients (6.7%) were classified as cT1 rectal cancer. Fifty-six patients (1.8%) were diagnosed with distant metastases, one patient was aged <18 years and surgical management

was not specified in five patients. After exclusion of these patients, a total of 3033 patients were included for further analysis. A flow diagram of patient selection, clinical nodal stage and given therapy is illustrated in Fig. 1. Baseline patient and tumour characteristics and therapy strategies divided per clinical nodal stage are depicted in Table 1.

Of all included patients, most were men (61.4%). Median age was 68 years (IQR 62–74) and most patients were diagnosed with clinical N0/x tumours (2867 out of 3033, 94.5%). The majority of all patients (2947 out of 3033, 97.2%) underwent some kind of endoscopic or surgical treatment. A total of 59 patients (1.9%) were registered as not having received treatment at all. The majority of them were male (n = 37, 62.7%) and their median age was 80 years (IQR 71–85). Twenty-seven patients (0.9%) were treated with chemotherapy, radiation therapy or chemoradiation therapy, without endoscopic or surgical therapy. In this group, most patients were male (n = 22, 81.5%) and their median age was 81 years (IQR 66 - 83).

Of the patients diagnosed with clinical N0/x stage, most did not receive NAT (90.8%) and were primarily treated by LE (80.0%). The patients diagnosed with clinical N1/2 stage usually received NAT (72.4%), frequently followed by a TME procedure (96.4%).

3.2. Trends in incidence and treatment over time

Throughout the incidence years, the absolute number of patients diagnosed with clinical T1 rectal cancer increased from 540 patients in 2005–2009, to 1643 patients in 2015–2018 (Fig. 2). In all time periods, most patients were classified as clinical N0/x stage (94.5%, 2867 out of 3033 patients).

3.2.1. Neoadjuvant therapy

During the study period, there was a significant decrease in the use of NAT in patients with cT1N0/x rectal cancer, from 26.6% in 2005–2009 to 0.6% in 2015–2018 (P < 0.001). For patients with cT1N1/2 rectal cancer NAT was administered in 75.0% of patients in 2005–2009 which was statistically not significantly different from 61.8% in 2015–2018 (P = 0.085).

3.2.2. Surgical/endoscopic treatment

3.2.2.1. cT1N0/x. There was a significant increase over time towards LE as definitive endoscopic/surgical treatment compared to TME (primary and cTME) in patients with cT1N0/x rectal cancer, from 43.4% in 2005–2009 to 70.9% in 2015–2018 (P < 0.001) (Fig. 3A). The number of primary TME significantly decreased over time, from 41.6% in 2005–2009 to 18.5% in 2015–2018 (P < 0.001), and simultaneously the number of cTME significantly decreased over time from 15.0% in 2005–2009 to 10.6% in 2015–2018 (P = 0.016) (Fig. 3A). In the group of patients primarily treated with LE (including those who eventually underwent cTME), the percentage of patients receiving endoscopic resection compared to transanal surgical excision significantly increased over time from 55.1% (157 out of 285 patients) in 2005–2009, to 52.6% (276 out of 525 patients) in 2010–2014, and finally to 64.7% (824 out of 1273 patients) in 2015–2018 (P < 0.001).

3.2.2.2. cT1N1/2. There was no significant difference in time towards TME (primary and cTME) compared to LE as definitive treatment in patients with cT1N1/2 rectal cancer (P = 0.320) (Fig. 3B). The number of primary TME significantly decreased over time from 95.0% in 2005–2009 to 74.5% in 2015–2018 (P = 0.017) and on the contrary the number of cTME significantly increased over time from 5.0% in 2005–2009 to 18.2% in 2015–2018 (P = 0.016) (Fig. 3B). There was no significant difference over time between endoscopic resections and transanal excisions in the small group of patients primarily treated with LE (including those who eventually underwent cTME), though a decreasing trend was observed for endoscopic resections namely 100% (1 out of 1 patients) in 2005–2009, 80.0% (8 out of 10 patients) in 2010–2014, and 42.9% (6 out of 14 patients) in 2015–2018 (P = 0.051).

