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Predictive value of selected geriatric parameters for postoperative outcomes in older patients with rectal cancer – A multicenter cohort study

T.E. Argillander [a,b,*,1], H.C. van der Hulst [c,1], H.J. van der Zaag-Loonen [b], P. van Duijvendijk [a], J. W.T. Dekker [c], J.M. van der Bol [d], E. Bastiaannet [e], J. Verkuyl [f], P. Neijenhuis [g], M. Hamaker [h], A.H. Schiphorst [i], T.S. Aukema [j], T.A. Burghgraef [k], D.J.A. Sonneveld [l], J.S. Schuijtemaker [m], W. van der Meij [n], F. van den Bos [o], J.E.A. Portielje [p], E.T.D. Souwer [p,2], B.C. van Munster [b,2]

[a] Department of Surgery, Gelre Hospitals, Apeldoorn, the Netherlands
[b] University of Groningen, University Medical Center Groningen, University Center of Geriatric Medicine, Groningen, the Netherlands
[c] Department of Surgery, Reinier de Graaff Hospital, Leiden, the Netherlands
[d] Department of Geriatric Medicine, Reinier de Graaf Hospital, Delft, the Netherlands
[e] Department of Surgery, Leiden University Medical Center, Leiden, the Netherlands
[f] Department of Geriatric Medicine, Martini Hospital, Groningen, the Netherlands
[g] Department of Surgery, Alrijne Hospital, Leiderdorp, the Netherlands
[h] Department of Geriatrics, Diakonessenhuis, Utrecht, the Netherlands
[i] Department of Surgery, Diakonessenhuis, Utrecht, the Netherlands
[j] Department of Surgery, Haga Hospital, The Hague, the Netherlands
[k] Department of Surgery, Meander Medical Center, Amersfoort, the Netherlands
[l] Department of Surgery, Dijklander Hospital, Hoorn, the Netherlands
[m] Department of Geriatrics, Dijklander Hospital, Hoorn, the Netherlands
[n] Department of Surgery, Bernhoven Hospital, Uden, the Netherlands
[o] Department of Geriatric Medicine, University Medical Center Utrecht, Utrecht, the Netherlands
[p] Department of Medical Oncology, Leiden University Medical Center, Leiden, the Netherlands

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ABSTRACT

Introduction: Older patients have a higher risk for complications after rectal cancer surgery. Although screening for geriatric impairments may improve risk prediction in this group, it has not been studied previously.
Methods: We retrospectively investigated patients ≥70 years with elective surgery for non-metastatic rectal cancer between 2014 and 2018 in nine Dutch hospitals. The predictive value of six geriatric parameters in combination with standard preoperative predictors was studied for postoperative complications, delirium, and length of stay (LOS) using logistic regression analyses. The geriatric parameters included the four VMS-questionnaire items pertaining to functional impairment, fall risk, delirium risk, and malnutrition, as well as mobility problems and polypharmacy. Standard predictors included age, sex, body mass index, American Society of Anesthesiologists (ASA)-classification, comorbidities, tumor stage, and neoadjuvant therapy. Changes in model performance were evaluated by comparing Area Under the Curve (AUC) of the regression models with and without geriatric parameters.
Results: We included 575 patients (median age 75 years; 32% female). None of the geriatric parameters improved risk prediction for complications or LOS. The addition of delirium risk to the standard preoperative prediction model improved model performance for predicting postoperative delirium (AUC 0.75 vs 0.65, $p = 0.03$).
Conclusions: Geriatric parameters did not improve risk prediction for postoperative complications or LOS in older patients with rectal cancer. Delirium risk screening using the VMS-questionnaire improved risk prediction for delirium. Older patients undergoing rectal cancer surgery are a pre-selected group with few impairments. Geriatric screening may have additional value earlier in the care pathway before treatment decisions are made.

* Corresponding author at: Department of Surgery, Gelre Hospitals, Albert Schweitzerlaan 31, 7334 DZ Apeldoorn, the Netherlands.
E-mail address: t.e.argillander@umcg.nl (T.E. Argillander).
[1] Contributed equally to this work and share first co-authorship.
[2] Share last co-authorship.

