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ABSTRACT

Introduction: In an era of exploring patient-tailored treatment options for colon cancer, preoperative staging is increasingly important. This study aimed to evaluate completeness and reliability of CT-based preoperative locoregional colon cancer staging in Dutch hospitals.
Materials and methods: Patients who underwent elective oncological resection of colon cancer without neoadjuvant treatment in 77 Dutch hospitals were evaluated between 2011 and 2021. Completeness of T-stage was calculated for individual hospitals and stratified based on a 60% cut-off. Concordance between routine CT-based preoperative locoregional staging (cTN) and definitive pathological staging (pTN) was examined.
Results: A total of 59,558 patients were included with an average completeness of 43.4% and 53.4% for T and N-stage, respectively. Completeness of T-stage improved from 4.9% in 2011–2014 to 74.4% in 2019–2021. Median completeness for individual hospitals was 53.9% (IQR 27.3–80.5%) and were not significantly different between low and high-volume hospitals. Sensitivity and specificity for T3-4 tumours were relatively low: 75.1% and 76.0%, respectively. cT1-2 tumours were frequently understaged based on a low negative predictive value of 56.8%. Distinction of cT4 and cN2 disease had a high specificity (>95%), but a very low sensitivity (<50%). Positive predictive values of <60% indicated that cT4 and cN1-2 were often overstaged. Completeness and time period did not influence reliability of staging.
Conclusion: Completeness of locoregional staging of colon cancer improved during recent years and varied between hospitals independently from case volume. Discriminating cT1-2 from cT3-4 tumours resulted in substantial understaging and overstaging, additionally cT4 and cN1-2 were overstaged in >40% of cases.

1. Introduction

Segmental resection is the mainstay of curative treatment for patients with colon cancer (CC) without distant metastases. Additionally, adjuvant chemotherapy is offered to patients with high-risk tumours. There is a growing interest in neoadjuvant chemotherapy (NAC) options for patients with locally advanced CC and (chemo)radiotherapy in case of cT4b sigmoid cancer [1–3]. The benefit of neoadjuvant therapy would be to achieve downsizing and downstaging of the tumour resulting in more radical (R0)

Abbreviations: CT, computed tomography; CC, colon cancer; DCRA, Dutch ColoRectal Audit; NAC, neoadjuvant chemotherapy; PPV, positive predictive value; NPV, negative predictive value; cTNM, clinical TNM stage; pTNM, pathological TNM stage.

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resections and reduction of tumour cell-shedding. Furthermore, systemic therapy might also eradicate circulating tumour cells and distant (micro)metastases [1,4,5]. NAC also has the potential to increase compliance of systematic therapy, because postoperative complications can often lead to postponing or canceling adjuvant chemotherapy [6–10]. In addition, NAC is generally well tolerated [5]. For patients with early-stage CC (T1-2N0M0) might benefit from organ-preserving resections, such as endoscopic resections or colonoscopy-assisted limited wedge resections [11,12]. Both treatment options necessitate adequate preoperative staging of tumours.

Computed tomography (CT) is standard of care for preoperative radiological staging of CC (cTNM) and is vital for a multidisciplinary team to recommend treatment strategy [13]. Most trials regarding NAC include patients with cT3(cd) or cT4 tumours.

In recent years, a growing number of patients with locally advanced CC received NAC in the Netherlands [14] and also in the United States [2]. Based on promising results of neoadjuvant treatment, the 2014 Dutch colorectal cancer treatment guidelines incorporated the use of neoadjuvant treatment in patients with CC [15].

However, studies on reliability of radiological staging show varying results regarding T-staging [16,17]. This questions whether patient-tailored treatment based on CT is justified [16]. Most studies only examined a limited number of cases by specialised radiologists, which might not reflect current daily practice.

This study aimed to evaluate completeness and reliability of CT-based preoperative locoregional colon cancer staging in Dutch hospitals.

2. Materials and methods

2.1. Data set

Data from all CC patients were obtained from the mandatory Dutch ColoRectal Audit (DCRA) database [18], providing information on patients, tumour and treatment characteristics, and postoperative outcomes in 77 participating Dutch hospitals. Ethics committee approval and patients' informed consent were not required due to the use of anonymised data.

2.2. Eligibility criteria

Patients who underwent surgical resection of CC between January 1st 2011 and December 31st 2021 were retrospectively evaluated. Patients with synchronous tumours of the colon, local excision, "watch and wait" strategy, emergency operation, and patients treated with neoadjuvant therapy were excluded.

