

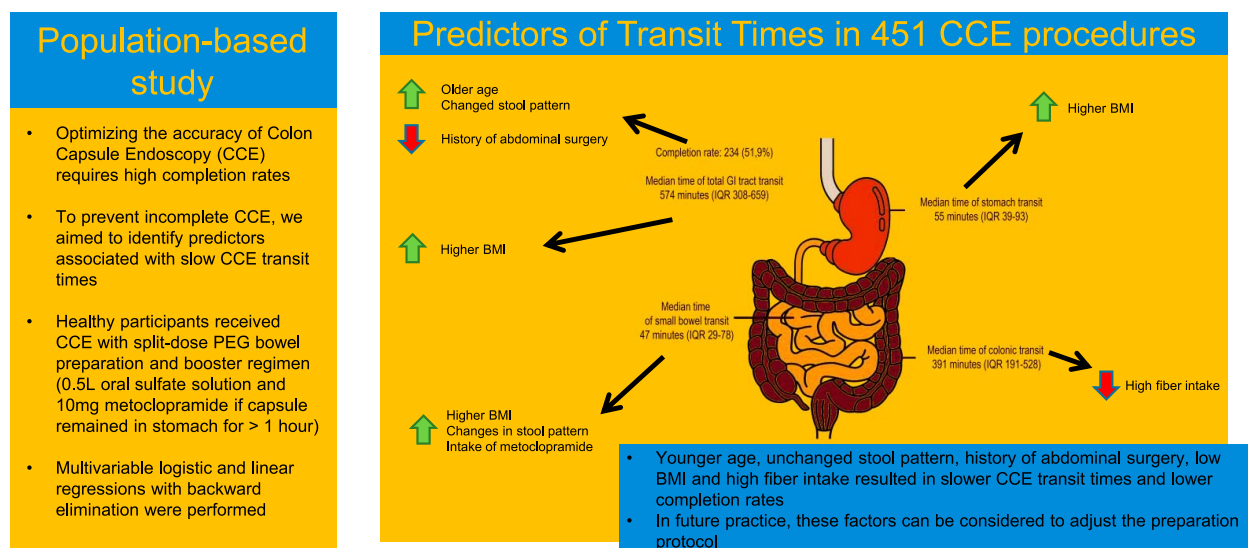
# Predictors of Gastrointestinal Transit Times in Colon Capsule Endoscopy

Sarah Moen, MD<sup>1</sup>, Fanny E. R. Vuik, MD<sup>1</sup>, Trudy Voortman, PhD<sup>2</sup>, Ernst J. Kuipers, MD, PhD<sup>1</sup> and Manon C. W. Spaander, MD, PhD<sup>1</sup>

**INTRODUCTION:** Optimizing the accuracy of colon capsule endoscopy (CCE) requires high completion rates. To prevent incomplete CCE, we aimed to identify predictors associated with slow CCE transit times.

**METHODS:** In this population-based study, participants received CCE with a split-dose polyethylene glycol bowel preparation and booster regimen (0.5 L oral sulfate solution and 10 mg metoclopramide if capsule remained in stomach for > 1 hour). The following predictors were assessed: age, sex, body mass index (BMI), smoking, coffee and fiber intake, diet quality, physical activity, dyspeptic complaints, stool pattern, history of abdominal surgery, medication use, and CCE findings. Multivariable logistic and linear regressions with backward elimination were performed.

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<sup>1</sup>Department of Gastroenterology and Hepatology, Erasmus MC University Medical Center, Rotterdam, the Netherlands; <sup>2</sup>Department of Epidemiology, Erasmus MC University Medical Center, Rotterdam, the Netherlands. **Correspondence:** Manon C. W. Spaander, MD, PhD. E-mail: v.spaander@erasmusmc.nl

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**RESULTS:** We analyzed 451 CCE procedures with a completion rate of 51.9%. The completion rate was higher among older participants (odds ratio [OR] 1.54, 95% confidence interval [CI] 1.04–2.28,  $P = 0.03$ ) and participants with a changed stool pattern (OR 2.27, 95% CI 1.20–4.30,  $P = 0.01$ ). Participants with a history of abdominal surgery had a lower completion rate (OR 0.54, 95% CI 0.36–0.80,  $P = 0.003$ ). Participants with higher BMI had faster stomach, small bowel, and total transit times ( $\beta = -0.10$ ,  $P = 0.01$ ;  $\beta = -0.14$ ,  $P = 0.001$ ;  $\beta = -0.12$ ,  $P = 0.01$ ). A faster small bowel transit was found in participants with a changed stool pattern ( $\beta = -0.08$ ,  $P = 0.049$ ) and the use of metoclopramide ( $\beta = -0.14$ ,  $P = 0.001$ ). Participants with high fiber intake had a slower colonic transit ( $\beta = 0.11$ ,  $P = 0.03$ ).

**DISCUSSION:** Younger age, unchanged stool pattern, history of abdominal surgery, low BMI, and high fiber intake resulted in slower CCE transit times and lower completion rates. In future practice, these factors can be considered to adjust preparation protocols.

**SUPPLEMENTARY MATERIAL** accompanies this paper at <http://links.lww.com/CTG/A812>

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## INTRODUCTION

Colon capsule endoscopy (CCE) provides a noninvasive technique that enables exploration of the colon without the need for sedation nor gas insufflation. Despite the framework for potential clinical indications that was provided by the European Society of Gastrointestinal Endoscopy and the US Food and Drug Administration, standardized use of CCE in daily practice is still limited (1–3).