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1. Introduction

Colorectal cancer (CRC) is the third most common malignancy in the West with rectal cancer accounting for 30% of the cases. The median age at diagnosis for rectal cancer patients is 63 years and a substantial proportion are above 70 years of age [1]. Surgery remains the cornerstone of treatment. Older patients are at an increased risk of postoperative complications and mortality [2], and the occurrence of any complication is associated with a decreased postoperative quality of life in older patients with rectal cancer [3]. However, older patients are also a heterogeneous group with regard to comorbidities, physical capabilities and the presence of geriatric impairments such as decreased mobility, malnutrition, polypharmacy and cognitive problems. Several studies have found an association between these geriatric impairments and adverse postoperative outcomes in older patients with CRC [4–7]. Adequate risk stratification in older patients is required to support informed decision-making and to adjust perioperative strategies such as the implementation of prehabilitation (preoperative physical optimization) programs.

One method to screen for possible geriatric impairments is the Dutch Patients Safety program ('VeiligheidsManagementSysteem', VMS) [8]. The VMS-questionnaire encompasses four geriatric domains: fall risk, malnutrition risk, delirium risk, and physical impairments [8], and is meant to be administered to all older patients (>70 years) admitted to the hospital. Patients diagnosed with impairments can receive additional care according to their needs (e.g., supplements in case of malnutrition, delirium prevention, or fall prevention measures). For hospitalized older patients, higher scores on the frailty screening using the VMS-questionnaire are associated with adverse outcomes and six-month mortality [9,10]. A recent study by Souwer et al. in 550 older patients with CRC showed that an increasing number of geriatric impairments as measured with the VMS was associated with postoperative complications and lower overall survival [6]. In their subsequent study, Souwer et al. developed a prediction model for severe postoperative complications in older patients with CRC. After adding the geriatric domains of the VMS, polypharmacy and the use of mobility aid to standard preoperative variables, the model's predictive value marginally improved [11]. Geriatric impairments have been incorporated in few other prediction models for older patients with CRC [11–14]. Although, compared to colon cancer, the treatment of rectal cancer is more often multimodal and rectal surgery is associated with higher morbidity rates [15], the predictive value of geriatric parameters has not been previously assessed specifically in patients undergoing surgery for rectal cancer [16].

Therefore, the aim of this study was to determine whether the addition of geriatric risk factors (physical impairment, fall risk, malnutrition risk, delirium risk, polypharmacy, and use of mobility aid) to standard preoperative prognostic variables improves the predictive value for adverse postoperative outcomes in older patients with rectal cancer.

2. Methods

2.1. Study Design and Patient Inclusion

In this retrospective multicenter study in nine hospitals in The Netherlands (Alrijne Hospital in Leiderdorp, Diakonessenhuis in Utrecht, Haga Hospital in the Hague, Martini Hospital in Groningen, Reinier de Graaf Hospital in Delft, Dijklander Hospital in Hoorn, Gelre Hospital in Apeldoorn, Meander Medical Center in Amersfoort, Bernhoven Hospital in Uden), patients aged 70 years and older who underwent elective surgery for non-metastatic rectal cancer were eligible for inclusion. Patients who underwent transanal endoscopic microsurgery or who received palliative treatment for other forms of cancer were excluded. All participating hospitals provided perioperative care according to the Enhanced Recovery After Surgery (ERAS) protocol [17]. In most hospitals in The Netherlands, all electively admitted patients 70 years and older are subjected to the VMS questionnaire. The inclusion periods ranged between the hospitals depending on when VMS-questionnaires were administered (Supplementary Table S1). The study complies with the Declaration of Helsinki and was approved by the institutional review boards of the participating hospitals.

2.2. Data Collection

Patients' demographics, tumor characteristics, and postoperative outcomes within 30 days after surgery were prospectively registered according to nationwide data collection for the Dutch ColoRectal Audit (DCRA): age, sex, American Society of Anesthesiologists (ASA)-score [18], comorbidities (Charlson Comorbidity Index [CCI] [19]), tumor stage according to the American Joint Committee on Cancer (AJCC) [20], surgical approach (laparoscopic or open), surgical procedure (low anterior resection (LAR) or abdominal perineal resection (APR)/ Hartmann's procedure), construction of a stoma, (neo)adjuvant therapy, and postoperative outcomes. The dataset was retrospectively manually completed in a cloud-based database (Castor EDC) [21] by a resident physician or a medical student with information from the Electronic Medical Records (EMR): body mass index (BMI), geriatric parameters, postoperative delirium, and discharge destination.