2.3. Dutch guidelines: preoperative staging and NAC

The Dutch guidelines during the study period stated that an abdominal CT should be performed for the detection of synchronous metastases of colorectal cancer. There were no specific recommendations for locoregional staging of colon cancer during the study period. The 2014 revised version stated that neoadjuvant chemo(radio)therapy should be considered in patients with CC that cannot be radically resected based on preoperative CT-scans [15]. The most recent 2019 guidelines further describe that NAC in patients with cT4bN0-2M0 CC, or chemoradiotherapy in case of cT4bN0-2M0 (recto)sigmoid tumours, might be considered to achieve more R0 resections [13].

2.4. Definitions

We defined completeness of locoregional staging as the percentage of documented cT and cN-staging of all registered patients with complete pT and pN-stage, since incomplete pT and pN-stage was negligible (0.6%, Fig. 1). Low-volume and high-volume hospitals were categorised by the lower three quarter and upper quarter number of procedures performed during the study period, respectively. Reliability of staging was defined as preoperative staging (cT/cN) that correctly predicts definitive pathological staging (pT/pN) and was expressed using the diagnostic test outcome measures described in section 2.5 *Statistical analysis*. The highest or positive TN-stage of two categories was defined as "positive" and the lowest or negative TN-stage was defined as "negative" in confusion matrixes. Understaging was defined as cT/cN-staging lower than the pT/pN-staging. Vice versa, overstaging was defined as cT/cN-staging higher than the pT/pN-staging.

2.5. Statistical analysis

We examined completeness of locoregional staging and concordance between CT-based preoperative locoregional staging and definitive pathological staging (pTN). Patient and tumour characteristics were expressed in numbers and proportions. Normally distributed data were expressed as mean and standard deviation, and non-normally distributed data as median and interquartile range. Fisher's F-test was used to compare variances of completeness between low-volume and high-volume hospitals. No other statistical hypothesis tests were deemed meaningful due to the large number of patients. Confusion matrixes were constructed for T1-2 vs T3-4, T1-3 vs T4, N0 vs N1-2, N0-1 vs N2, N0 vs N2. For T1-3 vs T4 tumours, subgroup analysis for the years 2020–2021 was performed in order to assess the impact of the 2019 guideline revision concerning NAC for cT4b tumours.

Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy with binomial proportion 95% confidence intervals were calculated. Overstaging and understaging were calculated as 1−PPV (false discovery rate) and 1−NPV (false omission rate) respectively [19]. Completeness of T-stage was calculated for individual hospitals and presented in a funnel plot by

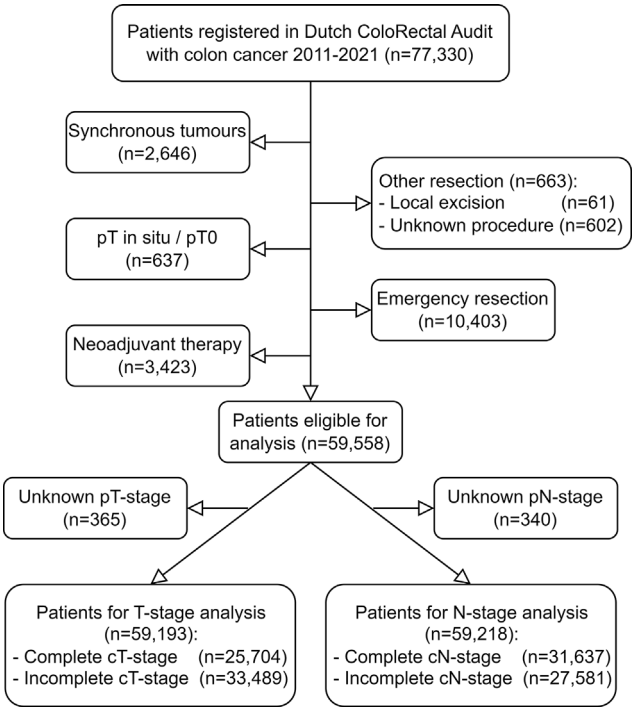

Fig. 1. Flowchart of patient selection.

hospital volume. Funnel plots were constructed for 2011–2014, 2015–2018, 2019–2021, and 2011–2021. To this end, complete T-stage of 60% was used for stratification of hospitals with regards to the potential association between completeness and reliability of pre-operative staging. Lastly, PPV and NPV were calculated for individual years as these are the most appropriate outcomes for predicting the presence or absence of a certain disease stage for individual patients [20]. Statistical analyses were performed with R version 4.2.1.

3. Results

3.1. Study population

A total of 77,330 patients with CC were registered in the DCRA database. In total, 23.0% patients were excluded due to synchronous tumours of the colon, local excision, pT in situ or pT0, emergency operation, or neoadjuvant therapy (Fig. 1). Thus 59,558 patients met the eligibility criteria. Baseline characteristics are described in Table 1. Men constituted 52.5% of patients, 57.2% was ≥70 years, and 77.3% had a BMI ≥18.5 - <30. The sigmoid was the most common tumour location (37.7%). The presence of lymph node metastases ranged from 12.3% to 63.6% in pT1 and pT4 tumours, respectively (Table 2).