CCE accurately detects various colonic abnormalities such as colorectal polyps and colorectal cancer (4–6). However, its accuracy highly depends on optimal bowel preparation to allow adequate visualization of the colonic mucosa and on capsule transit time (1,7). To obtain images of the entire colon, the optimal capsule transit time has to be fast enough to achieve completion within the battery time, but not so fast that lesions may be missed. CCE has a flexible frame rate of 4–35 images per second that adapts automatically based on the capsule speed (4). However, because the capsule is not equipped to actively move forward, capsule progression needs to be stimulated to achieve excretion within the battery time. This requires booster medication on the day of the capsule endoscopy in addition to the bowel preparation. Many studies have been performed to determine the optimal boosters for CCE, but completion rates still vary widely (6,8–10).

The wide variation in the CCE completion rate and transit times is not completely understood. Several factors that are known to influence the physiological gastrointestinal (GI) transit times might have an impact on CCE transit as well. Aging may delay gastric emptying or colonic transit time, and men have a faster transit than women (11–14). Different lifestyle-associated factors also affect GI transit times such as body mass index (BMI), exercise level, smoking, and coffee intake (15–17). The literature on factors that specifically influence transit times in CCE is scarce. One study identified a BMI above 25 and the absence of constipation as CCE transit time-accelerating factors (18). Another study concluded that coffee and chewing gum did not improve the CCE completion rate (19).

To optimize CCE transit times, more knowledge is needed on which factors can predict the CCE speed through the different segments of the GI tract. In future practice, such factors could be used to anticipate capsule transit times and possibly adapt the preparation protocol for certain patient groups. The aim of this study was to identify possible predictors for CCE transit times in a prospective population-based cohort.

## METHODS

### Participants

This study was embedded in the Rotterdam Study, an ongoing prospective population-based cohort study in Rotterdam, the Netherlands (20). A subset of participants with ages ranging from 50 to 75 years underwent CCE, as described in more detail elsewhere (21). This study was approved by the Institutional Review Board of Erasmus MC (registration number MEC-2015-453). The protocol of the original ORCA trial was registered in the Netherlands National Trial Register (NTR6321). All participants signed written informed consent before participation in this study.

### Colon capsule endoscopy

The second-generation colon capsule (Medtronic, Minneapolis, MN) was used. The ingestion of the capsule usually took place at 9 AM in the presence of a physician. A sensor belt was provided, which received transmission data from the capsule and sent the images to the corresponding recorder. The belt was taken off by the participants at 8 PM or earlier if the capsule had left the body.

Before the ingestion of the capsules, the participants received bowel preparation consisting of 5 mg bisacodyl, 2 L polyethylene glycol with ascorbic acid (MoviPrep; Norgine, Amsterdam, the Netherlands), and 2 L water, both split-dose. After ingestion of the capsule, the participants received a booster regimen. When the capsule remained in the stomach for longer than 1 hour, an alarm went off and participants were instructed to take 10 mg metoclopramide. After small bowel recognition, another alarm went off and participants were instructed to take 0.25 L oral sulfate solution as a booster (Eziclen, Zambon, the Netherlands), and 3 h after small bowel recognition, they had to take another 0.25 L oral sulfate solution.

### Predictors of CCE transit times

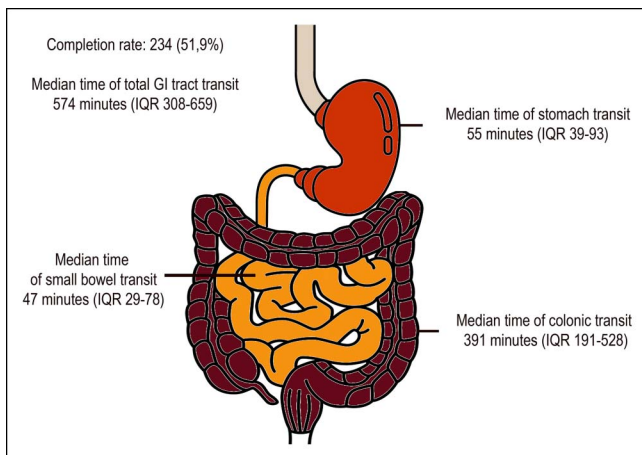
For each CCE video, segmental transit times were calculated for the stomach, small bowel, and colon by Rapid Software v8.0 (Medtronic, Minneapolis, MN). The procedure was classified as “complete” when the capsule observed the anal verge within the battery time. Possible transit time predictors were obtained through questionnaires and included patient characteristics, relevant symptoms, relevant medical history, relevant medication, CCE procedure-related factors, and CCE findings.

**Table 1. Baseline characteristics**

Total study cohort (n = 451)	
Patient characteristics	
Mean age (SD), yr	67.3 (4.8)
Sex, male, n (%)	208 (46.1%)
Mean BMI (SD), kg/m <sup>2</sup>	26.3 (3.8)
History of smoking, n (%)	306 (67.8%)
Mean coffee intake (SD), g/d	418.6 (266.5)
Mean fiber intake (SD), g/d	28.1 (8.1)
Mean diet quality score (SD)	7.3 (1.8)
Mean physical activity score (SD), MET h/wk	57.7 (58.0)
Relevant symptoms	
Dyspeptic complaints, n (%)	33 (7.3%)
Changes in stool pattern, n (%)	51 (11.3%)
Relevant medical history	
Abdominal surgery, n (%)	171 (37.9%)
Relevant medication	
Medication use, n (%)	343 (76.1%)
Stomach protectors, n (%)	109 (24.2%)
Procedure CCE	
Intake metoclopramide, n (%)	151 (33.5%)
Findings CCE	
Presence of diverticula in SB, n (%)	15 (3.3%)
Presence of diverticula in the colon, n (%)	392 (86.9%)

BMI, body mass index; CCE, colon capsule endoscopy; MET, metabolic equivalent of task; SB, small bowel.