3.3. Clinical tumour accuracy

Results for clinical tumour accuracy per time period and per clinical N stage are presented in Table 2. In the patients treated with endoscopic/surgical therapy (without neoadjuvant therapy except neoadjuvant short-course radiation therapy followed by early surgery), pathological confirmation of clinical T1 stage was observed in 2071 out of 2613 patients (79.3%).

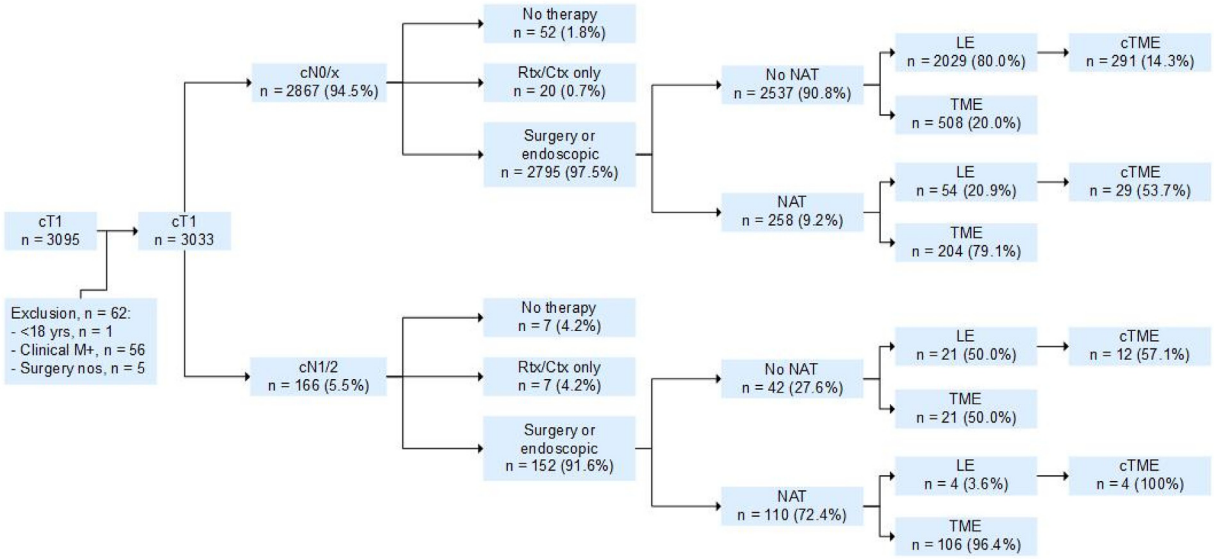

Fig. 1. Flow diagram patient selection, nodal status and given therapy
Abbreviations: LE, local excision; TME, total mesorectal excision; cTME, completion TME; NAT, neoadjuvant therapy; CTx, chemotherapy; RTx, radiotherapy; nos = not otherwise specified.

Table 1
Baseline characteristics Dutch patients with cT1 rectal cancer, subdivided by N stage, N (%) or median [IQR].

Characteristic	All (*n* = 3033)	N0/x (*n* = 2867)	N1/2 (*n* = 166)
Gender			
Female	1172 (38.6)	1108 (38.6)	64 (38.6)
Male	1861 (61.4)	1759 (61.4)	102 (61.4)
Age	68 [62 - 74]	68 [62 - 75]	67 [60 - 74]
Treatment category			
No treatment	59 (1.9)	52 (1.8)	7 (4.2)
RTx/CTx only	27 (0.9)	20 (0.7)	7 (4.2)
Endoscopic/surgical	2947 (97.2)	2795 (97.5)	152 (91.6)
NAT [a]	*n* = 2947	*n* = 2795	*n* = 152
No	2579 (87.5)	2537 (90.8)	42 (27.6)
Yes	368 (12.5)	258 (9.2)	110 (72.4)
NAT category [b]	*n* = 368	*n* = 258	*n* = 110
CTx	1 (0.3)	1 (0.4)	0 (0)
RTx	325 (88.3)[c]	241 (93.4)[c]	84 (76.4)[c]
CRTx	42 (11.4)	16 (6.2)	26 (23.6)
Surgical treatment [a]	*n* = 2947	*n* = 2795	*n* = 152
LE only	1772 (60.1)	1763 (63.1)	9 (5.9)
Primary TME	839 (28.5)	712 (25.5)	127 (83.6)
LE + cTME	336 (11.4)	320 (11.4)	16 (10.5)
Type of LE [d]	*n* = 2108	*n* = 2083	*n* = 25
Endoscopic resection	1272 (60.3)	1257 (60.3)	15 (60.0)
Transanal surgical excision	836 (39.7)	826 (39.7)	10 (40.0)