3.2. Completeness of locoregional staging

No clinically significant differences were found between patients with complete and incomplete cT-stage (Table 1). Median completeness for individual hospitals was 53.9% (IQR 27.3–80.5%). There was a high variability in completeness of cT-staging between hospitals since 82% of hospitals fell outside the 95% confidence interval control limits of the funnel plot (Fig. 2D). However, variance of completeness between low-volume and high-volume hospitals did not significantly differ ($p = 0.87$). Complete registration of cT-stage ranged from 2.4 to 6.8% in 2011–2014, 55.4–62.1% in 2015–2018, and 72.7–76.2% in 2019–2021 (Fig. 2A-C). Complete cN-stage varied from 2.4 to 6.9% in 2011–2014, 69.7–83.4% in 2015–2018, and 85.1–86.8% in 2019–2021 (Appendix A.1).

3.3. Diagnostic reliability of T-stage

For differentiating cT3-T4 from cT1-T2, a sensitivity, specificity, PPV, NPV, and accuracy of 75.1%, 76.0%, 87.9%, 56.8%, and 75.4% were found, respectively (Table 3). Distinction of cT4 from cT1-3 resulted in higher specificity, NPV, and accuracy. However, sensitivity and PPV were lower if discriminating cT3-4 from cT1-2. In 2020–2021, specificity, PPV, and accuracy were comparable with previous years regarding the distinction of cT4 and cT1-3, although sensitivity and NPV were slightly lower in more recent years (29.9% vs 37.1% and 87.8% vs 90.3%). In 2018–2021, 50.0% of patients with a cT4b tumour (n = 518) were overstaged: 14.1% (n = 73) were pT4a tumours and 35.9% were pT2-3 (pT2: n = 7, pT3: n = 179).

3.4. Diagnostic reliability of N-stage

For detection of lymph node metastases (N1-2 vs N0), sensitivity, specificity, PPV, NPV, and accuracy were 48.2%, 81.5%, 59.4%, 73.7%, and 69.5%, respectively (Table 4). Distinction of N2 from N0-1 resulted in substantially higher specificity, NPV, and accuracy. However, sensitivity and PPV if discriminating N2 from N0-1 were lower compared to the distinction between N1-2 vs N0. For differentiating between N2 and N0, there was a high specificity (96.8%), NPV (92.8%), and accuracy (90.5%), but sensitivity and PPV were low (38.6% and 59.1%, respectively).

3.5. Reliability of cTN-staging at hospital level

During the years 2011–2021, 12 hospitals had >60% complete registration, thus 65 hospitals had ≤60% complete cT-stage. All results of reliability after stratification can be found in Appendix A.2. Most notable differences after stratification were a sensitivity of 37.1% and 27.7% for differentiating cT1-3 from cT4 tumours and a sensitivity of 46.6% and 54.3% for differentiating cN0 from cN1-2 tumours in the groups with ≤60% and >60% completeness, respectively. Positive and negative predictive values differed <5% between hospitals with ≤60% and >60% completeness.