**Patient characteristics.** Patient characteristics that were used as possible transit time predictors were age, sex, BMI, smoking status, habitual coffee and fiber intake, diet quality, and physical activity. Smoking status was classified as either “ever smoked” or



**Figure 1.** Heat map illustrating gastrointestinal transit times and completion rates. IQR, interquartile range.

“never smoked.” Habitual coffee intake and fiber intake were both obtained through a food frequency questionnaire and expressed in grams per day. Both variables were adjusted for the total energy intake (22). Diet quality was defined as a score from 0 to 14 based on the adherence to 14 items of the Dutch dietary guidelines (23). Physical activity was measured by the Longitudinal Aging Study Amsterdam questionnaire and expressed in metabolic equivalent of task-hours per week. This value gives an indication of both the duration and the intensity by expressing the sum of the duration of all activities weighed with the metabolic equivalent of task-value of each activity (24).

**Relevant symptoms, medical history, and medication.** Relevant symptoms, medical history, and medication that were used as possible predictors for CCE transit times were presence of dyspeptic complaints, changes in stool pattern, history of abdominal surgery, general medication use, and the use of gastro-protectant drugs. Dyspeptic complaints included general dyspeptic complaints, heart burn, feeling of being full, and belches. Stomach protectors included proton pump inhibitors, H<sub>2</sub> antagonists, antiemetics, and gastric acid binders. For history of abdominal surgery, it should be noted that participants were not included when they had prior abdominal surgery likely to cause bowel obstruction (21).

**CCE procedure-related factors and CCE findings.** CCE procedure-related factors and CCE findings that were used as possible predictors for CCE transit times were the intake of metoclopramide, the presence of diverticula in the small bowel found by CCE, and the presence of diverticula in the colon found by CCE.

## STATISTICAL ANALYSIS

Baseline characteristics were presented as mean with SD for the numerical data or as number with percentage for the categorical data. Transit times were presented as median with interquartile range (IQR). The completion rate was also presented as number with the corresponding percentage.

Owing to missing values in some of the variables (see Supplementary Table 1, Supplementary Digital Content 1, <http://links.lww.com/CTG/A812>), multiple imputation was performed to improve the validity of the results (25). The assumption was made that the missing values were missing at random. A total of 5 imputations were performed using all variables from each model and some additional variables including history of lung disease, use of laxatives, and presence of diverticula in the medical history as predictors.

Univariable linear regression and multivariable linear regression, with and without backward elimination, were performed to predict CCE stomach, small bowel, colonic, and total transit times. For each of these analyses, cases were excluded from the analysis when they did not have a complete transit of the investigated GI segment because the actual transit time of this GI segment was then unknown (e.g., when predicting stomach transit, cases where the capsule did not reach the small bowel within the battery time were excluded). Univariable and multivariable logistic regression models were performed to predict the CCE completion rate in all cases. The main conclusions were based on the multivariable analyses with backward elimination.

For all tests, a 2-sided statistical significance level of 0.05 was used. Analyses were performed in IBM SPSS v.25 (IBM, Armonk, NY).

**Table 2. Predictors of stomach transit time (dependent variable) among participants with complete stomach transit (n = 450)**

	Univariable analysis			Multivariable analysis			Multivariable analysis with backward elimination		
	$\beta$	95% CI	Pvalue	$\beta$	95% CI	Pvalue	$\beta$	95% CI	Pvalue
Patient characteristics									
Age	0.04	-0.05 to 0.12	0.40	0.04	-0.05 to 0.12	0.37			
Sex, male	0.06	-0.02 to 0.15	0.13	0.07	-0.02 to 0.16	0.11	0.08	-0.01 to 0.16	0.07
BMI	-0.11	-0.20 to -0.03	0.01	-0.11	-0.20 to -0.03	0.01	-0.10	-0.19 to -0.02	0.01
History of smoking	-0.05	-0.13 to 0.03	0.22	-0.06	-0.14 to 0.02	0.16			
Coffee intake	0.02	-0.08 to 0.11	0.70	0.02	-0.07 to 0.12	0.66			
Diet quality	-0.02	-0.10 to 0.07	0.68	-0.03	-0.11 to 0.06	0.55			
Physical activity	0.11	0.03-0.20	0.01	0.09	0.004-0.173	0.04	0.10	0.02-0.18	0.02
Relevant symptoms									
Dyspeptic complaints	-0.02	-0.11 to 0.06	0.57	-0.01	-0.10 to 0.07	0.79			
Relevant medical history									
Abdominal surgery	-0.02	-0.11 to 0.06	0.57	-0.001	-0.09 to 0.09	0.99			
Relevant medication									
Medication use	-0.07	-0.15 to 0.02	0.12	-0.04	-0.12 to 0.05	0.43			
Stomach protectors	-0.04	-0.12 to 0.04	0.34	-0.01	-0.10 to 0.08	0.83			

$\beta$ , standardized beta; BMI, body mass index; CI, confidence interval; t, t-value.

Linear regression analyses were performed. Univariable models (each predictor one by one), a multivariable model (including all predictors in the table), and a multivariable model after backward selection (subsequent removal of the predictor with the highest *P* value until all *P* values were <0.1) are included in this table.  $\beta$  values are standardized regression coefficients and here represent differences in stomach transit times per SD higher predictor variables.

## RESULTS

### Baseline characteristics

Four hundred fifty-one participants were included, and they all underwent CCE. Participants had a mean (SD) age of 67.3 (4.8) years, and 46.1% was male. All baseline characteristics after imputation are given in Table 1. Baseline characteristics of the original data are included in Supplementary Table 2 (see Supplementary Digital Content 1, <http://links.lww.com/CTG/A812>). In total, 450 videos had a complete transit of the stomach, 449 videos had a complete transit of the small bowel, and 234 videos had a complete colonic transit. The entire GI tract was visualized in 234 videos (completion rate 51.9%).

