### **ORIGINAL CONTRIBUTIONS**





# Roux Limb Motility in Gastric Bypass Patients with Chronic Abdominal Pain—Is There an Association to Prescribed Opioids?

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## Abstract

**Background/Aim** A number of patients continue to suffer from chronic abdominal pain of unknown origin, which may also lead to a prolonged use of opioid analgesics. Symptoms of abdominal pain, nausea and vomiting in this patient group resemble the characteristics of the Roux stasis Syndrome. The aim was to elucidate relationships between chronic abdominal pain, Roux limb motor activity and opioid analgesics.

**Methods** Roux limb high-resolution manometry and ratings of abdominal pain and quality of life were analysed in 15 gastric bypass patients reporting abdominal pain of unknown origin. Effect of acute opiate administration (morphine i.v.) on fasting Roux limb motor activity was assessed in asymptomatic and morphine-naïve gastric bypass patients (n = 9) and compared with an untreated control group (n = 11).

**Results** In the symptomatic patient group, we found disturbed Roux limb motor patterns in 10 out of 15 examinations, but no signs of Roux stasis syndrome. A high prevalence of prescribed opioid analgesics as well as a high number of reoperations in this group. The worst quality of life and the highest number of pain-killing medications were observed among the patients with distal pacemaker activity in Roux limb. In the morphine-naïve and asymptomatic patients, morphine increased the muscular tone in the Roux limb during phase III-like motor activity.

**Summary and Conclusions** A majority of the RYGBP patients with chronic abdominal pain had a disturbed Roux limb fasting motility, and there was a high prevalence of prescribed opioid analgesics. In opiate-naïve RYGBP patients, acute morphine intravenously increased the muscular tone of the Roux limb.

Keywords Bariatric · Opiates · Intestinal motility · Manometry

## Abbreviations

HAC	High activity complex
MMC	Migrating motor complex
NBS	Narcotic bowel syndrome
RSS	Roux stasis syndrome
RYGBP	Roux-en-Y gastric bypass

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# Introduction

Obesity is an important worldwide public health problem. The WHO reports that, in 2014, 39% of adults aged 18 years and over was overweight and 13% was obese [1]. Obesity surgery is regarded as the most effective treatment for achieving sustained weight loss [2]. Angrisani et al. present in the IFSO Worldwide Survey of the year 2014 that 579,517 bariatric/metabolic surgical procedures were performed worldwide, and of these 39.6% was Roux-en-Y Gastric Bypass (RYGBP) [3]. RYGBP has long been the most common bariatric procedure but is now surpassed by vertical sleeve gastrectomy [4]. The RYGBP involves a profound change in the gastrointestinal continuity with the creation of a small gastric pouch and Roux limb [5, 6]. Along with a marked and sustained weight loss, it has, however, by time become evident that the RYGBP procedure may bring a number of complications. In a cohort study from 2016, Gribsholt et al. report that 54% of RYGBP-operated patients had

symptoms of abdominal pain and that 34% had been in contact with the healthcare system because of such symptoms [7]. Greenstein and O'Rourke list a number of causes for abdominal pain in the gastric bypass-operated patient spanning from more general functional disorders and cholelithiasis to procedure dependent internal herniations and gastro-gastric fistulas [8]. These authors state that in the absence of a clear diagnosis, the threshold for surgical exploration should be low. Despite a competent surgical follow-up, there will be a number of patients with persisting abdominal pain. In a 5-year follow-up study by Høgestøl et al., chronic abdominal pain was reported in 34% of patients operated with RYGBP [9]. Underlying mechanisms of chronic abdominal pain after gastric bypass are still enigmatic and of paramount importance to elucidate.

In some patients, chronic abdominal pain can occur together with nausea and vomiting, symptoms similar to Roux stasis syndrome (RSS) described by Mathias et al. [10]. Moreover, the majority of RYGBP patients with chronic abdominal pain use opioids, which are well known for causing symptom-generating gastrointestinal dysmotility and may further complicate the clinical picture in this patient group. However, the Roux limb motor activity of RYGBP patients with longstanding symptoms has so far not been reported. The aim of the present study was to analyse retrospectively Roux limb manometry examinations of RYGBP patients who complain of chronic abdominal pain, and to investigate morphine influence on Roux limb manometry in asymptomatic RYGBP patients.