Abbreviations: LE, local excision; TME, total mesorectal excision; cTME, completion TME; NAT, neoadjuvant therapy; CTx, chemotherapy; RTx, radiotherapy; CRTx, chemoradiotherapy.
[a] In the subgroup of patients who were treated with an endoscopic/surgical procedure.
[b] In the subgroup of patients who received NAT and were subsequently treated with an endoscopic/surgical procedure.
[c] Short-course radiation with early surgery was presumed in n = 184 patients (56.6%), cN0/x n = 134 (55.6%) and cN1/2 n = 50 (59.5%).
[d] In the subgroup of patients who primarily underwent LE.

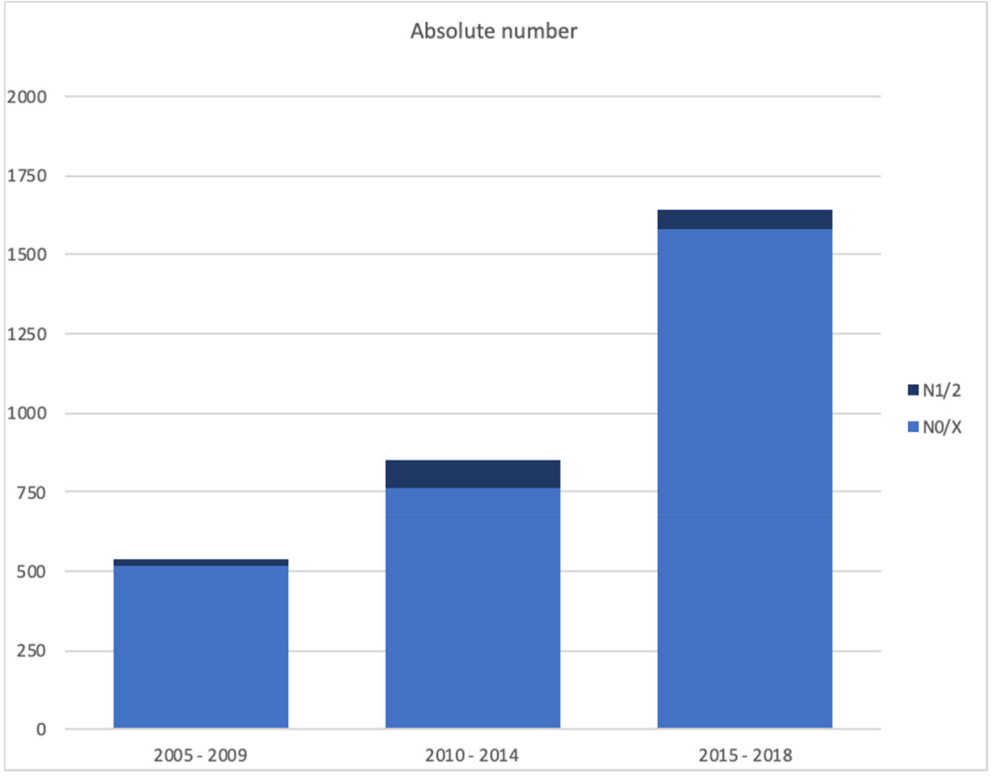

Fig. 2. The absolute number of patients diagnosed with clinical T1 rectal cancer in The Netherlands.

During the study period, there was a significant increase in pathological confirmation of T1 stage, from 67.2% in 2005–2009 to 85.9% in 2015–2018 (P < 0.001). Between patients staged with clinical N0/x stage and clinical N1/2 stage, there was a significant difference in this pathological confirmation (80.6% versus 52.7% respectively, P < 0.001). There was considerable understaging in tumour stage in patients with clinical N1/2 disease, as 45.1% were diagnosed with pT2-4 stage.