### CCE transit times

The median transit times were 55 minutes (IQR = 39–93) in the stomach, 47 minutes (IQR = 29–78) in the small bowel, and 391 minutes (IQR = 191–528) in the colon (Figure 1). The median total transit time was 574 minutes (IQR = 308–659).

### Predictors of CCE transit times

**Stomach transit.** Participants with a higher BMI had a faster stomach transit (0.10 SD faster transit per 1 SD higher BMI [standardized  $\beta$  = -0.10, 95% confidence interval [CI] -0.19 to -0.02, *P* = 0.01]), whereas those with higher physical activity had a slower stomach transit ( $\beta$  = 0.10, 95% CI 0.02–0.18, *P* = 0.02) (Table 2). A trend was shown for a slower stomach transit in men ( $\beta$  = 0.08, 95% CI -0.01 to 0.16, *P* = 0.07).

**Small bowel transit.** Participants with a higher BMI ( $\beta$  = -0.14, 95% CI -0.22 to -0.05, *P* = 0.001), higher physical activity

( $\beta$  = -0.14, 95% CI -0.22 to -0.05, *P* = 0.002), and changes in stool pattern ( $\beta$  = -0.08, 95% CI -0.167 to 0.000, *P* = 0.049) had a faster small bowel transit, all independent of the other predictors (Table 3). Participants who took metoclopramide because of a long stomach transit also had a significantly faster small bowel transit ( $\beta$  = -0.14, 95% CI -0.23 to -0.05, *P* = 0.001).

**Colonic transit.** Participants with higher fiber intake had a slower colonic transit ( $\beta$  = 0.11, 95% CI 0.01–0.21, *P* = 0.03). A trend was shown for a slower colonic transit in the presence of colonic diverticula ( $\beta$  = 0.10, 95% CI -0.004 to 0.204, *P* = 0.06) (Table 4).

**Total transit.** Participants with a higher BMI had a faster total transit ( $\beta$  = -0.12, 95% CI -0.22 to -0.03, *P* = 0.01), whereas participants who took metoclopramide because of a long stomach transit had a slower total transit ( $\beta$  = 0.15, 95% CI 0.04–0.25, *P* = 0.01) (Table 5). A trend was shown for a slower total transit with higher fiber intake ( $\beta$  = 0.08, 95% CI -0.01 to 0.18, *P* = 0.09) and in the presence of diverticula (both small bowel [ $\beta$  = 0.08, 95% CI -0.004 to 0.156, *P* = 0.06] and colonic diverticula [ $\beta$  = 0.09, 95% CI -0.01 to 0.19, *P* = 0.09]).

### Predictors of CCE completion rate

The overall completion rate was higher among older participants (odds ratio [OR] 1.54 per SD higher age, 95% CI 1.04–2.28, *P* = 0.03) and among those with changes in stool pattern (OR 2.27, 95% CI 1.20–4.30, *P* = 0.01) (Table 5). A trend was shown for a higher completion rate with the presence of small bowel diverticula (OR 2.94, 95% CI 0.91–9.49, *P* = 0.07). A lower completion rate was seen in those participants with a history of

**Table 3.** Predictors of small bowel transit time (dependent variable) among participants with complete small bowel transit (n = 449)

	Univariable analysis			Multivariable analysis			Multivariable analysis with backward elimination		
	$\beta$	95% CI	P value	$\beta$	95% CI	P value	$\beta$	95% CI	P value
Patient characteristics									
Age	0.002	−0.08 to 0.09	0.96	0.03	−0.05 to 0.12	0.43			
Sex, male	0.04	−0.05 to 0.12	0.38	0.06	−0.03 to 0.15	0.17			
BMI	−0.10	−0.18 to −0.01	0.02	−0.14	−0.22 to −0.05	0.002	−0.14	−0.22 to −0.05	0.001
History of smoking	−0.04	−0.13 to 0.04	0.31	−0.06	−0.14 to 0.03	0.20			
Coffee intake	−0.05	−0.15 to 0.05	0.31	−0.05	−0.14 to 0.05	0.33			
Fiber intake	0.02	−0.08 to 0.12	0.73	−0.003	−0.10 to 0.09	0.96			
Diet quality	0.04	−0.06 to 0.15	0.43	0.04	−0.06 to 0.15	0.42			
Physical activity	−0.11	−0.20 to −0.03	0.01	−0.15	−0.24 to −0.06	0.001	−0.14	−0.22 to −0.05	0.002
Relevant symptoms									
Changes in stool pattern	−0.06	−0.15 to 0.02	0.16	−0.08	−0.166 to 0.001	0.054	−0.08	−0.167 to 0.000	0.049
Relevant medical history									
Abdominal surgery	0.06	−0.02 to 0.15	0.16	0.09	0.000–0.174	0.049			
Relevant medication									
Medication use	−0.05	−0.13 to 0.04	0.25	−0.07	−0.16 to 0.02	0.12			
Procedure CCE									
Intake metoclopramide	−0.12	−0.20 to −0.03	0.01	−0.14	−0.22 to −0.05	0.002	−0.14	−0.23 to −0.05	0.001
Findings CCE									
Presence of diverticula	−0.01	−0.10 to 0.07	0.75	−0.003	−0.09 to 0.08	0.94			

$\beta$ , standardized beta; BMI, body mass index; CCE, colon capsule endoscopy; CI, confidence interval; t, t-value.

Linear regression analyses were performed. Univariable models (each predictor one by one), a multivariable model (including all predictors in the table), and a multivariable model after backward selection (subsequent removal of the predictor with the highest *P* value until all *P* values were <0.1) are included in this table.  $\beta$  values are standardized regression coefficients from linear regression models and here represent differences in small bowel transit times per SD higher predictor variables.

abdominal surgery (OR 0.54, 95% CI 0.36–0.80, *P* = 0.003) and in those who had to take metoclopramide because of a long stomach transit (OR 0.60, 95% CI 0.40–0.91, *P* = 0.02).