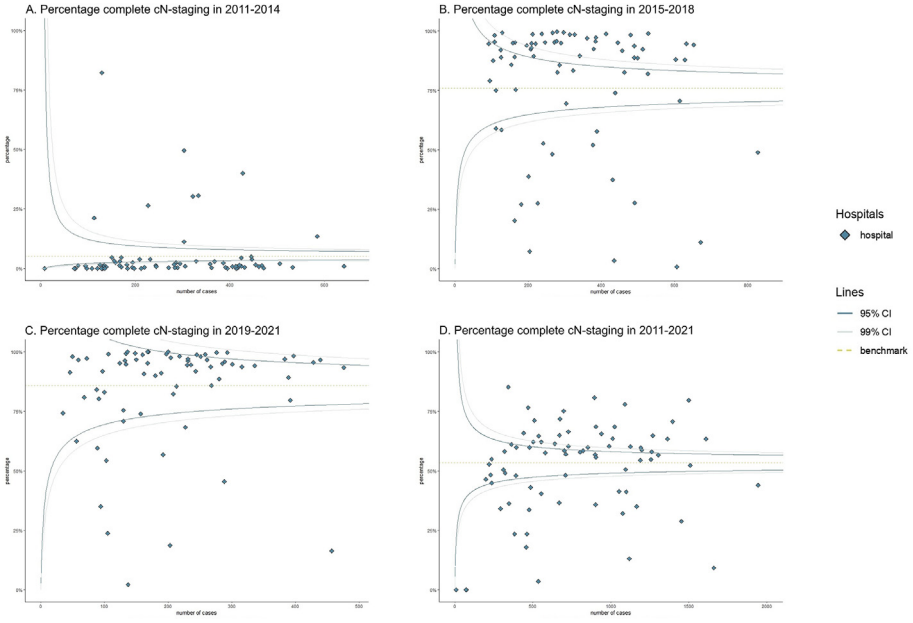

Fig. A.1. Percentage complete cN-staging in 2011-2021
Percentage complete cN-staging in different time periods: (A) 2011–2014, (B) 2015–2018, (C) 2019–2021, and (D) for the entire 2011–2021 study period. Completeness of cN-staging increased between time periods: from 5.2% in 2011–2014%, to 76.0% in 2015–2018, and to 85.9% in 2019–2021.

Table A.2
Concordance between cTN-stage and pTN-stage compared between hospitals with >60% and ≤60% complete T-stage

Groups	≤60% or >60% complete T-stage	Total patients	Number of patients				Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
			TP	TN	FP	FN					
A. Reliability of preoperative staging in differentiating T-stages											
T3-4 vs T1-2	>60%	6,408	3,369	1,542	478	1,019	76.8	76.3	87.6	60.2	76.6
	≤60%	19,296	10,123	4,342	1,382	3,449	74.6	75.9	88.0	55.7	75.0
T4 vs T1-3	>60%	6,408	237	5,372	179	620	27.7	96.8	57.0	89.7	87.5
	≤60%	19,296	1,069	15,648	766	1,813	37.1	95.3	58.3	89.6	86.6
B. Reliability of preoperative staging in differentiating N-stages											
N1-2 vs N0	>60%	6,505	1,288	3,265	868	1,084	54.3	79.0	59.7	75.1	70.0
	≤60%	25,132	4,190	13,252	2,880	4,810	46.6	82.2	59.3	73.4	69.4
N2 vs N0-1	>60%	6,505	212	5,484	232	577	26.9	95.9	47.8	90.5	87.6
	≤60%	25,132	589	21,696	684	2,163	21.4	96.9	46.3	90.9	88.7
N2 vs N0	>60%	3,878	212	3,265	140	261	44.8	95.9	60.2	92.6	89.7
	≤60%	15,268	589	13,252	414	1,013	36.8	97.0	58.7	92.9	90.7

Note: TP = true positive, TN = true negative, FP = false positive, FN = false negative, PPV = positive predictive value, NPV = negative predictive value.

Table 1
Baseline characteristics of patients with complete and incomplete cT-stage.

Baseline characteristic	Complete/Total cT-stage*		Complete/Total cN-stage*	
	n = 25,704/59,193	*%*	*n = 31,637/59,218*	*%*
Gender				
Female	12,276/28,112	43.7	15,086/28,134	53.6
Male	13,428/31,081	43.2	16,551/31,084	53.2
Age				
<70	11,207/25,322	44.3	13,743/25,376	54.2
≥70	14,497/33,871	42.8	17,894/33,842	52.9
BMI				
Unknown	14/65	21.5	15/66	22.7
<18.5	730/1,873	39.0	827/1,881	44.0
≥18.5 - <30	19,817/45,752	43.3	24,300/45,782	53.1
≥30	5,143/11,503	44.7	6,495/11,489	56.5
Tumour location				
Caecum	4,873/11,501	42.4	6,015/11,510	52.3
Ascending colon	6,913/15,701	44.0	8,448/15,707	53.8
Transverse colon	2,007/4,489	44.7	2,476/4,467	55.4
Descending colon	2,357/5,158	45.7	2,922/5,157	56.7
Sigmoid	9,554/22,344	42.8	11,776/22,377	52.6
Date of surgery				
2011	316/4,622	6.8	321/4,674	6.9
2012	226/5,099	4.4	270/5,161	5.2
2013	121/5,008	2.4	119/5,010	2.4
2014	351/6,049	5.8	372/6,052	6.1
2015	3,696/6,666	55.4	4,649/6,672	69.7
2016	3,438/6,154	55.9	4,439/6,167	72.0
2017	3,330/5,570	59.8	4,492/5,558	80.8
2018	3,386/5,450	62.1	4,469/5,357	83.4
2019	3,786/5,206	72.7	4,449/5,200	85.6
2020	3,186/4,293	74.2	3,652/4,293	85.1
2021	3,868/5,076	76.2	4,405/5,074	86.8
pT-stage				
pT unknown	NA		76/297	25.6
pT1	2,753/6,465	42.6	3,773/6,405	58.9
pT2	4,991/11,904	41.9	6,709/11,843	56.6
pT3	14,221/32,947	43.2	16,979/32,831	51.7
pT4	3,739/7,877	47.5	4,100/7,842	52.3
pN-stage				
pN unknown	107/272	39.3	NA	
pN0	15,911/36,968	43.0	20,265/37,242	54.4
pN1	6,547/14,562	45.0	7,831/14,579	53.7
pN2	3,139/7,391	42.5	3,541/7,397	47.9

* = Patients with complete preoperative stage divided by all patients.