2.3. Geriatric Parameters

The VMS-questionnaire consists of four geriatric parameters: fall risk, delirium risk, malnutrition risk, and functional impairment. The questionnaire was administered preoperatively by nursing staff and entered into the EMR. Fall risk was present if the patient had experienced a fall in the previous six months. Delirium risk was present if at least one out of the three questions (presence of cognitive problems, needing help with self-care in the past 24 h, or a history of delirium) was answered with "yes". Malnutrition risk was assessed using the Short Nutritional Assessment Questionnaire [22] or the Malnutrition Universal Screening Tool [23]. Patients with a score of ≥2 were considered at risk. Functional impairment was defined as a Katz activities of daily living (ADL) score ≥ 2 based on six items (one point if assistance was needed): bathing, dressing, toileting, eating, transferring from bed to chair, and the use of any incontinence material [24]. In Martini hospital, the item 'need help with eating' was replaced with 'use of a walking aid', and only the total score (≥2 vs <2) was available. Information on polypharmacy (use of five or more medications) and the use of mobility aid (with the exception of Martini hospital) were also collected from the EMR.

2.4. Outcomes

The primary outcome was the occurrence of any complications within 30 days after surgery. The secondary outcomes were severe complications (Clavien-Dindo classification [25] ≥3) requiring reintervention, unplanned intensive care unit (ICU) admission, or leading to death, postoperative delirium, 30-day mortality, discharge to another institution, and length of stay (LOS). Prolonged LOS was defined as >14 days, based on the DCRA definition of a complicated postoperative course. Postoperative delirium was present if the diagnosis delirium was registered by the treating physician or a geriatrician, haloperidol was prescribed, or a Delirium Observation Screening Scale ≥3 was registered in the medical record. Discharge to another institution was defined as a (temporary) discharge to a rehabilitation center or nursing home if the patient was living at home prior to surgery. Patients who died during hospital admission were excluded from the analyses for this outcome.

2.5. Statistical Analysis

Continuous variables were presented as mean and standard

deviation (SD) or as median and interquartile range (IQR). Frequencies were presented as number and percentage.

We aimed to assess whether geriatric parameters can improve risk prediction compared to only standard preoperative predictors regarding the primary and secondary study outcomes. First, we built a logistic regression model for each outcome using only standard preoperative parameters (standard model). The parameters that were considered included age, sex (male vs female), ASA-score (III-IV vs I-II), CCI (score $\geq$ 2 vs <2), tumor stage (III vs 0-II), neoadjuvant therapy (present vs absent), and obesity (BMI $\geq$30 vs <30). Univariable logistic regression analyses were performed to determine associations between each variable and outcome and reported as odds ratios (OR) with 95% confidence intervals (CI). The standard model was then built using manual forward selection where predictor variables were added one by one starting with the variable that had the strongest association with the outcome (smallest *p*-value). At each step, changes in model performance were evaluated by comparing the Area Under the Curves (AUC) and 95% CIs using the Hanley & McNeil method [26]. Each new variable was retained in the standard model if it significantly improved the model performance (significant difference between AUCs [$p < 0.05$]).

Second, we evaluated whether geriatric parameters (functional impairment, delirium risk, fall malnutrition risk, fall risk, mobility aid, or polypharmacy) could be used to improve the predictive ability of the standard model. For each outcome, the model performance between the standard model and the model including each geriatric parameter was again compared by measuring differences in the AUCs using the Hanley & McNeil method [26]. To avoid overfitting, a maximum of one variable per ten outcome events was allowed in each model [27]. Comparisons between AUCs were performed using MedCalc (MedCalc Software LtD, Ostend, Belgium). All other analyses were performed using SPSS version 25.0. A two-tailed *p*-value <0.05 was considered statistically significant for all analyses.

3. Results

3.1. Patient Inclusion

Flow chart of study inclusion is depicted in Fig. 1. A total of 632 patients underwent resection for rectal cancer during the inclusion periods. Of these, 57 patients were excluded due to the prespecified exclusion criteria, leaving 575 patients for the analyses.

3.2. Baseline and Treatment Characteristics of Included Patients

The baseline characteristics of included patients are summarized in Table 1. The median age was 75 years (IQR 73–80) and 185 (32.2%) patients were female. The ASA-score was III-IV in 145 (25.2%) patients and 140 (24.3%) patients had CCI score of 2 or higher.

The tumor stage was I in 213 (37.0%) patients, II in 171 (29.7%) patients and III in 162 (28.2%) patients. For two patients (0.3%), the T-stage was not known (these patients had AJCC stage I-II).

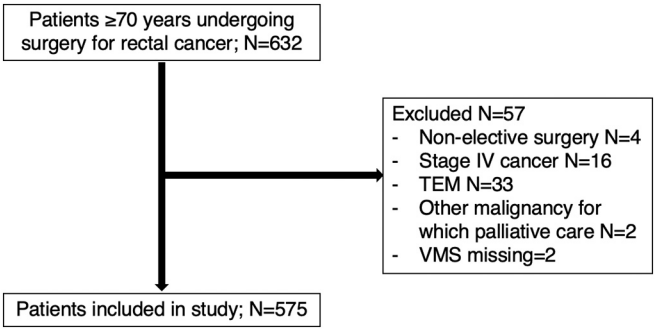

Fig. 1. Flow chart of patient inclusion.