## DISCUSSION

To the best of our knowledge, this is the largest prospective population-based cohort study identifying predictors of CCE GI transit times. The low completion rate of 51.9% in this study emphasizes the need for entry points which can be used to anticipate and prevent incomplete CCE procedures. We observed that lower BMI, unchanged stool pattern, higher fiber intake, younger age, and history of abdominal surgery were significant predictors for slower CCE transit times and a lower completion rate. In future practice, these factors can be used to anticipate a longer capsule transit time and possibly adjust the preparation protocol. The subsequent faster SB transit in participants who took metoclopramide because of a delayed stomach transit compared with those who did not take metoclopramide suggests that it might be beneficial to use metoclopramide in all CCE procedures instead of waiting for a delay in stomach transit.

Some of the associations in our study can be explained according to what is already known about the etiology of differences in physiological GI transit times. For example, participants with a higher BMI generally had faster CCE stomach, small bowel, and total transit times. Although a higher BMI is associated with delay in

physiological colonic transit, previous literature has shown that it actually has an accelerating effect on gastric emptying and small bowel transit, which could have resulted in a faster CCE total transit time (15). Participants with higher physical activity had a faster CCE small bowel transit but a slower stomach transit, with no apparent effect on total transit time. In line with this, previous literature has shown that physical activity can accelerate small bowel transit, but with increasing intensity, it can cause delayed gastric emptying (16, 26). This delayed gastric emptying seen in heavy exercise might be due to the inhibitory effects of increased catecholamine on splanchnic blood flow and gastric motility (27). Furthermore, our data showed a lower CCE completion rate in participants with a history of abdominal surgery, which may be explained by the possible presence of abdominal adhesions and its associated bowel obstructing effects (28, 29). On top of that, our study revealed trends for a slower colonic and total transit in the presence of diverticula, which may be due to possible causes of these diverticula such as disordered intestinal motility and obstipation (30). Participants with changes in stool pattern had a faster CCE small bowel transit and a higher completion rate. Unfortunately, our data did not differentiate what type of changed stool pattern was present. A possible explanation for this result can be that these changes in stool pattern could have been mostly diarrhea instead of obstipation.

The intake of metoclopramide in those participants with a prolonged stomach transit subsequently led to a significantly

**Table 4. Predictors of colonic transit time (dependent variable) among participants with complete colonic transit (n = 234)**

	Univariable analysis			Multivariable analysis			Multivariable analysis with backward elimination		
	$\beta$	95% CI	P value	$\beta$	95% CI	P value	$\beta$	95% CI	P value
Patient characteristics									
Age	0.02	-0.08 to 0.11	0.75	0.01	-0.09 to 0.11	0.84			
Sex, male	0.02	-0.08 to 0.12	0.67	0.04	-0.06 to 0.14	0.48			
BMI	-0.06	-0.11 to -0.01	0.22	-0.08	-0.18 to 0.03	0.14			
History of smoking	0.02	-0.07 to 0.12	0.62	0.02	-0.07 to 0.12	0.64			
Coffee intake	-0.02	-0.13 to 0.08	0.70	-0.01	-0.11 to 0.10	0.93			
Fiber intake	0.12	0.02-0.21	0.02	0.11	-0.004 to 0.215	0.06	0.11	0.01-0.21	0.03
Diet quality	0.05	-0.04 to 0.15	0.29	0.01	-0.10 to 0.11	0.93			
Physical activity	-0.02	-0.12 to 0.07	0.63	-0.05	-0.15 to 0.06	0.37			
Relevant symptoms									
Changes in stool pattern	0.02	-0.03 to 0.06	0.67	-0.002	-0.09 to 0.09	0.96			
Relevant medical history									
Abdominal surgery	0.02	-0.08 to 0.13	0.64	-0.001	-0.11 to 0.11	0.99			
Relevant medication									
Medication use	0.06	0.01-0.11	0.79	0.06	-0.04 to 0.17	0.23			
Findings CCE									
Presence diverticula	0.11	0.002-0.208	0.045	0.12	0.01-0.24	0.03	0.10	-0.004 to 0.204	0.06

$\beta$ , standardized beta; BMI, body mass index; CCE, colon capsule endoscopy; CI, confidence interval; t, t-value.

Linear regression analyses were performed. Univariable models (each predictor one by one), a multivariable model (including all predictors in the table), and a multivariable model after backward selection (subsequent removal of the predictor with the highest P value until all P values were <0.1) are included in this table.  $\beta$  values are standardized regression coefficients from linear regression models and here represent differences in colonic transit times per SD higher predictor variables.

faster CCE small bowel transit. This can be explained by the known stimulating effect of metoclopramide on the peristalsis of the entire upper GI channel (31). Still, intake of metoclopramide in this study was associated with a slower total transit time and lower completion rate, likely due to the fact that the medication was only administered in the event of a delayed stomach transit which could have caused the lengthening of the total transit time.

Some of the observed associations in our study were opposite to what we expected based on human physiology. It has been reported that aging may delay gastric emptying or slow down colonic transit time possibly because of nerve dysfunction (11-13), but our study population (with ages ranging from 50 to 75 years) showed a higher CCE completion rate with older age. Our study also observed a nonsignificant trend for a slower CCE stomach transit in men, whereas a previous study has shown that men have physiological faster gastric emptying (14). Perhaps these differences can be explained by possible differences in commitment to the CCE protocol in different age groups and sexes. In addition, it was expected that a higher fiber intake would lead to a faster colonic transit, but we found that a higher habitual fiber intake was associated with a slower colonic transit. A previous meta-analysis showed a faster transit with higher wheat dietary fiber intake, but only among those with an initial transit time greater than 48 h. The effect was not shown for those with a faster initial transit time (32). If our participants had an overall faster initial transit time, this could partly explain our result, but unfortunately, this parameter was unknown for our study population. On top of that, the fiber intake reported in our study

included all types of dietary fibers. Although insoluble fibers (such as wheat) can accelerate colonic transit, some soluble fibers can actually have a constipating effect (33), which may explain the slower colonic transit with higher fiber intake that we observed in our participants. Furthermore, there was a nonsignificant trend for a higher completion rate in those participants with small bowel diverticula, which cannot be explained. Possibly the number of participants (15) with small bowel diverticula was too low to provide a reliable outcome. Finally, we did not observe any association between (history of) smoking, coffee intake, diet quality, dyspeptic complaints, medication use in general, and stomach protectors with any of the transit times.