Table 2
pT-stage with corresponding pN-stage of patients.

pT-stage	Number of patients	
	n	%
pT1	6,465	
unknown	60	0.9
pN0	5,608	86.7
pN1	695	10.8
pN2	102	1.6
pT2	11,904	
unknown	61	0.5
pN0	9,529	80.0
pN1	1,964	16.5
pN2	350	2.9
pT3	32,947	
unknown	116	0.4
pN0	18,999	57.7
pN1	9,285	28.2
pN2	4,547	13.8
pT4	7,877	
unknown	35	0.4
pN0	2,832	36.0
pN1	2,618	33.2
pN2	2,392	30.4

3.6. Reliability of staging during the years

Mean complete registration of cT-stage was 4.9% in 2011–2014 (Table 1). Therefore, these years were not included for reliability calculations. During the years 2015–2021, absolute improvement of PPV for all groups did not exceed 1.2% while only NPV improved by 1.8% for cN0-1 vs cN2 and decreased for all other groups, most notably 13.7% for cT1-2 vs cT3-4 (Appendix A.3).

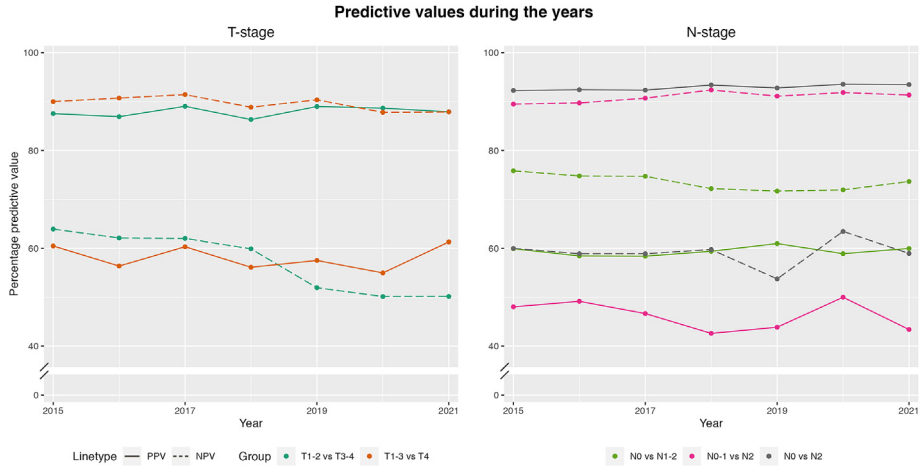

Fig. A.3. Positive predictive values (PPV) and negative predictive values (NPV) during 2015–2021. Improvement of PPV or NPV did not exceed 1.8% in any category, contrarily, predictive values decreased in some categories.

4. Discussion

Preoperative clinical staging of colon cancer is essential for patient-tailored treatment strategies. Therefore, completeness and reliability of CT-based preoperative CC staging in the Netherlands were assessed. In total, 59,787 patients were included of which 43.4% had a registered cT-stage and 53.4% a registered cN-stage. Completeness of preoperative radiological work-up varied in both low-volume and high-volume hospitals, but improved during the study period (from 4.9% in 2011–2014 to 74.4% in 2019–2021). However, hospitals with high completeness did not have clinically significant improved reliability of preoperative staging. Reliability of staging was highly variable: >40% of cT1-2 tumours were understaged, and >40% of cT4 and cN1-2 were overstaged, while 12.1% of cT3-4 were overstaged. In addition, overstaging and understaging did not clinically significantly improve during the study period.

Completeness of locoregional staging is low compared to other variables in the DCRA that often achieve 99% completeness [21] and compared to registries from other countries. For example,

