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SHORT COMMUNICATION

# Normal colonic transit time predicts the outcome of colonic manometry in patients with chronic constipation—an exploratory study

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## Abstract

**Purpose** Colonic manometry (CM) can be of additive value in the diagnostic workup of colonic motility in chronic constipated patients. However, it is claimed that colonic motor disturbances occur in normal-transit constipation (NTC) and slow-transit (STC) constipation, as measured using a radio-opaque marker study, and therefore, the relationship between colonic motor disturbances on CM and colonic transit time (CTT) remains unclear. Our aim was to compare results from colonic marker study with the outcome of CM in patients with treatment-refractory chronic constipation (CC).

**Method** Eighty-seven CC patients and 12 healthy volunteers, undergoing both a CTT study and a 24-h CM in a Dutch tertiary referral center, were included. CTT was measured using radio-opaque markers (X-ray at day 4 after ingestion of 20 markers at day 0). CM was performed using a catheter with 6 solid-state pressure sensors, endoscopically clipped to the mucosa in the right colon. CM was defined as normal when at least three high-amplitude propagating contractions (HAPCs), i.e., propagating waves with amplitude ≥ 80 mmHg over at least three sensors, were identified.

**Results** In total, 70 patients showed STC on CTT, of which 21 (30%) showed normal CM. All 17 NTC patients and healthy volunteers showed normal CM. The negative predictive value of CTT for normal CM was 100%.

**Conclusion** Colonic manometry should be considered in therapy-refractory STC patients in order to further delineate colonic motility. However, in this exploratory study, for patients presenting with NTC on a radio-opaque marker study, colonic manometry does not appear to have added value.

**Keywords** Chronic constipation · Colonic manometry · Colonic transit time

## Introduction

Colonic transit time (CTT) using radio-opaque markers [1, 2] is a useful tool in clinical practice to determine the presence or absence of slow colonic transit in the workup of chronic constipation [1, 3]. In our tertiary center, colonic manometry is regularly performed in addition to a colonic marker study, in order to further delineate disturbances in colonic motility and transport. Colonic motor disturbances on colonic manometry have been described not only in patients with slow-transit constipation (STC) but also in patients with normal-transit constipation (NTC). Therefore, the association between colonic motor disturbances and colonic transit remains unclear [2]. Moreover, the added value of colonic manometry in the diagnostic workup of chronic constipation is disputable and there is no clear guideline recommendation for which patients colonic manometry is indicated [2, 3]. Colonic manometry is an invasive, time-consuming, and expensive procedure that is not readily available in every gastrointestinal (GI) motility center. Being able to identify patients, in whom colonic manometry could have added value in the diagnostic workup and management of

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chronic constipation, will result in a reduction of unnecessary invasive procedures and healthcare costs.

The aim of the current exploratory study was to compare the results of colonic marker studies with the outcome of colonic manometry in patients with treatment-refractory chronic constipation, in order to assess the predictive value of colonic transit time for colonic motor abnormalities on colonic manometry.

## Method

All adult chronic constipation patients referred to our outpatient clinic in whom rectal evacuatory disorders had been excluded by history taking and physical examination underwent both a colonic marker study and colonic manometry in our tertiary referral center (Maastricht University Medical Center+ (MUMC+), The Netherlands) between 2012 and 2017, and were included for exploratory retrospective analysis. In addition, data from a control group of 12 healthy volunteers, that had previously participated in a prospective study for which they had undergone both procedures, were available. The study has been approved by our Medical Ethics Committee. Data analysis was performed using IBM SPSS Statistics, version 23 (IBM Statistics for Macintosh, Chicago, IL, USA). Continuous outcomes are expressed as mean ± standard deviation (SD) and differences between groups were tested using ANOVA and/or independent samples *t* test. Categorical outcomes are expressed as proportions (%) and differences between groups were tested using the $\chi^2$ test. A $p$ value of $< 0.05$ was considered statistically significant.

### Colonic transit study

Colonic transit was investigated using the Hinton method [4]. Patients ingested two gelatine capsules each containing 10 radio-opaque markers (polyurethane; 40% barium sulfate) (P. & A. Mauch, CH-4142 Münchenstein) on day 0. On day 4, a single abdominal X-ray was taken to assess the number of markers still present in the GI tract. Delayed transit was defined as retention of > 20% of the markers (> 4 markers) at the time of the X-ray. Laxatives were discontinued for at least 3 days prior to testing.

### Colonic manometry

Colonic manometry was performed using a solid-state probe with six sensors, with sensor spacing of 15 cm (Medical Measurement Systems, etc.). Colonoscopy and placement of the manometer at the hepatic flexure was performed under minimal sedation (Midazolam 2.5 mg and Fentanyl 25 μg or Pethidine 25 mg). The manometer was anchored to the colonic wall using hemostatic clips, and correct positioning of the manometer was verified using fluoroscopy. Recordings were started after a 2-h adaptation period (i.e., bed rest), in order to reduce the effects of endoscopic placement of the catheter and sedation. During the following measurement period of 24 h, subjects received standardized meals and were allowed to move about throughout the day.

The number of high-amplitude propagating contractions (HAPCs) was evaluated using MMS database software (Medical Measurement Systems, version 9.5f (February 25, 2016)). An HAPC was defined as a propagating wave with an amplitude ≥ 80 mmHg over at least three sensors [5]. Colonic manometry was defined as normal when at least three HAPCs were present over 24 h [6].