Previous literature on influential factors of transit times in CCE specifically is scarce. One study identified a high BMI and the absence of constipation as promoting factors for CCE transit time (18), which is in accordance with our results. Contrary to our current study, the previous study did not investigate the effect of possible predictors on stomach, small bowel, and colonic transit separately.

Major strengths of our study are the prospective population-based cohort design and the examination of predictors for each GI segment transit separately. To the best of our knowledge, this study with 451 participants is the largest study so far to investigate the possible predictors of CCE transit times. However, this study also has some limitations to address. First, in the analysis for stomach, small bowel, colonic, and total transit times, cases were excluded from the analysis when they did not have a complete transit of the investigated GI segment within the battery time. This was necessary because the actual transit time of that GI segment was then unknown. Because

**Table 5.** Predictors of total GI tract transit time (dependent variable) among participants with complete transit (n = 234) and predictors of the completion rate (dependent variable) among all participants (n = 451)

Total GI tract transit	Univariable analysis			Multivariable analysis			Multivariable analysis with backward elimination		
	β	95% CI	P value	β	95% CI	P value	β	95% CI	P value
Patient characteristics									
Age	0.04	−0.06 to 0.13	0.47	0.01	−0.09 to 0.11	0.78			
Sex, male	0.04	−0.06 to 0.14	0.40	0.07	−0.03 to 0.17	0.16			
BMI	−0.13	−0.22 to −0.03	0.01	−0.12	−0.22 to −0.02	0.02	−0.12	−0.22 to −0.03	0.01
History of smoking	−0.003	−0.10 to 0.09	0.96	0.004	−0.09 to 0.10	0.93			
Coffee intake	−0.04	−0.14 to 0.06	0.47	−0.03	−0.13 to 0.08	0.62			
Fiber intake	0.10	0.01–0.20	0.04	0.08	−0.03 to 0.19	0.14	0.08	−0.01 to 0.18	0.09
Diet quality	0.05	−0.04 to 0.15	0.26	0.01	−0.10 to 0.12	0.87			
Physical activity	0.03	−0.07 to 0.13	0.59	0.004	−0.10 to 0.11	0.94			
Relevant symptoms									
Dyspeptic complaints	0.01	−0.10 to 0.12	0.85	−0.01	−0.13 to 0.10	0.80			
Changes in stool pattern	0.04	−0.05 to 0.12	0.42	0.03	−0.06 to 0.12	0.53			
Relevant medical history									
Abdominal surgery	0.02	−0.08 to 0.12	0.70	0.02	−0.08 to 0.13	0.66			
Relevant medication									
Medication use	0.04	−0.07 to 0.14	0.50	0.03	−0.07 to 0.14	0.56			
Stomach protectors	0.03	−0.07 to 0.13	0.57	0.02	−0.09 to 0.12	0.72			
Procedure CCE									
Intake metoclopramide	0.15	0.05–0.26	0.003	0.15	0.05–0.25	0.004	0.15	0.04–0.25	0.01
Findings CCE									
Presence of diverticula in SB	0.09	0.01–0.17	0.04	0.07	−0.01 to 0.16	0.10	0.08	−0.004 to 0.156	0.06
Presence of diverticula in the colon	0.08	−0.02 to 0.19	0.13	0.09	−0.02 to 0.20	0.12	0.09	−0.01 to 0.19	0.09

Completion rate	Univariable analysis			Multivariable analysis			Multivariable analysis with backward elimination		
	OR	95% CI	P value	OR	95% CI	P value	OR	95% CI	P value
Patient characteristics									
Age	1.01	0.97–1.05	0.67	1.001	0.960–1.043	0.97	1.54	1.04–2.28	0.03
Sex, male	1.66	1.14–2.41	0.01	1.52	1.01–2.29	0.04			
BMI	1.05	1.00–1.10	0.08	1.04	0.98–1.10	0.21			
History of smoking	0.86	0.58–1.28	0.45	0.80	0.52–1.22	0.29			
Coffee intake	1.000	0.999–1.001	0.60	1.000	0.999–1.001	0.70			
Fiber intake	0.98	0.95–1.01	0.12	0.98	0.95–1.02	0.27			
Diet quality	0.95	0.84–1.08	0.44	0.99	0.85–1.15	0.91			
Physical activity	1.000	0.997–1.003	0.91	1.001	0.997–1.004	0.62			
Relevant symptoms									
Dyspeptic complaints	0.66	0.32–1.36	0.26	0.81	0.36–1.78	0.59			
Changes in stool pattern	2.18	1.17–4.07	0.01	2.27	1.18–4.36	0.01	2.27	1.20–4.30	0.01
Relevant medical history									
Abdominal surgery	0.53	0.36–0.78	0.001	0.50	0.33–0.77	0.002	0.54	0.36–0.80	0.003
Relevant medication									
Medication use	1.28	0.83–1.97	0.27	1.43	0.87–2.36	0.16			

Table 5. (continued)