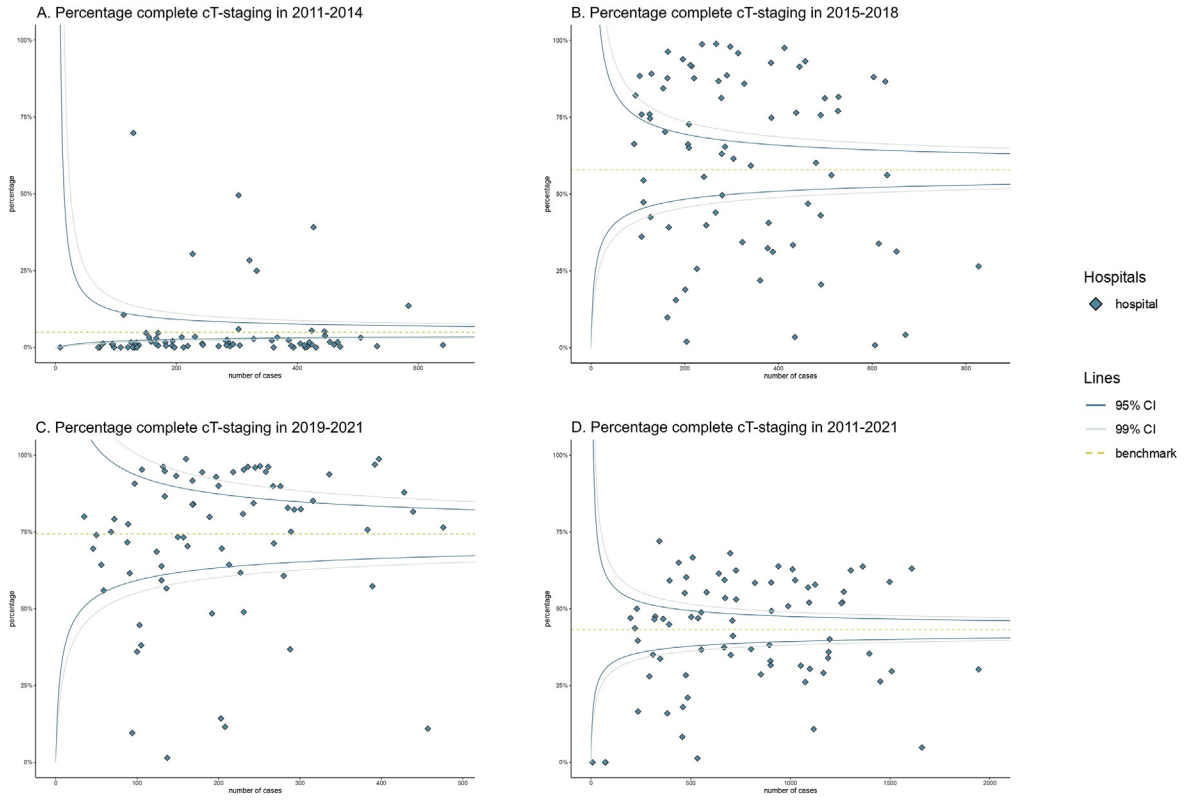

Fig. 2. Percentage complete cT-staging in 2011-2021
Percentage complete cT-staging in different time periods: (A) 2011–2014, (B) 2015–2018, (C) 2019–2021, and (D) for the entire 2011–2021 study period. Completeness of cT-staging increased between time periods. In 2011–2021, 82% of hospitals were outside the 95% confidence interval control limits, thus, indicating a high variability in completeness. Variance of completeness between low-volume and high-volume hospitals did not significantly differ ($p = 0.87$).

Table 3
Concordance between cT-stage and pT-stage.

Radiology, cT-stage	Pathology, pT-stage				
	pT1	pT2	pT3	pT4	Total
cT1	1,673	314	274	41	2,302
cT2	849	3,048	3,685	468	8,050
cT3	226	1,579	9,372	1,924	13,101
cT4	5	50	890	1,306	2,251
Total	2,753	4,991	14,221	3,739	25,704

A. Reliability of preoperative staging in differentiating pT3-4 from pT1-2	
Sensitivity	75.1% (74.5–75.8)
Specificity	76.0% (75.0–76.9)
Positive predictive value	87.9% (87.5–88.3)
Negative predictive value	56.8% (56.1–57.5)
Accuracy	75.4% (74.9–75.9)
B. Reliability of preoperative staging in differentiating pT4 from pT1-3	
Sensitivity	34.9% (33.4–36.5)
Specificity	95.7% (95.4–96.0)
Positive predictive value	58.0% (56.2–59.9)
Negative predictive value	89.6% (89.4–89.8)
Accuracy	86.9% (86.4–87.3)
C. Reliability of preoperative staging in differentiating pT4 from pT1-3 in 2011–2019	
Sensitivity	37.1% (35.2–39.0)
Specificity	95.6% (95.3–95.9)
Positive predictive value	57.9% (55.8–60.0)
Negative predictive value	90.3% (90.1–90.6)
Accuracy	87.4% (86.9–87.9)
D. Reliability of preoperative staging in differentiating pT4 from pT1-3 in 2020–2021	
Sensitivity	29.9% (27.2–32.7)
Specificity	96.0% (95.4–96.4)
Positive predictive value	58.3% (54.6–62.0)
Negative predictive value	87.8% (87.4–88.2)
Accuracy	85.4% (84.6–86.2)

Note: Values in parentheses are 95% confidence intervals.