A total of 468 (81.4%) patients underwent a LAR (226 [48.3%] without a stoma, 242 [51.7%] with stoma). Sixty (10.4%) patients underwent APR or Hartmann's procedure. For 47 (8.2%) patients the type of resection was not known but all received a stoma without anastomosis. Laparoscopic or open surgery was performed in 467 (81.2%) and 108 (18.8%) patients, respectively. A total of 287 (49.9%) patients underwent neoadjuvant therapy (radiotherapy (N = 180, 31.3%) or chemoradiation (N = 107, 18.6%). Twenty-four (4.2%) patients received adjuvant chemotherapy.

3.3. Geriatric Parameters

Data on geriatric parameters are shown in Table 2. A total of 329 (57.2%) had at least one geriatric risk factor. The most often reported geriatric parameters were polypharmacy (N = 241 [41.9%]), malnutrition risk (N = 84 [14.6%]), and delirium risk (N = 82 [14.3%]). Most patients were at risk for delirium due to reporting having cognitive problems (N = 42 [51.2%]). Fall risk and functional impairment were reported for 43 (7.5%) and 25 (4.3%) patients, respectively. Forty-two (7.3%) patients used a mobility aid.

3.4. Baseline and Treatment Characteristics Between Patients with at Least One Geriatric Risk Factor and Patients Without Geriatric Risk Factors

Table 3 shows the baseline characteristics between patients with at least one geriatric risk factor (N = 329) and patients without any risk factors (N = 155). For 91 (15.8%) patients, data on at least one geriatric

Table 1
Patient, tumor and treatment characteristics.

		Total N = 575 (%)
Age, median (IQR)		75.5 (72.9–80.4)
Sex		
	Male	390 (67.8)
	Female	185 (32.2)
BMI, median (IQR) (missing: 22)		26.0 (23.8–28.1)
ASA-score		
	I/II	430 (74.8)
	III/IV	145 (25.2)
Charlson Comorbidity Index		
	0–1	435 (75.7)
	≥2	140 (24.3)
AJCC stage[a]		
	Stage 0	27 (4.7)
	Stage I	213 (37.0)
	Stage II	171 (29.7)
	Stage III	162 (28.2)
Surgical approach		
	Laparoscopic	467 (81.2)
	Open	108 (18.8)
Type of surgery		
	LAR without stoma	226 (39.3)
	LAR with stoma	242 (42.1)
	Abdominoperineal resection / Hartmann surgery	60 (10.4)
	Not specified	47 (8.2)
Neoadjuvant therapy		
	None	288 (50.1)
	Short course radiotherapy	180 (31.3)
	Chemoradiation	107 (18.6)
Adjuvant chemotherapy		
	No	548 (95.3)
	Yes	24 (4.2)
	Missing	3 (0.5)

Abbreviations: *AJCC* American Joint Committee on Cancer; *ASA* American Society of Anesthesiologists; *APR* abdominoperineal resection; *BMI* body mass index; *IQR* interquartile range; *LAR* low anterior resection.

[a] For two patients, the T-stage was missing, but the N-stage was 0 (AJCC stage I-II).

Table 2
Geriatric parameters.

	Total N = 575 (%)
VMS: Risk of delirium	
No (score 0)	474 (82.4)
Yes (score 1–3)	82 (14.3)
Missing	19 (3.3)
VMS: Risk of falls	
No	493 (85.7)
Yes	43 (7.5)
Missing	39 (6.8)
VMS: Risk of malnutrition	
No (SNAQ 0–1)	461 (80.2)
Yes (SNAQ 2–6)	84 (14.6)
Missing	30 (5.2)
VMS: Functional impairment (KATZ-ADL)	
Not impaired (score 0–1)	537 (93.4)
Impaired (score 2–6)	25 (4.3)
Missing	13 (2.3)
Polypharmacy (≥5 medications)	
No	327 (56.9)
Yes	241 (41.9)
Missing	7 (1.2)
Use of mobility aid	
No	405 (70.4)
Yes	42 (7.3)
Missing	128 (22.2)

Abbreviations: *ADL* Activities of Daily Living; *SNAQ* Short Nutritional Assessment Questionnaire; *VMS* 'VeiligheidsManagementsSysteem' Safety Management System.

parameter was missing and they were not included in the analyses. Patients with at least one risk factor were older ($p < 0.001$), more often female ($p = 0.02$), had higher ASA-scores ($p < 0.001$) and more comorbidities ($p < 0.001$). They more often underwent open surgery ($p < 0.001$) and APR or Hartmann's procedure ($p < 0.001$).