Completion rate	Univariable analysis			Multivariable analysis			Multivariable analysis with backward elimination		
	OR	95% CI	P value	OR	95% CI	P value	OR	95% CI	P value
Stomach protectors	0.997	0.647–1.537	0.99	0.995	0.606–1.635	0.99			
Procedure CCE									
Intake metoclopramide	0.63	0.42–0.94	0.02	0.61	0.40–0.94	0.03	0.60	0.40–0.91	0.02
Findings CCE									
Presence of diverticula in SB	2.51	0.78–8.04	0.12	2.83	0.85–9.47	0.09	2.94	0.91–9.49	0.07
Presence of diverticula in the colon	1.19	0.67–2.11	0.55	1.19	0.63–2.26	0.59			

$\beta$ , standardized beta; BMI, body mass index; CCE, colon capsule endoscopy; CI, confidence interval; GI, gastrointestinal; OR, odds ratio; SB, small bowel; t, t-value. For determining predictors of the total GI tract transit time, linear regression analyses were performed. Univariable models (each predictor one by one), a multivariable model (including all predictors in the table), and a multivariable model after backward selection (subsequent removal of the predictor with the highest *P* value until all *P* values were <0.1) are included in this table.  $\beta$  values are standardized regression coefficients from linear regression models and here represent differences in total GI tract transit times per SD higher predictor variables.

For determining predictors of the GI tract completion rate, logistic regression analyses were performed. Univariable models (each predictor one by one), a multivariable model (including all predictors in the table), and a multivariable model after backward selection (subsequent removal of the predictor with the highest *P* value until all *P* values were < 0.1) are included in this table. Odds represent the chances of completion per SD higher predictor variables.

the excluded cases probably had relatively longer transit times compared with the included cases, this might have affected the results. Second, the completion rate of 51.9% in our study is low compared with completion rates in previous studies, and therefore, the results might not be generalized. However, high completion rates of 70%–100% are mostly seen with the use of oral sodium phosphate (NaP), which has been withdrawn from many markets because of safety concerns (6). Studies using a similar preparation protocol to our study, however, show lower completion rates. Third, compliance to the bowel preparation protocol was not included as a confounder in our analysis. However, in daily practice, not everyone will be compliant to the preparation protocol and it is impossible to know this beforehand. Therefore, we believe that the found predictors for slow transit times and a low completion rate can still be used to anticipate longer transit times in certain patients, regardless of the reason behind it (e.g. physiological such as lower bowel motility or noncompliance). Fourth, to improve the validity of the results, multiple imputation was performed where the assumption was made that the missing values were missing at random. With this assumption, there is always a small chance that the results might be biased. However, the imputed and original data showed almost no differences in its baseline characteristics (see Supplementary Table 2, Supplementary Digital Content 1, <http://links.lww.com/CTG/A812>). Therefore, we believe the current results based on the imputed data set are reliable.

To conclude, lower BMI, unchanged stool pattern, higher fiber intake, younger age, and history of abdominal surgery were significant predictors for slower CCE transit times and a lower completion rate. Clinicians can use these factors to anticipate a longer capsule transit time and adapt the preparation protocol. On top of that, those participants to whom metoclopramide was administered because of a delayed stomach transit subsequently had a faster small bowel transit compared with those who did not take metoclopramide. This suggests that the completion rate might be optimized by using metoclopramide in all CCE procedures instead of waiting for a delay in stomach transit.

#### CONFLICTS OF INTEREST

**Guarantor of the article:** Manon C.W. Spaander, MD, PhD.

**Specific author contributions:** S.M.: collecting data, interpretation of data and statistical analysis, and writing the manuscript. F.V.: study design, collecting data, and writing the manuscript. T.V.: statistical analysis and writing the manuscript. E.K.: study design and writing the manuscript. M.C.W.S.: study design, interpretation of data, and writing the manuscript. **Financial support:** This manuscript was submitted on behalf of all authors and they have all contributed to the content of this study.

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**Potential competing interests:** None to report.

## Study Highlights

### WHAT IS KNOWN

- ✓ Colon capsule endoscopy (CCE) provides a noninvasive technique for exploration of the colon.
- ✓ To visualize the entire colon, the capsule has to be fast enough to achieve completion within the battery time.
- ✓ The wide variation in the CCE completion rate and transit times is not completely understood.
- ✓ The literature on factors influencing CCE transit times is scarce.

### WHAT IS NEW HERE

- ✓ Slower CCE transit times and a lower completion rate were shown with younger age, low body mass index, unchanged stool pattern, history of abdominal surgery, and high fiber intake.
- ✓ Clinicians can consider these factors to select patients with an anticipated longer capsule transit time.
- ✓ Those participants who took metoclopramide because of a delayed stomach transit subsequently had a faster small bowel transit compared with those who did not take metoclopramide.
- ✓ This suggests that the chance of completion might be optimized by using metoclopramide in all CCE procedures instead of waiting for a delay in stomach transit.