## **Material and Methods**

#### Study Design, Patients and Ethical Statement

The first part of the present study was a retrospective review of hospital records concerning sixteen consecutive RYGBP patients that had accepted a referral for upper gastrointestinal motility assessment due to abdominal pain between 2010 and 2017 (Table 1). One patient was unable to tolerate the instrument. Recordings of the fifteen patients were included into the final analysis, 14 female and one man. All patients had undergone laparoscopic gastric bypass, either as a primary surgery (n = 12), or as a conversion from another bariatric surgical procedure (n = 3), and were treated as a single group. The reason for the referral was chronic abdominal pain in all cases. Before referral to manometry, all patients underwent gastroscopy and barium meal investigations to exclude apparent obstruction at gastroenterostomy or enteroenterostomy. Severity of gastrointestinal symptoms, intensity of pain, depression/anxiety and quality of life was evaluated by Gastrointestinal Symptom Rating Scale (GSRS), being organised in five dimensions; diarrhoea, indigestion, constipation, abdominal pain and gastroesophageal reflux. The score below 3 is considered normal [12]. Brief Pain Inventory—Short Form (BPI-SF) asks the participant to rate pain or influence on activity (0 no pain and influence; 10 with worst imaginable pain and completely interference with daily activities) [14]. Euroqual (EQ-5D) estimated on a scale quality of life as best (100) and worst (0) imaginable health-related quality of life [15].

The second part of this study is a cross-sectional comparison of fasting Roux limb motility with or without acute administration of morphine in two cohorts of volunteering un-complicated RYBGP patients being naïve to opiate treatments. The main inclusion criterion was uncomplicated primary surgery with an antecolicantegastric RYGBP as described in detail elsewhere [5, 6]. The time after primary surgery was at least 2 years to ensure stable weight loss. Exclusion criteria were as follows: organic gastrointestinal disease or other substantial comorbidity, recurrent problems with abdominal pain or continuous use of NSAID or opioid analgesics, history of substance abuse or hypersensitivity to given pharmaceuticals. Basic characteristics are shown in Table 2.

All procedures and data collection performed were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The study protocol was approved by the Regional Ethical Review Board in Gothenburg (Dnr: S 447-16). Informed consent was obtained from all individual participants in the second (prospective) part of the study.

## Intraintestinal Pressure Recording Technology

The motility recordings were obtained by use of highresolution manometry catheters straddling the lower oesophageal sphincter, the gastric pouch and the upper part of the Roux limb. During the study period, the laboratory changed from water-perfused side-hole catheters to solid-state Manoscan catheters. Both techniques have similar recording characteristics with pressure sensing at 1-cm intervals, but the latter one covered a longer segment (35 cm) than the former technique (21 cm).

Water-Perfused Catheters Manometry was performed using a multi-lumen Silastic catheter (a customised Ch12 gastrointestinal manometric catheter, CE4-1024, Dentsleeve International LTD, Mississauga, Ontario, Canada). The catheter had a diameter of 4.2 mm and included 22 separate channels with corresponding side holes positioned 10 mm apart, thus covering 21-cm length. Each side hole was connected to a pressure transducer that was separately fed with a low flow of 3 mL/h of NaCl (150 mmol/L). Pressure measurements via fluid-perfused catheters with externally placed transducers are sensitive to body movements. A correction factor

#### Table 1 Patients characteristics (part 1, symptomatic)

	Normal manometry $(n = 5)$	Phase II abnormalities $(n = 6)$	Retrograde propulsion in Roux limb $(n = 4)$	ANOVA <i>p</i> value
Age (years)	40.6 (5.9)	39.7 (11.7)	48.0 (5.9)	0.337
Sex, M/F	1/4	0/6	0/4	0.343
Years after primary operation	4.8 (1.3)	3.0 (1.7)	6.7 (3.2)	0.081
Reoperations	3.8 (1.9)	5.3 (4.0)	3.0 (2.6)	0.493
EQ5D VAS ( $0 = $ worst and $100 = $ best)	53.0 (11.0)#	43.0 (17.8)	20 (8.2)#	0.011
BPI pain $(0 = \text{no pain}, 10 = \text{worst})$	5.4 (1.5)##	6.7 (0.4)	7.9 (1.4)##	0.023
BPI pain influence on general activities ( $0 = no$ influences, 10 = large influences)	5.0 (2.6)	6.3 (1.6)	6.5 (2.6)	0.536
Pain medications (number of analgetics)	0.6 (0.9)	0.8 (1.0)	2.0 (0.8)	0.092
Opiates <i>n</i> (% of above)	2 (40)	3 (50)	4 (100)	0.153

Means (SD); ANOVA is calculated in relation to manometric findings for each variable to the left; significant pairs: p = 0.011; p = 0.023

compensated for the increased hydrostatic pressure along the manometric catheter secondary to the fixed semi-recumbent body position. Each manometry was recorded and analysed using specially designed LabView-software (National Instruments, Austin, TX, USA).