Table 3
Comparison of baseline and treatment characteristics between patients without any geriatric risk factors and patients with at least one geriatric risk factor.

	No risk factors N = 154 (%)	At least one risk factor N = 329 (%)	p-value
Age, median (IQR)	74.8 (72.4–78.6)	76.2 (73.3–81.3)	<0.001
Sex			0.02
Male	116 (75.3)	213 (64.7)	
Female	38 (24.7)	116 (35.3)	
BMI, median (IQR)	25.8 (23.6–28.0)	26.3 (24.0–28.4)	0.17
ASA-classification			<0.001
I-II	137 (89.0)	209 (63.5)	
III-IV	17 (11.0)	120 (36.5)	
Charlson Comorbidity Index			<0.001
0–1	138 (89.6)	221 (67.2)	
≥2	16 (10.4)	108 (32.8)	
Tumor stage			0.62
0-II	108 (70.1)	238 (72.3)	
III	46 (29.9)	91 (27.7)	
Neoadjuvant therapy	79 (52.3)	167 (51.4)	0.85
Surgical approach			<0.001
Open	7 (4.5)	65 (19.8)	
Laparoscopic	147 (95.5)	264 (80.2)	
Type of surgery			<0.001
LAR without stoma	81 (52.6)	104 (31.6)	
LAR with stoma	56 (36.4)	151 (45.9)	
APR/Hartmann	5 (3.2)	42 (12.8)	
Not specified (no anastomosis)	12 (7.8)	32 (9.7)	

Abbreviations: ASA American Society of Anesthesiologists; APR abdominoperineal resection; BMI body mass index; IQR interquartile range; LAR low anterior resection; VMS 'VeiligheidsManagementSysteem' Safety Management System.

3.5. Outcomes

Results of the univariable logistic regression analyses for the outcomes are shown in Table 4.

3.5.1. Overall Complications

Overall complications occurred in 253 (44.0%) patients. Of the standard preoperative predictors, ASA-score and CCI were associated with overall complications in univariable analysis. The final prediction model only included ASA score (AUC 0.57, 95% CI 0.52–0.62) as CCI did not significantly improve model performance. Although functional impairment, delirium risk and mobility aid were associated with overall complications in univariable analyses, the addition of any of these geriatric parameters to the standard model did not improve model performance.

3.5.2. Severe Complications

Seventy-one (12.3%) patients had severe complications. None of the standard preoperative variables were associated with severe complications in univariable analyses. Regarding the geriatric parameters, only mobility aid was associated with the outcome. However, use of mobility aid did not discriminate between patients with and without severe complications (AUC 0.56, 95% CI 0.47–0.64).

3.5.3. Postoperative Delirium

Forty-five (8.0%) patients had postoperative delirium. Age, ASA-score and CCI were associated with this outcome in univariable analysis. Only ASA-score remained in the final model with standard preoperative variables (AUC 0.65, 95% CI 0.56–0.74).

When delirium risk was added to the standard model, the discriminative ability of the model improved significantly (AUC 0.75, 95% CI 0.71–0.78, $p = 0.03$). Other geriatric parameters did not improve the model performance.

3.5.4. Length of Stay

The median LOS was six days (IQR 5–10); 73 (12.7%) patients were admitted for more than fourteen days (prolonged LOS). The final prediction model of standard preoperative variables only included age (AUC 0.60, 95% CI 0.54–0.67). None of the geriatric parameters improved the model performance for prolonged LOS.

3.5.5. Discharge to Another Care Facility

Forty-five (8.0%) patients were discharged to another institution. The standard variables associated with this outcome included age and female sex. Only age remained in the final prediction model (AUC 0.71, 95% CI 0.63–0.80). Regarding the geriatric parameters, adding functional impairment (Katz-ADL score ≥ 2) to the model resulted in a modest increase in the model performance (AUC 0.73, 95% CI 0.69–0.76, $p = 0.049$). Other geriatric parameters did not increase the predictive ability of the model.

3.5.6. Thirty-day Mortality

Fifteen (2.6%) patients died within 30 days of surgery. Of the standard preoperative variables, age and CCI were associated with mortality in univariable analysis. No prediction model was developed due to the low numbers of events.