## REFERENCES

1. Spada C, Hassan C, Galmiche JP, et al. Colon capsule endoscopy: European Society of Gastrointestinal Endoscopy (ESGE) Guideline. *Endoscopy* 2012;44:527–36.
2. Spada C, Hassan C, Bellini D, et al. Imaging alternatives to colonoscopy: CT colonography and colon capsule. *European Society of Gastrointestinal Endoscopy (ESGE) and European Society of Gastrointestinal and Abdominal Radiology (ESGAR) Guideline - Update 2020*. *Eur Radiol* 2021;31:2967–82.
3. Rex DK, Boland CR, Dominitz JA, et al. Colorectal cancer screening: Recommendations for physicians and patients from the U.S. Multi-society task force on colorectal cancer. *Am J Gastroenterol* 2017;112:1016–30.
4. Spada C, Pasha SF, Gross SA, et al. Accuracy of first- and second-generation colon capsules in endoscopic detection of colorectal polyps: A systematic review and meta-analysis. *Clin Gastroenterol Hepatol* 2016;14:1533–43.e8.
5. Pecere S, Senore C, Hassan C, et al. Accuracy of colon capsule endoscopy for advanced neoplasia. *Gastrointest Endosc* 2020;91:406–14 e1.
6. Kjølhede T, Olholm AM, Kaalby L, et al. Diagnostic accuracy of capsule endoscopy compared with colonoscopy for polyp detection: Systematic review and meta-analyses. *Endoscopy* 2021;53:713–21.
7. Yamada K, Nakamura M, Yamamura T, et al. Clinical factors associated with missing colorectal polyp on colon capsule endoscopy. *Digestion* 2020;101:316–22.
8. Kobaek-Larsen M, Krojger R, Dyrvig AK, et al. Back-to-back colon capsule endoscopy and optical colonoscopy in colorectal cancer screening individuals. *Colorectal Dis* 2018;20:479–85.
9. Krojger R, Dyrvig AK, Kobaek-Larsen M, et al. Booster medication to achieve capsule excretion in colon capsule endoscopy: A randomized controlled trial of three regimens. *Endosc Int Open* 2018;6:E1363–8.
10. Togashi K, Fujita T, Utano K, et al. Gastrografin as an alternative booster to sodium phosphate in colon capsule endoscopy: Safety and efficacy pilot study. *Endosc Int Open* 2015;3:E659–61.
11. Madsen JL, Graff J. Effects of ageing on gastrointestinal motor function. *Age Ageing* 2004;33:154–9.
12. Brogna A, Ferrara R, Bucci AM, et al. Influence of aging on gastrointestinal transit time. An ultrasonographic and radiologic study. *Invest Radiol* 1999;34:357–9.
13. Nandhra GK, Mark EB, Di Tanna GL, et al. Normative values for region-specific colonic and gastrointestinal transit times in 111 healthy volunteers using the 3D-Transit electromagnet tracking system: Influence of age, gender, and body mass index. *Neurogastroenterol Motil* 2020;32:e13734.
14. Degen LP, Phillips SF. Variability of gastrointestinal transit in healthy women and men. *Gut* 1996;39:299–305.
15. Mushref MA, Srinivasan S. Effect of high fat-diet and obesity on gastrointestinal motility. *Ann Transl Med* 2013;1:14.
16. Keeling WF, Martin BJ. Gastrointestinal transit during mild exercise. *J Appl Physiol* 1987;63:978–81.
17. Bohlin J, Dahlin E, Dreja J, et al. Longer colonic transit time is associated with laxative and drug use, lifestyle factors, and symptoms of constipation. *Acta Radiol Open* 2018;7:2058460118807232.
18. Sato J, Nakamura M, Watanabe O, et al. Prospective study of factors important to achieve observation of the entire colon on colon capsule endoscopy. *Therap Adv Gastroenterol* 2017;10:20–31.
19. Buijs MM, Kobaek-Larsen M, Kaalby L, et al. Can coffee or chewing gum decrease transit times in colon capsule endoscopy? A randomized controlled trial. *BMC Gastroenterol* 2018;18:95.
20. Ikram MA, Brusselle G, Ghanbari M, et al. Objectives, design and main findings until 2020 from the Rotterdam Study. *Eur J Epidemiol* 2020;35:483–517.
21. Vuik FER, Nieuwenburg SAV, Moen S, et al. Population-based prevalence of gastrointestinal abnormalities at colon capsule endoscopy. *Clin Gastroenterol Hepatol* 2022;20:692–700.e7.
22. Willett WC, Howe GR, Kushi LH. Adjustment for total energy intake in epidemiologic studies. *Am J Clin Nutr* 1997;65:1220S–31S.
23. Voortman T, Kieffe-de Jong JC, Ikram MA, et al. Adherence to the 2015 Dutch dietary guidelines and risk of non-communicable diseases and mortality in the Rotterdam Study. *Eur J Epidemiol* 2017;32:993–1005.
24. Stringa N, van Schoor NM, Milanesechi Y, et al. Physical activity as moderator of the association between APOE and cognitive decline in older adults: Results from three longitudinal cohort studies. *J Gerontol A Biol Sci Med Sci* 2020;75:1880–6.
25. Sterne JA, White IR, Carlin JB, et al. Multiple imputation for missing data in epidemiological and clinical research: Potential and pitfalls. *BMJ* 2009;338:b2393.
26. Neuffer PD, Young AJ, Sawka MN. Gastric emptying during walking and running: Effects of varied exercise intensity. *Eur J Appl Physiol Occup Physiol* 1989;58:440–5.
27. Mittal R, Debs LH, Patel AP, et al. Neurotransmitters: The critical modulators regulating gut-brain Axis. *J Cell Physiol* 2017;232:2359–72.
28. Strik C, Stommel MW, Schipper LJ, et al. Long-term impact of adhesions on bowel obstruction. *Surgery* 2016;159:1351–9.
29. ten Broek RPG, Issa Y, van Santbrink EJ, et al. Burden of adhesions in abdominal and pelvic surgery: Systematic review and met-analysis. *BMJ* 2013;347:f5588.
30. Matrana MR, Margolin DA. Epidemiology and pathophysiology of diverticular disease. *Clin Colon Rectal Surg* 2009;22:141–6.
31. Schulze-Delrieu K. Metoclopramide. *Gastroenterology* 1979;77(4 pt 1):768–79.
32. de Vries J, Miller PE, Verbeke K. Effects of cereal fiber on bowel function: A systematic review of intervention trials. *World J Gastroenterol* 2015;21(29):8952–63.
33. McRorie JW Jr, McKeown NM. Understanding the physics of functional fibers in the gastrointestinal tract: An evidence-based approach to resolving enduring misconceptions about insoluble and soluble fiber. *J Acad Nutr Diet* 2017;117(2):251–64.

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