



University of Michigan Health System

Impairment of Overall and Regional High Amplitude Colon Contractions in Severe Slow Transit Constipation Measured by Wireless Motility Capsules

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ABSTRACT

Background: Severe slow transit constipation (STC) is characterized by reduced high amplitude propagating contractions (HAPCs) on colon manometry, but we previously reported that colon pressure activity is increased in chronic constipation using wireless motility capsules (WMC) (Hasler et al., AJP 2009). A possible reason for this discrepancy is the relatively small number of patients with severe STC recruited in our original WMC study. **Aims:** (i) to compare overall colon pressure activity and high amplitude, long duration contractions (HAC) in a large cohort of patients with severe STC vs. those with lesser colon transit delays, (ii) to assess if contractile deficits in severe STC show variation in different colon regions, and (iii) to test if HAC activity in severe STC is affected by associated dyssynergic defecation. **Methods:** WMC (SmartPill Corp.) colon pressure waves were compared in 30 normal transit constipation (NTC) patients (colon transit <59 hr by WMC), 17 patients with moderate STC (transit 59-100 hr), and 35 patients with severe STC (transit >100 hr). Transit was divided into quartiles by time to characterize regional colon motor activities. Overall numbers of contractions >25 mmHg in amplitude and areas under pressure curves (AUC) per 15 min were quantified. HACs (>100 mmHg in amplitude and >14 sec duration) were defined by similar criteria as for HAPCs on colon manometry. Dyssynergia was detected if balloon expulsion time was >1 min. **Results:** Overall numbers of colon contractions and AUCs in severe STC were lower vs. NTC and moderate STC (P<0.01)(Table 1). HACs represented 0.7% of overall contractions in NTC, 0.9% in moderate STC, and 0.2% in severe STC (P<0.05). HACs per hr were significantly reduced in severe STC vs. NTC and moderate STC (P<0.01)(Table 1). In the 1st colon transit quartile, HACs were similar in severe STC (0.001±0.001), NTC (0.001±0.001), and moderate STC (0.008±0.006)(P=NS). In the 4th quartile, HACs occurred less often in severe STC (0.01±0.01) vs. NTC (0.17±0.02) and moderate STC (0.19±0.02)(P<0.05). Severe STC patients with and without dyssynergia had similar overall contractions, AUCs, and HACs (all P=NS)(Table 2). **Conclusions:** Patients with severe slow transit constipation exhibit significantly reduced overall colon contractile activity compared to those with less severe transit delays. High amplitude contractions with similar amplitude and duration characteristics as manometrically-defined HAPCs are especially reduced in severe STC. Deficits in high amplitude contractions in severe STC are most prominent in the latter phases of transit. Contraction defects in severe STC are unaffected by concurrent dyssynergia. Our findings provide pathophysiologic insight into slow transit constipation and suggest that characterization of high amplitude contractions with WMC testing may provide clinically useful information.

	NTC	Moderate STC	Severe STC	P Value
Overall contraction numbers/15 min	9.0±0.8	8.4±0.6	4.8±0.4	<0.01
AUC values per 15 min	32.8±3.8	35.1±3.6	13.4±1.7	<0.01
HACs per hr	0.26±0.02	0.30±0.03	0.03±0.01	<0.01

	Severe STC		P Value
	With Dyssynergia	Without Dyssynergia	
Overall contraction numbers/15 min	4.2±2.5	5.0±2.2	0.38
AUC values per 15 min	9.2±2.9	15.3±2.0	0.12
HACs per hr	0.02±0.01	0.03±0.01	0.64

BACKGROUND

- Wireless motility capsules (WMC) have been used to measure whole gut, small bowel, and colonic transit times.
- Severe slow transit constipation (STC) is characterized by reduced high amplitude propagating contractions (HAPCs) on colon manometry.
- We previously showed colon pressure activity increases in chronic constipation using WMC (Hasler et al., AJP 2009).
- A possible reason for the discrepancy is the relatively small number of patients with severe STC recruited into the original WMC study.

AIMS OF STUDY

- To compare overall colon pressure activity and high amplitude, long duration contractions (HAC) in a larger cohort of patients with severe STC vs. patients with lesser transit delays
- To assess if contractile deficits in severe STC show variation in different colon regions.
- To test if HAC activity in severe STC is affected by the presence of associated dyssynergic defecation.