4. Discussion

In our cohort of 575 older patients undergoing surgery for rectal cancer, adding geriatric parameters to standard preoperative risk factors did not improve risk prediction for postoperative complications. The VMS-items delirium risk and functional impairment were of added value in predicting postoperative delirium and post-discharge institutionalization, respectively. To our knowledge, this is the first study exploring the value of assessing geriatric parameters to improve risk prediction for

Table 4
Results from univariable analyses for overall complications, severe complications, postoperative delirium, prolonged length of stay, discharge to another care facility and 30-day mortality.

Standard preoperative risk predictors	*Missing (n)*	Overall complications (*N* = 253)		Severe complications (*N* = 71)		Postoperative delirium (*N* = 45)		Prolonged length of stay (*N* = 73)		Discharge to another care facility (N = 45)		30-day mortality (N = 15)	
		OR (95% CI)	*p-value*	*OR (95% CI)*	*p-value*	*OR (95% CI)*	*p-value*	*OR (95% CI)*	*p-value*	*OR (95% CI)*	*p-value*	*OR (95% CI)*	*p-value*
Age	0	1.0 (1.0–1.1)	0.13	0.2 (1.0–1.1)	0.23	**1.1 (1.0–1.2)**	**0.003**	**1.1 (1.0–1.1)**	**0.02**	**1.2 (1.1–1.2)**	**<0.001**	**1.1 (1.0–1.3)**	**0.005**
Male sex	0	1.4 (1.0–1.9)	0.09	1.3 (0.8–2.4)	0.30	1.7 (0.8–3.6)	0.14	1.4 (0.8–2.5)	0.23	**0.5 (0.3–0.9)**	**0.02**	1.3 (0.4–4.2)	0.65
ASA III-IV	0	**2.1 (1.4–3.0)**	**<0.001**	1.4 (0.8–2.4)	0.23	**3.9 (2.1–7.2)**	**<0.001**	1.4 (0.8–2.5)	0.19	1.3 (0.7–2.5)	0.49	2.7 (1.0–7.5)	0.06
CCI 2 or higher	0	**1.9 (1.3–2.8)**	**0.001**	1.6 (0.9–2.7)	0.09	**3.3 (1.8–6.2)**	**<0.001**	1.3 (0.8–2.3)	0.35	1.7 (0.9–3.3)	0.11	**3.7 (1.3–10.4)**	**0.01**
BMI ≥ 30	22	1.1 (0.7–1.8)	0.68	1.3 (0.6–2.5)	0.53	0.3 (0.1–1.3)	0.10	1.0 (0.5–2.0)	0.98	0.4 (0.1–1.3)	0.14	1.6 (0.4–5.8)	0.49
Neoadjuvant therapy	8	1.0 (0.7–1.4)	0.96	1.0 (0.6–1.7)	0.89	0.9 (0.5–1.7)	0.81	0.9 (0.6–1.5)	0.72	1.0 (0.5–1.7)	0.86	0.7 (0.2–2.1)	0.56
AJCC stage III	0	1.1 (0.8–1.6)	0.68	1.3 (0.8–2.3)	0.28	0.9 (0.5–1.8)	0.82	1.4 (0.8–2.3)	0.24	0.8 (0.4–1.7)	0.57	1.7 (0.6–4.9)	0.31
Geriatric risk predictors													
VMS: functional impairment	13	**3.4 (1.4–8.4)**	**0.007**	1.8 (0.6–4.9)	0.27	2.3 (0.8–7.0)	0.14	2.2 (0.9–5.7)	0.11	2.5 (0.8–7.6)	0.12	3.5 (0.7–16.0)	0.12
VMS: delirium risk	19	**2.4 (1.5–4.0)**	**<0.001**	1.7 (0.9–3.2)	0.09	**5.7 (2.9–10.9)**	**<0.001**	**2.3 (1.2–4.1)**	**0.008**	**4.2 (2.2–8.1)**	**<0.001**	1.5 (0.4–5.2)	0.57
VMS: fall risk	39	0.7 (0.4–1.4)	0.74	1.7 (0.7–3.8)	0.22	0.6 (0.1–2.5)	0.47	0.7 (0.2–2.0)	0.68	0.6 (0.1–2.5)	0.46	3.0 (0.8–11.)	0.10
VMS: malnutrition risk	30	1.3 (0.8–2.2)	0.22	1.1 (0.5–2.1)	0.90	**2.2 (1.1–4.5)**	**0.03**	1.6 (0.9–3.1)	0.12	**2.5 (1.2–5.1)**	**0.01**	2.9 (1.0–8.7)	0.06
Mobility aid	128	**2.4 (1.2–4.5)**	**0.009**	**2.7 (1.2–5.9)**	**0.01**	1.2 (0.3–4.0)	0.81	1.6 (0.7–3.6)	0.27	**4.0 (1.9–8.8)**	**<0.001**	1.0 (0.1–7.7)	0.97
Polypharmacy (≥5 medications)	7	1.4 (1.0–2.0)	0.05	1.2 (0.7–2.0)	0.48	**2.4 (1.3–4.5)**	**0.006**	1.2 (0.8–2.0)	0.40	1.7 (0.9–3.0)	0.11	2.8 (0.9–8.2)	0.07