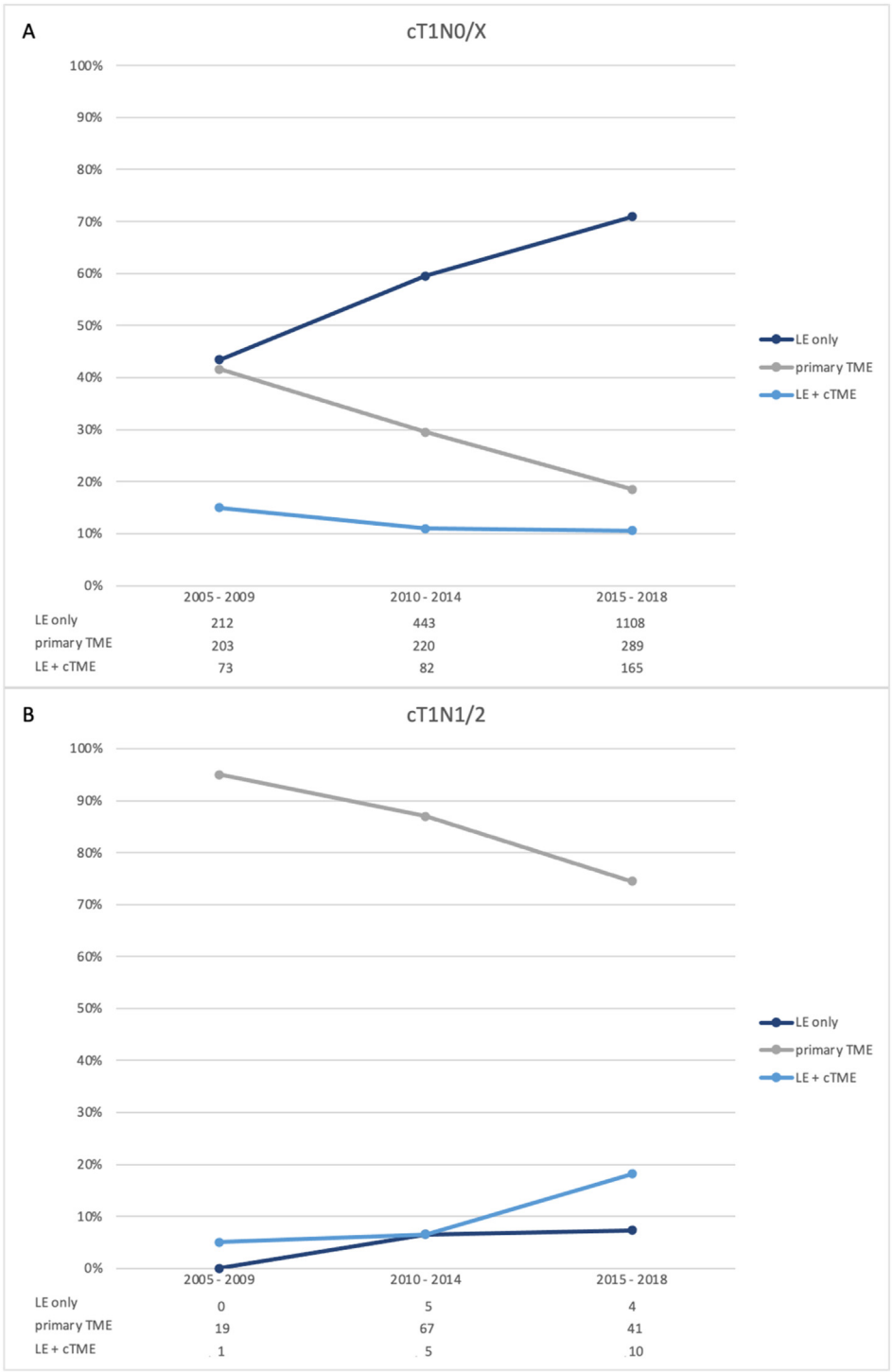

Fig. 3. The proportion of patients with cT1N0/X (A) and cT1N1/2 (B) rectal cancer who were treated with LE only, primary TME or LE + cTME throughout the incidence years.