EQUIPMENT

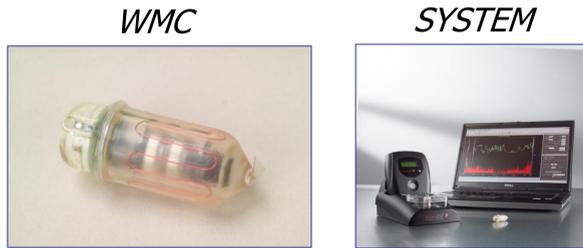


Figure 1: The photo on the right shows the wireless motility capsule (WMC) used to record luminal pH and pressure. The photo on the right shows the data recorder, docking station, and laptop computer for data analysis.

METHODS

- WMC (SmartPill®) colon pressure profiles were compared in subjects from two clinical trial datasets and University of Michigan GI Physiology clinical database:
 - 30 with normal transit constipation (NTC) (colon transit <59 hrs by WMC)
 - 17 with moderate STC (colon transit 59-100 hrs)
 - 35 with severe STC (colon transit >100 hrs)
- Transit was divided into quartiles by time to permit characterization of regional colon activities.
- Patients underwent balloon expulsion testing (BET). Dyssynergia defined by BET >1 minute.

DATA ANALYSIS

- Overall numbers of colon contractions >25 mmHg in amplitude and areas under the pressure curves (AUC) per 15 minutes were quantified.
- HACs were defined as contractions >100 mmHg in amplitude and >14 sec in duration (similar to manometric criteria for colon HAPCs).
- Overall numbers of contractions, AUCs, and HACs were compared in:
 - Patients with NTC, moderate STC, and severe STC.
 - Severe STC patients with and without dyssynergia.
- Numbers of contractions, AUCs, and HACs in each quartile of colon transit were compared in the 3 groups.

SAMPLE WMC TRACING—NTC

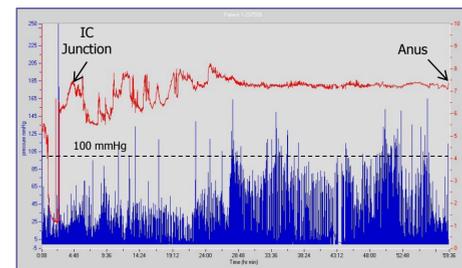


Figure 2: This is a tracing from a patient with normal transit constipation (NTC). From the pH tracing, a colon transit time of 53 hr is documented. The pressure tracing shows an increasing gradient from the early to late phase of colon transit with several contractions >100 mmHg in amplitude in the latter phase of transit.

SAMPLE WMC TRACING—SEVERE STC

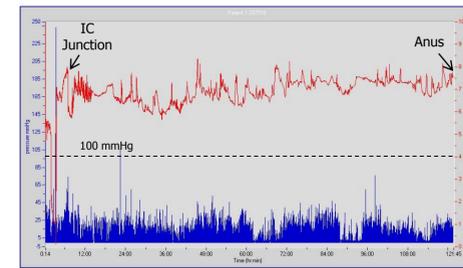


Figure 3: This is a tracing from a patient with severe slow transit constipation (STC). From the pH tracing, a colon transit time of 115 hr is documented. In contrast to the NTC patient, the pressure tracing shows low amplitude contractions throughout the period of colon transit with only one contraction >100 mmHg in amplitude.