Table 4
Concordance between cN-stage and pN-stage.

Radiology, cN-stage	Pathology, pN-stage			
	pN0	pN1	pN2	Total
cN0	16,517	4,620	1,274	22,411
cN1	3,194	2,849	1,466	7,509
cN2	554	362	801	1,717
Total	20,265	7,831	3,541	31,637

A. Reliability of preoperative staging in differentiating pN1-2 from pN0	
Sensitivity	48.2% (47.3–49.1)
Specificity	81.5% (81.0–82.0)
Positive predictive value	59.4% (58.5–60.2)
Negative predictive value	73.7% (73.3–74.1)
Accuracy	69.5% (69.0–70.0)
B. Reliability of preoperative staging in differentiating pN2 from pN0-1	
Sensitivity	22.6% (21.3–24.0)
Specificity	96.7% (96.5–96.9)
Positive predictive value	46.6% (44.5–48.9)
Negative predictive value	90.9% (90.7–91.0)
Accuracy	88.5% (88.1–88.8)
C. Reliability of preoperative staging in differentiating pN2 from N0	
Sensitivity	38.6% (36.5–40.7)
Specificity	96.8% (96.5–97.0)
Positive predictive value	59.1% (56.7–61.5)
Negative predictive value	92.8% (92.6–93.1)
Accuracy	90.5% (90.0–90.9)

Note: Values in parentheses are 95% confidence intervals.

completeness of locoregional staging was 65.7–71.6% in the Swedish Colorectal Cancer Registry [22]. Incomplete registration could be due to multiple reasons: limited entry of preoperative staging in the database since it is an optional variable, not reporting according to the TNM classification (i.e. description of tumour growth pattern and size instead of cT-stage) [23], and missing reports of the radiologist or the multidisciplinary team. Unfortunately, no distinction could be made due to the retrospective nature of the study. The increased completeness in our study, especially since 2014, is conceivably related to the first mention of NAC in the 2014 Dutch guidelines. Similarly, an increase in locoregional staging was found in a Swedish hospital during this period [23].

In the context of patient-tailored treatment, understaging could lead to under-treatment, such as inappropriate use of organ-preserving surgery or omitting neoadjuvant treatment. Vice versa, overstaging may lead to over-treatment with risk of associated morbidity.

Regarding differentiating cT1-T2 from cT3-T4, 43.2% of patients with cT1-2 were understaged and 12.1% of patients with cT3-4 were overstaged. A meta-analysis (n = 300) concerning the diagnostic reliability of CT found similar overstaging (11%) of cT3-4 tumours, but a far lower understaging (13%) of cT1-T2 tumours [17]. A study with 105,569 patients from the United States national database had just 0–1% overstaging of cT3-4, which is not in line with any other study and may have resulted from differential misclassification bias [24]. More in line with our results, a large cohort study and a Swedish registry study had 7% and 12% overstaging of cT3-4, and 64% and 51% understaging of cT1-2, respectively [25,26].

Regarding the detection of lymph node metastases (cN1-2 vs cN0), there was a PPV and NPV of 59.4% and 73.7%, respectively. Even if the radiologist reports a cN2, 32.3% of patients had no confirmed lymph node metastases, which is slightly better than the 45.9% pN0 after cN2 staging found in a Danish registry [16]. Other studies also found a low diagnostic value for predicting lymph node metastases [17,25–29]. Therefore, N-stage is often not used as an inclusion criterion for NAC. A prospective cohort study on the administration of NAC to patients with cT4N2 tumours found that NAC resulted in significant downstaging of N-stage (and T-stage) compared to baseline cTN-staging [4]. Likewise, in another prospective study, downstaging of N-stage after NAC was observed in 60.0% of patients staged as cN1-2 [3]. In our cohort, 44.5% of cN1-2 had a lower N-stage. Downstaging of N-stage in these NAC studies can, at least partially, be explained by overstaging as evident from our results, and this hypothesis is further supported by the PRODIGE-22 study [30]. PRODIGE-22 is the only randomised controlled trial in which N-stage (cN2) was a criterion in addition to T-staging for NAC, which contributed to overstaging of 33% patients in the control group that were ineligible for adjuvant chemotherapy.

The 2020 NICE guidelines mention, in line with the 2014 Dutch guidelines, that neoadjuvant chemo(radio)therapy could be considered for patients with cT4 tumours to increase R0 resections [15,31]. In our cohort, 42.0% of patients with a cT4 tumour were overstaged, similar to overstaging of 43.8–52.8% of patients with cT4 tumours in three large cohorts [25,26,32], but only 2.4% of patients with a cT4 tumour had a pT1-2 tumour. The most recent 2019 Dutch guidelines mention that NAC could be considered for cT4bN0-2M0 [13], similar to the NCCN guidelines [33]. Since 2018, the DCRA subdivides cT4-stage in cT4a and cT4b tumours. In 2018–2021, 50.0% of patients with a cT4b tumour were overstaged and 35.9% of cT4b tumours were in fact pT2-3.