The significant difference in pathological confirmation between patients staged with clinical N0/x stage and clinical N1/2 stage remained throughout all time periods (2005-2009: 68.5% versus 25.0%, P = 0.009; 2010-2014: 74.2% versus 51.2%, P = 0.004; 2015-2018: 86.5% versus 63.9%, P = 0.001).

4. Discussion

In this large nationwide study, we investigated the trends in incidence and treatment of clinically staged T1 rectal cancer in the Netherlands between 2005 and 2018. The absolute number of patients with cT1 rectal cancer more than tripled over this time period, from 540 patients in 2005–2009 to 1643 patients in 2015–2018. Furthermore, there was a significant increase in the use of LE and concurrently, a significant decrease in the use of neoadjuvant therapy and TME surgery for patients with clinical node negative T1 tumours.

In the Netherlands, an organized (not opportunistic) national

Table 2
Clinical tumour accuracy divided per time period and per clinical N stage, N = 2613.[a].

		pT0	pT1	pT2-4
All time periods	cT1N0/x (n = 2522)	25 (1.0)	2032 (80.6)	465 (18.4)
	cT1N1/2 (n = 91)	2 (2.2)	48 (52.7)	41 (45.1)
2005–2009	cT1N0/x (n = 387)	4 (1.0)	265 (68.5)	118 (30.5)
	cT1N1/2 (n = 12)	0 (0)	3 (25.0)	9 (75.0)
2010–2014	cT1N0/x (n = 644)	12 (1.9)	478 (74.2)	154 (23.9
	cT1N1/2 (n = 43)	1 (2.3)	22 (51.2)	20 (46.5)
2015–2018	cT1N0/x (n = 1491)	9 (0.6)	1289 (86.5)	193 (12.9)
	cT1N1/2 (n = 36)	1 (2.8)	23 (63.9)	12 (33.3)

[a] Patients treated with neoadjuvant chemoradiation therapy, neoadjuvant radiation therapy with delayed endoscopic/surgical therapy or unknown time from incidence to endoscopic/surgical therapy or those classified as pTx were excluded.

screening program for colorectal cancer, coordinated by the National Institute of Public Health and Environment (RIVM) with biennial faecal immunochemical tests followed by a colonoscopy when positive, was gradually implemented in 2014 for all adults aged 55–75 years. In the years 2014–2018, approximately 76% of the invited people responded to the invitation [20]. Although the screening program caused a steep increase of cT1 rectal tumours, an increasing incidence was already observed before the actual start of the program. Pilot studies performed in densely populated areas in the Netherlands prior to this screening might be an explanation for this increasing incidence as well as an increasing awareness and improvements in diagnostic modalities.

Most patients were diagnosed without suspected nodal disease and thus potential candidates for LE (without NAT). Over time, in clinically node negative patients, the use of LE has gained ground. This is supported by recent literature increasingly recommending LE as an attractive alternative to TME surgery due to less procedure-related morbidity and mortality [4–6,8–10,12]. For patients with low risk pT1N0/x rectal cancer, organ preservation is the preferred approach in the Dutch colorectal cancer guidelines. However, the ideal endoscopic or transanal technique for such tumours is still debated as there is a clear lack of high-quality comparative studies [21]. The current study found that most patients with cT1N0/x rectal cancer who underwent LE received a form of endoscopic resection (~60%), and over a time a slight increase in endoscopic resections was observed.

Organ preservation strategies are also more commonly used in higher stages of rectal cancer in several ongoing clinical trials [22]. The current study observed that patients with cT1N1/2 rectal cancer were most frequently treated with TME, but a shift was observed in type of TME. Namely, a significant decrease of primary TME was observed and a significant increase in cTME. This finding may be partially explained by patients entering ongoing clinical trials on organ preservation strategies. Other reasons may be patient's choice or doctor's preference which are influenced by treatment related morbidity and oncologic control. Of note, the numbers in these analyses were very small.