## Results

Data from 87 chronic constipation patients and 12 healthy volunteers were included in the analysis. Mean age was 41.60 ± 14.0 years and 86 (86.9%) subjects were female. Baseline characteristics per subgroup are shown in Table 1.

Based on the radio-opaque marker study, 70 chronic constipation patients were categorized as slow colonic transit, whereas 17 were defined as normal colonic transit. Of the subjects with slow transit, 21 (30%) had a normal colonic manometry. This percentage was significantly lower compared with that in the group with normal transit ($n = 17$; 100%), and healthy controls ($n = 12$; 100%). These results demonstrate a negative predictive value of a colonic transit study for normal colonic manometry of 100%. Additionally, the number of HAPCs per 24 h was indeed significantly lower in slow-transit patients (1.89 ± 2.2) as compared with normal-transit patients (5.00 ± 1.5), and healthy subjects (5.25 ± 3.0).

## Discussion

In this exploratory analysis of standardized diagnostic workup data, 70% of STC patients showed colonic motor disturbances on colonic manometry, whereas all NTC patients and all healthy subjects had normal colonic manometry. These findings point to a negative predictive value of colonic transit time for normal colonic manometry of 100%, indicating that colonic manometry does not add any value to the diagnostic or therapeutic processes for constipation in patients with normal colonic transit. Moreover, this suggests that a colonic marker study could be used to predict for which patients an additional colonic manometry is indicated.

Previous research demonstrated that a subgroup of STC patients did not show pathophysiologic abnormalities on colonic manometry [7] and differences in colonic motor activity between STC, NTC, and healthy subjects have also been observed previously [8, 9]. The current study is the first, albeit exploratory and retrospective in nature, to directly compare

**Table 1** Demographic characteristics and results from colonic manometry for slow-transit patients, normal-transit patients, and healthy controls

| | Slow transit ($n = 70$) | Normal transit ($n = 17$) | Controls ($n = 12$) |
|---|---|---|---|
| Female sex, *n* (%) | 60 (85.7) | 16 (94.1) | 10 (83.3) |
| Age, mean years ± SD | 41.76 ± 14.7 | 43.06 ± 12.1 | 38.58 ± 11.7 |
| BMI, mean ± SD | 23.33 ± 4.8[a] | 22.55 ± 5.1[b] | c |
| Normal colonic manometry, *n* (%) | 21 (30) | 17 (100)* | 12 (100)[#] |
| Number of HAPCs in 24 h | 1.89 ± 2.2 | 5.00 ± 1.5* | 5.25 ± 3.0[#] |

Continuous outcomes expressed as mean ± SD and tested using ANOVA; categorical outcomes expressed as number (%) and tested using $\chi^2$ test

*Significant difference slow transit vs. normal transit ($p < 0.001$). [#] Significant difference slow transit vs. control ($p < 0.001$)

[a] Missing data of 20 subjects. [b] Missing data of 4 subjects. [c] Missing data of all subjects

the results of colonic transit time and full colonic manometry in both NTC and STC patients, in an adult population, in terms of determining whether the result of a colonic marker study could predict the manometric outcome.

In the 2013 American Gastroenterological Association medical position statement on constipation, colonic manometry is similarly placed in the treatment algorithm for both NTC and STC [2]. Our results, however, demonstrate that this invasive procedure should not be considered useful for NTC patients. These findings might have important implications for clinicians involved in the management of chronic constipation patients. As colonic marker study is readily available in secondary care, whereas colonic manometry is only offered in specialized tertiary motility centers, our findings could form a basis for the decision whether or not to refer an individual patient. In fact, a recent study has shown that a plain abdominal radiograph can be a good surrogate for the colonic marker test [10].

It should be noted that CTT data in this study are based on the Hinton method [4], as compared with the more refined Metcalf method [11]. As the latter method measures over a longer period of 7 days and allows to differentiate transit between different colonic segments, a more detailed comparison between CTT and colonic manometry could be made when using this method. At the time of the initiation of the study, the single capsule technique was considered sufficient for routine clinical practice [12]. Furthermore, recent developments have shifted future perspectives from conventional manometric studies to high-resolution colonic manometry (HRCM). Our analysis of HAPCs was based on rather rough estimate to define colonic motor response, yet the aim of this study was not to dissect more subtle differences. The newer technique has shown to define colonic motility patterns more detailed, and should be considered more useful over conventional 24 h manometry when assessing colonic motility into detail in patients suspected of motility disorders [13, 14]. Ideally, the findings of this study should be confirmed by assessing whether colonic transit studies also predict the outcome on HRCM. In addition, our study is limited by the fact that no systematic evaluation was performed of potential other causes of constipation, in particular rectal evacuatory disorders, the presence of which might have influenced outcomes of the radio-opaque marker studies, albeit this was not confirmed in a larger study [15]. Further, our sample included a relatively small percentage of normal-transit constipation patients; results with regard to the negative predictive value of CTT ought therefore be corroborated in larger and more well-defined populations.

## Conclusion

Colonic manometry should be considered in therapy-refractory slow-transit constipation patients in order to further delineate colonic motility. However, for patients presenting with normal transit on a radio-opaque marker study, colonic manometry does not appear to have added value on the basis of our exploratory findings. Findings need corroboration in larger, well-characterized populations.

### Compliance with ethical standards

The study has been approved by our Medical Ethics Committee.



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