OVERALL COLON CONTRACTILE ACTIVITY MEASURED BY WMC

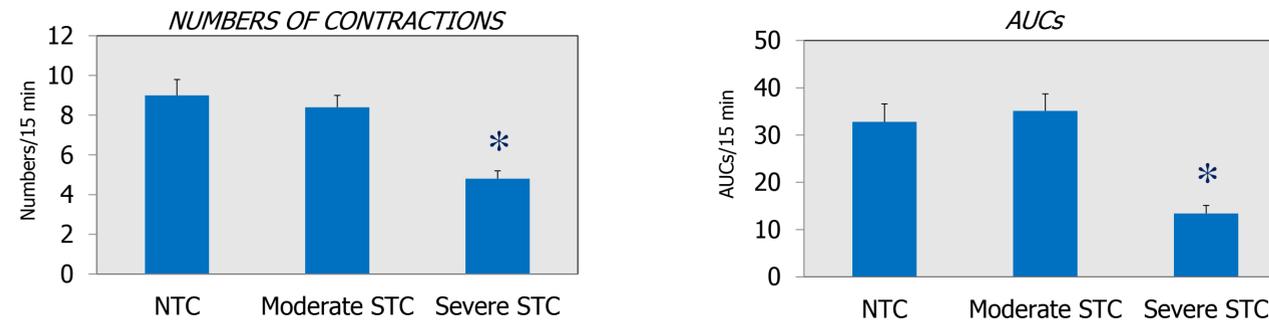


Figure 4: These graphs plot the overall numbers of contractions (left) and areas under the pressure curves (AUCs)(right) for patients with normal transit constipation (NTC), moderate slow transit constipation (STC, and severe STC). Both numbers of contractions and AUCs were significantly reduced in severe STC patients (both P<0.01).

HIGH AMPLITUDE CONTRACTIONS (HACs) MEASURED BY WMC

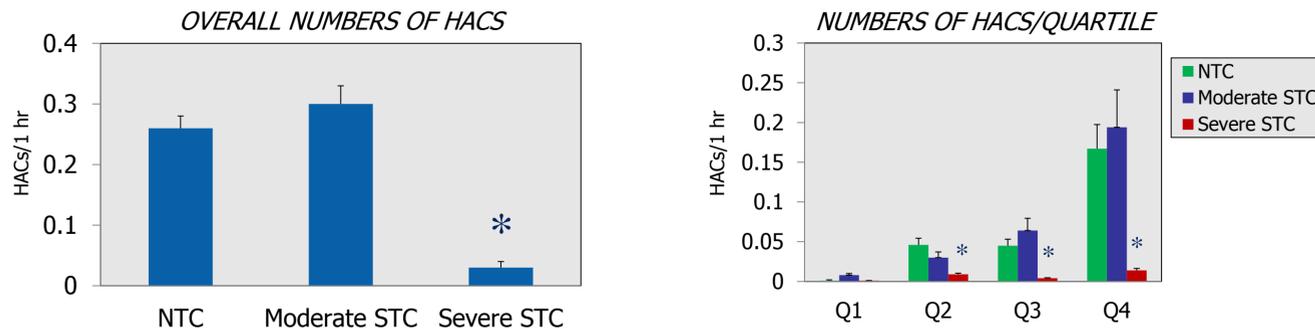


Figure 5: These graphs plot the overall numbers of high amplitude contractions (HACs)(left) and HACs in each quartile of colon transit (right) for patients with NTC, moderate STC, and severe STC. Overall numbers of HACs and numbers of HACs in quartiles 2, 3, and 4 of colon transit were significantly reduced in severe STC patients (all P<0.05).

HACs—% OF TOTAL CONTRACTIONS

	Colon Region				
	Q1	Q2	Q3	Q4	Overall
NTC	0.004%	0.139%	0.107%	0.407%	0.181%
Moderate STC	0.039%	0.087%	0.155%	0.505%	0.219%
Severe STC	0.007%	0.052%	0.021%*	0.064%*	0.038%*

Table 1: This table plots the percent of colon contractions in each quartile of transit and overall that are HACs. HACs represent a very small percent of all contractions in each group. However, they represent a significantly smaller percent in the 3rd and 4th quartiles and overall in STC patients vs. the other groups (P<0.05).

HACs—RELATION TO DYSSYNERGIA

	Severe STC		P Value
	With Dyssynergia	Without Dyssynergia	
Overall contraction numbers/15 min	4.2±2.5	5.0±2.2	0.38
AUC values per 15 min	9.2±2.9	15.3±2.0	0.12
HACs per hr	0.02±0.01	0.03±0.01	0.64

Table 2: This table plots the overall number of colon contractions, the AUC values, and the number of HACs in severe STC patients with and without dyssynergia. There were no differences in any parameter in relation to the presence of dyssynergia.

CONCLUSIONS

- Patients with severe slow transit constipation exhibit significantly reduced overall colon contractile activity on WMC versus patients with less severe transit delays.
- High amplitude, long duration contractions on WMC with similar amplitude and duration profiles as HAPCs defined by manometry are especially reduced in severe STC.
- Deficits in high amplitude contractions in severe STC are most prominent in the latter phases of colon transit.
- Colon contraction defects in severe STC are unaffected by the concurrent presence of dyssynergia.
- These findings provide insight into STC and suggest that characterizing high amplitude contractions with WMC testing may provide clinically relevant information.