Simultaneous to the increase in LE, the use of (unjustified) NAT in clinical node negative patients decreased. However, in 2005–2009 still 27% of the patients with cT1N0/x received NAT (predominantly radiation therapy). We presume this relatively high number of patients can be partly explained by results from the Dutch prospective randomized TME trial published in 2001. In this trial a significant lower risk of recurrence was observed in patients treated with short-course radiation therapy followed by TME versus TME alone. This led to an increase of radiation therapy in all rectal cancer patients, including early-stage rectal cancer. Later, it became evident that patients with early rectal cancer without nodal involvement do not benefit from short-course radiation therapy and therefore surgery alone was proposed in the Dutch colorectal cancer guidelines as standard approach [23]. This led to a significant decrease in radiation therapy over time in these early rectal cancer patients.

If a suspected T1 rectal cancer proves to be a T2 or more invasive carcinoma after LE, cTME is recommended, leading to similar oncological results as primary TME surgery [24].

In the present study, the proportion of cTME has significantly decreased over time for patients with clinical node negative disease. This might indicate that patient selection has improved, due to more accurate pre-operative staging. Another explanation might be the growing role for a rectal preserving strategy, in which high-risk pT1 and pT2 rectal carcinomas are subject of several studies. In those patients, adjuvant chemoradiotherapy is given as an alternative to cTME [25]. Although this strategy is not yet evidence based, this might contribute to the lower proportion of patients in whom cTME is performed. However, in earlier studies it was also found that fewer patients than expected were subject to cTME, possibly explained by patients and/or doctors' preference. [19] Whether these strategies achieve similar outcomes as compared to cTME, should be looked at with caution, and only be offered within clinical trials [15,26].

In the current study, clinical staging of pT1 tumours was accurate in 77%, which increased to 81% when only cN0/x patients were selected. Over the years, diagnostic accuracy for detection of pT1 tumours improved in patients clinically staged cT1N0/x, from 67% in 2005–2009 to 86% in the period from 2015 until 2018. This major improvement is likely caused by the implementation of high resolution MRI, enabling a more accurate preoperative assessment of the location of the tumour and locoregional disease extent [27]. Nonetheless, nodal staging in rectal cancer remains challenging as has been described in a previous study with data of the NCR [26]. This study reported that during the interval of our study period, clinical nodal staging was insufficient due to limitations in the capacity of MRI in detecting lymph node metastases and recommendations in the Dutch guidelines on criteria used for establishing suspected lymph nodes e.g., >3 mm in the first version of the guideline, >5 mm in the second version and the addition of morphological features in the revised version in 2014.

The use of preoperative MRI in rectal cancer is mandatory since 2011 in the Netherlands and is used in >95% of all rectal cancer patients [17]. More accurate tumour staging might (partially) explain the reduction in cTME procedures over time during the study period. Interestingly, correct diagnosis of pT1 was significantly worse in patients who had suspected positive lymph nodes as 45% of the patients had a higher pathological T stage (compared with 18% in cN0/x patients). This may have a biological explanation, as higher tumour stages harbour a greater metastatic potential (i.e. 6-14% for T1 tumours, 17-23% for T2 tumours and 49-66% for T3 tumours) [28,29]. Although operator-dependent, endorectal ultrasound (ERUS) is an accurate method to preoperatively stage rectal cancers, especially early rectal cancers [30]. Three-dimensional ERUS may further improve staging accuracy [31].

A small number of patients (27 out of 2613, 1%) revealed pT0 at histopathological examination after surgery. One of the possible explanations might be that the tumour was removed at biopsy and final results showed no tumour remnant. A pathological complete response after radiation therapy might be another explanation. As is reported previously, the rate of pathological complete response after short-course radiation therapy followed by early surgery is low (1.7% in the pre-planned interim analysis of the Stockholm III trial) [32]. Unfortunately, our database does not contain exact dates of initiated neoadjuvant therapy, only date of primary diagnosis and date of surgery. Therefore, we choose a time period of 8 weeks from date of diagnosis to date of surgery, as this will have excluded most patients with reasonable potential for downstaging (e.g.,

those with short-course radiation therapy but delayed surgery after 4-8 weeks), but we cannot dispute that few patients with down-staging have been included.