Significant associations between risk factors and postoperative outcomes are shown in boldface.
Abbreviations: *ADL* Activities of Daily Living, *AJCC* American Joint Committee on Cancer, *ASA* American Society of Anesthesiologists, *BMI* body mass index, *CCI* Charlson Comorbidity Index, *CI* confidence interval, *OR* odds ratio, *VMS* (VeiligheidsManagementSysteem "Safety Management System").

short-term outcomes in older patients undergoing surgery for rectal cancer.

Our findings are not in line with previous studies that have focused on older patients undergoing CRC surgery. Whereas geriatric parameters did not predict severe complications in our study, Souwer et al. [6] found a marginally improved prediction of severe complications after adding geriatric impairments (previous delirium, self-reported cognitive impairment, need for ADL assistance, use of mobility aid, and polypharmacy) to standard variables. In the studies by Kiran et al., Murray et al., and Cohen et al., functional dependency predicted 30-day mortality [13,14] and 30-day morbidity [12]. This is in contrast to our finding that functional dependency (or functional impairment) only improved the prediction for discharge to another care facility and not for other outcomes. However, as our cohort consisted exclusively of patients with rectal cancer, a direct comparison of our results and the results of the aforementioned studies is not feasible.

The fact that our findings do not support frailty screening using the current geriatric risk factors to predict overall or severe complications in rectal cancer surgery can be due to several reasons. First, we included older patients who had already been selected for surgery. The prevalence of geriatric risk factors was relatively low when compared to the previous cohort of Souwer et al. [6] that also included patients with colon cancer. The treatment of rectal cancer is multidisciplinary and many different treatment options exist, ranging from chemoradiation followed by watch-and-wait [28] or transanal microsurgery [29] to direct surgical resection. It is highly likely that frailer patients with more impairments more often received non-surgical treatment [30]. The modest discriminative value of the standard predictor variables (e.g., age or ASA-score) also supports this hypothesis. Second, although we assessed the risk for several geriatric impairments, there are other preoperative risk factors that may have more predictive value in older surgical patients. Physical decline contributes to the development of geriatric impairments such as falling and needing help with ADL, and measuring markers of physical decline may improve risk prediction in the older patient population. For example, low muscle mass and poor aerobic capacity have been shown to be strongly associated with adverse outcomes in colorectal surgery [31,32]. Third, rectal surgery is complex and postoperative outcomes (such as anastomotic leak) are strongly influenced by surgical factors (extent of resection, invasiveness of surgery, height of anastomosis, deviating ostomy) [15]. In our cohort, patients with at least one geriatric risk factor had open surgery and received a stoma more often. Preoperative prediction models cannot rely on intraoperative surgical variables which were thus not included in the logistic regression analyses. However, patient characteristics that were associated with having at least one geriatric risk factor in our cohort (advanced age, higher ASA-scores, and a higher comorbidity burden) likely had influence on perioperative decision-making, for example regarding stoma construction. More vulnerable patients thus received different surgical treatment.

Interestingly, we noted the relatively low percentage of patients receiving APR in our cohort (10%). In other recent Dutch cohorts in which patients of all ages were included, the percentages of patients undergoing APR were higher (27–46%) [33–35]. We also observed that most patients underwent surgery for stage I/II cancer which may in part explain the lower percentage of APR. Older patients with very distal cancers who would have to undergo APR as well as patients with more

advanced disease may have instead opted for non-surgical treatment and were thus not included in our study.

Postoperative delirium is associated with an increased risk for cognitive decline and mortality [36]. Identifying at-risk patients can be used to implement delirium prevention measures. Previous studies in other cohorts of older surgical patients have shown that a history of delirium and cognitive problems are associated with a higher risk of postoperative delirium [37–39]. Both items are a part of the delirium risk screening incorporated in the VMS-questionnaire. In the present cohort, we showed that delirium risk screening together with ASA-score resulted in a fair discriminative ability for postoperative delirium of the prediction model (AUC 0.75), implying that delirium risk screening with the VMS-questionnaire is a useful addition to the preoperative risk assessment in patients with rectal cancer.