It is important to note that our study results show that there is a proportion of overstaging. Therefore, some patients would receive NAC as a result of overstaging that would not be indicated according to current guidelines or study protocols.

The FOxTROT randomised controlled trial showed promising results and a good tolerability of NAC in 2012 [1] with more studies investigating NAC since then [3,4,29,30,34–37]. The long-term results of the FOxTROT trial show better disease control at 2-years with an absolute 4% improvement, but no significant long-term survival benefits [38]. Therefore, more randomised controlled trials are needed to better define the patients who might benefit from NAC [38–40]. Based on the present data, overstaging by CT should be considered as an important clinical issue if this results in overtreatment by NAC.

4.1. Strengths and limitations

This study is the largest nationwide cohort on reliability and completeness of CT-based locoregional CC staging. The DCRA is a mandatory registration for all Dutch hospitals, thus this study demonstrates clinical practice and trends during an eleven-year time period. Despite incompleteness of staging, reliability of preoperative staging in this study was representative for patients with a single colonic cancer undergoing elective surgery without NAC, since pTN-stage of patients with complete and incomplete cT-stage did not clinically significantly differ.

A limitation was that data about radiologists' experience and their expertise was lacking, but it does represent daily-practice in the Netherlands. Literature about the influence of experience provides inconsistent results. In two studies, radiologists trained for the FOxTROT trial independently assessed cases for eligibility in the study, but PPV did not exceed 86.0% while having only moderate interobserver agreement [41–43]. In contrast, a Dutch study showed improved preoperative staging after training concerning some outcomes, but not regarding PPV [27]. In our study, there were no clinically significant differences in reliability of preoperative staging between hospitals stratified for 60% completeness of staging registration. This could suggest that increased awareness and attention of the radiologists and multidisciplinary teams do not improve reliability of cTN-staging.

Secondly, no information about the CT-scanners could be obtained from the DCRA. Nerad et al. demonstrated that slice thickness <5 mm improved reliability. Some studies found that MRI, either without or in combination with CT, could improve diagnostic reliability [44–46]. In addition, interobserver agreement with MRI for T-stage might be higher than with CT [46–48]. However, lymph node staging with MRI remains unreliable [45,47–50]. Other modalities, such as CT-colonography [17], PET-CT [51–53], or ultrasound [54,55] have been suggested as alternatives to CT or MRI, but studies are limited and results vary.

5. Conclusion

In Dutch hospitals, completeness of locoregional CC staging improved in recent years. Completeness varied between hospitals independently from case volume, but this did not substantially influence reliability of preoperative staging. Likewise, reliability of staging did not improve during recent years. Nearly half of cT1-2 tumours were understaged while 12% of cT3-4 tumours were overstaged. In contrast, >40% of cT4 and cN1-2 categories were overstaged. Therefore, selecting patients with CC for future tailored treatment options will be challenging using current CT-based staging techniques.

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CRediT authorship contribution statement

Daan J. Sikkenk: Conceptualization, Methodology, Software, Validation, Formal analysis, Investigation, Resources, Data curation, Writing – original draft, Visualization, Funding acquisition. **Julie M.L. Sijmons:** Conceptualization, Methodology, Software, Validation, Formal analysis, Investigation, Resources, Data curation, Writing – original draft, Visualization, Project administration. **Thijs A. Burghgraef:** Conceptualization, Methodology, Formal analysis, Writing – review & editing, Supervision. **Ilias Asaggau:** Conceptualization, Methodology, Writing – review & editing. **Annelotte Vos:** Conceptualization, Methodology, Writing – review & editing, Supervision. **David W. da Costa:** Conceptualization, Methodology, Writing – review & editing, Supervision. **Inne Somers:** Conceptualization, Methodology, Writing – review & editing, Supervision. **Paul M. Verheijen:** Conceptualization, Methodology, Writing – review & editing, Supervision, Funding acquisition. **Jan-Willem T. Dekker:** Conceptualization, Methodology, Writing – review & editing, Supervision. **Wouter B. Nagengast:** Conceptualization, Methodology, Writing – review & editing, Supervision. **Pieter J. Tanis:** Conceptualization, Methodology, Validation, Formal analysis, Investigation, Resources, Data curation, Writing – review & editing, Supervision, Project administration. **Esther C.J. Consten:** Conceptualization, Methodology, Validation, Formal analysis, Investigation, Resources, Data curation, Writing – review & editing, Supervision, Project administration, Funding acquisition.

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