Although this is an extensive and large nationwide study of 3033 patients with cT1 rectal cancer who have been treated over a time period of 14 years, this study has some limitations. First, diagnostic procedures, standards of care and follow-up strategies have changed over the course of time. Unfortunately, data on specific diagnostic modalities used throughout the study period is not available in the NCR. Therefore, possible relevant information on the various imaging modalities is lacking. Secondly, in the database of the NCR no specific tumour characteristics were registered for the total study population. Consequently, differentiation between low risk and high risk T1 rectal cancer could not be performed. This is valuable information, as the absence of lymphatic invasion, budding, submucosal invasion $\geq$1 mm, and poor histological differentiation are each associated with low risk of lymph node metastases [28]. Thirdly, no information regarding the performance status of patients was available for the total study population (e.g. preoperative Charlson Comorbidity Index or ASA classification). In addition, data on quality of life is also lacking. The current study did not focus on survival outcomes. This was previously addressed by our study group [24]. Finally, there is no consensus on the specified time interval for when to still define additional surgery as 'completion surgery' or when to define it as 'salvage surgery' [33]. A 6-month cut-off has been described previously [18,19]. This time period will most likely include all 'completion surgeries', but on the other hand may also include some patients with an early recurrence who by definition received 'salvage surgery'.

5. Conclusion

The current study shows an increase in the incidence of cT1 rectal cancer throughout the years, and a concurrent increase in the use of LE was observed in clinical node negative patients. In addition, neoadjuvant therapy was prescribed less often for these patients, which is in line with national guidelines. Finally, pathological confirmation of pT1 rectal carcinomas increased throughout the years but was significantly higher in clinical node negative patients compared to clinical node positive patients, stressing the need for optimal preoperative staging.

Declarations

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CRediT authorship contribution statement

M. Verseveld: Data curation, Funding acquisition, Formal analysis, Writing – review & editing, Study concepts, Study design, Data acquisition, Quality control of data and algorithms, Data analysis and interpretation, Statistical analysis, Manuscript preparation, Manuscript editing, Manuscript review. **D. Verver:** Data curation, Funding acquisition, Formal analysis, Writing – review & editing, Data acquisition, Quality control of data and algorithms, Data analysis and interpretation, Statistical analysis, Manuscript preparation, Manuscript editing, Manuscript review. **B.J. Noordman:** Data curation, Formal analysis, Writing – review & editing, Quality control of data and algorithms, Data analysis and interpretation, Manuscript preparation, Manuscript editing, Manuscript review. **S. Pouwels:** Data curation, Formal analysis, Writing – review & editing, Quality control of data and algorithms, Data analysis and interpretation, Manuscript preparation, Manuscript editing, Manuscript review. **M.A.G. Elferink:** Data curation, Funding acquisition, Formal analysis, Writing – review & editing, Study concepts, Study design, Data acquisition, Quality control of data and algorithms, Data analysis and interpretation, Statistical analysis, Manuscript preparation, Manuscript editing, Manuscript review. **E.J.R. de Graaf:** Data curation, Formal analysis, Writing – review & editing, Study concepts, Study design, Quality control of data and algorithms, Data analysis and interpretation, Manuscript preparation, Manuscript editing, Manuscript review. **C. Verhoef:** Data curation, Formal analysis, Writing – review & editing, Study concepts, Study design, Quality control of data and algorithms, Data analysis and interpretation, Manuscript preparation, Manuscript editing, Manuscript review. **P.G. Doornebosch:** Data curation, Formal analysis, Writing – review & editing, Study concepts, Study design, Quality control of data and algorithms, Data analysis and interpretation, Manuscript preparation, Manuscript editing, Manuscript review. **J.H.W. de Wilt:** Data curation, Formal analysis, Writing – review & editing, Study concepts, Study design, Quality control of data and algorithms, Data analysis and interpretation, Manuscript preparation, Manuscript editing, Manuscript review.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ejso.2021.11.002.

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