Preoperative frailty screening serves two main purposes: first, it aids in risk stratification and helps to guide the decision-making process regarding the surgical trajectory, and second, it provides opportunities to address modifiable risk factors [40,41]. Frailty screening may, therefore, have the most value for older patients with rectal cancer when it is implemented directly after diagnosis and before decisions on treatment trajectory are made. Ideally, an initial frailty screening is quick and has adequate discriminatory power to determine which patients require further work-up, for example in the form of a Comprehensive Geriatric Assessment [42]. Future studies should determine whether frailty screening with the geriatric parameters addressed here would have additional prognostic value in an earlier phase in the treatment pathway for rectal cancer. It should be noted that measuring modifiable risk factors would be especially advantageous as it helps to target preoperative interventions such as prehabilitation for selected patients [43].

The major strength of this study was the large sample size and the inclusion of only older patients with rectal cancer. We were able to collect data in multiple hospitals, which increases the generalizability of the results. The limitations of the study include the previously mentioned selection bias for the fittest older patients, which probably limited the number of patients with more geriatric impairments as these patients did not undergo surgery. Furthermore, frailty screening with VMS was an implemented practice in the participating hospitals and patients at risk most likely received a geriatric consultation and/or additional care, for example consultation by a physiotherapist or a dietician, nutritional supplements, delirium prevention measures (such as counseling, early signaling, single room, or rooming in), or fall prevention measures. Some of these interventions may have weakened the association between the geriatric parameters and outcomes. Lastly, we measured a set of parameters that were readily available from the medical records. The VMS-questionnaire is a short screening tool, and even though we augmented the screening instrument with two additional geriatric parameters (polypharmacy and mobility issues), the method has its shortcomings. There are other parameters that may have stronger prognostic value in the older surgical population (such as cognition, muscle mass, aerobic capacity), and prospective data collection focusing especially on modifiable risk factors would be needed to determine which set of variables would have optimal prognostic value.

5. Conclusion

In this multicenter study in 575 older patients with rectal cancer, preoperative screening for geriatric parameters did not improve risk prediction for postoperative overall or severe complications. However, delirium risk screening with the VMS-questionnaire significantly improved risk prediction for postoperative delirium. Geriatric risk screening may have additional value when performed early after diagnosis and before treatment decisions are made. Future studies should determine which risk factors should be considered when making treatment decisions for older patients with rectal cancer in a prospective setting. Focus on modifiable risk factors is especially warranted in order to find targets for preoperative optimization and to further improve postoperative outcomes.

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Author Contribution Statement

T.E. Argillander: Conceptualization, Methodology, Data curation, Formal analysis, Investigation, Visualization, Writing – original draft, Writing – review & editing. **H.C. van der Hulst:** Conceptualization, Methodology, Formal analysis, Investigation, Visualization, Writing – original draft, Writing – review & editing. **H.J. van der Zaag-Loonen:** Conceptualization, Methodology, Writing – review & editing. **P. van Duijvendijk:** Conceptualization, Methodology, Resources, Supervision, Writing – review & editing. **J.W.T. Dekker:** Conceptualization, Methodology, Resources, Supervision, Writing – review & editing. **J.M. van der Bol:** Conceptualization, Methodology, Resources, Supervision, Writing – review & editing. **E. Bastiaannet:** Conceptualization, Methodology, Writing – review & editing. **J. Verkuyl:** Resources, Writing – review & editing. **P. Neijenhuis:** Resources, Writing – review & editing. **M. Hamaker:** Writing – review & editing. **A.H. Schiphorst:** Resources, Writing – review & editing. **T.S. Aukema:** Resources, Writing – review & editing. **T.A. Burghgraef:** Resources, Writing – review & editing. **D.J.A. Sonneveld:** Resources, Writing – review & editing. **J.S. Schuijtemaker:** Writing – review & editing. **W. van der Meij:** Resources, Writing – review & editing. **F. van den Bos:** Supervision, Writing – review & editing. **J.E.A. Portielje:** Methodology, Supervision, Writing – review & editing. **E.T.D. Souwer:** Conceptualization, Methodology, Data curation, Investigation, Resources, Writing – review & editing. **B.C. van Munster:** Conceptualization, Methodology, Resources, Supervision, Writing – review & editing.

Declaration of Competing Interest

None.

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