**Solid-State Catheters** These manometries were performed using a solid-state catheter assembly with a diameter of 4.2 mm and supplied with 36 circumferential pressure sensors spaced at 1-cm intervals (Manoscan; Given Scientific Instruments Inc., Los Angeles, CA, USA). The instrument was calibrated according to the manufacturer's instructions. The data analyses were carried out using Mano View analysis software (Sierra Scientific Instruments Inc.; Los Angeles, CA).

#### Investigational Procedures

All manometries were performed in the morning after an overnight fast. The subject rested in a comfortable semi-recumbent position. Following a small amount of local anaesthetic gel (Xylocain® Gel 2% (lidocain), AstraZeneca, Sweden), the manometry probe was inserted transnasally and positioned with the proximal 2–3 sensors in the distal oesophagus and then covering the lower oesophageal sphincter (LES), the gastric pouch and the proximal Roux limb. The position of the catheter was confirmed by fluoroscopy and the catheter was fixed to the nostril. 'Manometric landmarks' were recorded at the beginning and end of the examination, i.e. the highpressure zone (HPZ) indicating LES and the pressure inversion point (PIP) following forced inspiration. In the first (retrospective) part of the study, the patients were examined according to a previously published protocol [10, 11]. The fasting motor activity was recorded to obtain at least one full cycle of the migrating motility complex (MMC). Different phases of MMC in the Roux limb were defined as follows: phase I was motor quiescence with two contractions per 10 min or less, occurring after a phase III period;

Phase II was a period with contractions between 2 and 8 per minute and with irregular rhythm; Phase III was a distinct and >2-min-long period of coordinated powerful contractions between 10 and 12 per min, propagating in the aboral direction [12, 13]. Roux limb high activity complexes (HAC) not fulfilling the MMC phase III criteria were noted. After the 2-h recording of fasting motility, and at least 15 min after the last MMC high activity complex, the study subject was served a mixed meal and was allowed to eat until feeling comfortably full. The meal consisted of either 300 g of a mixture of meat, potatoes and onions (examinations with water-perfused catheters) or small portions of white bread (approximately  $1 \text{ cm}^3/$ portion) with butter, one at the time (examinations with solidstate catheter). The manometry recording was maintained for 15 min after end of meal ingestion after which the manometric landmarks were reconfirmed and the subject was extubated.

The second part of the study focussed on Roux limb MMC phase III HAC, with or without intravenous morphine

**Table 2**Study participants (part 2, asymptomatic)

	Number (females)	Age in years; median (range)	Months after surgery; median (range)	%TBWL; median (range)	Persisting co-morbidity
Time controls	11 (3)	48 (24 to 60)	35 (28 to 53)	33.7 (16.7 to 39.5)	None
Morphine intervention	10 (9)	44 (23 to 52)	39 (32 to 44)	35.5 (25 to 46)	None

%TBWL, total body weight loss in percent; mean (min to max)

infusion. These examinations started with a recording of a baseline period until the occurrence of one phase III-like activity complex. In one group (n = 9), an intravenous infusion of morphine hydrochloride (Morfin Epidural Meda® 10 mg/mL, Meda, Sweden, in 100 mL NaCl 9 mg/mL, Braun, Germany) at 40 µg/kg/h was started and was then maintained over 90 min. The other group (n = 11) served as time controls and did not receive any drug.

#### Analyses

In the first retrospective part of the study, all manometry records were reviewed independently by two examiners (PB and LF). The clinical examination was performed by one single examiner (AM). In the second part of the study, the first and second phase III-like HAC (termed HAC1 and HAC2, respectively) were analysed in all study subjects. The Roux limb intraluminal pressure was assessed by converting the Manoscan recording to numerical values. To standardise the measurements, the intraintestinal pressure was related to the intraesophageal recording: Mean Roux limb pressure was defined as the recorded mean luminal Roux-pressure minus the intraluminal pressure of the distal (non-sphincteric) oesophagus. Furthermore, the oscillating pressure due to contractions was termed contractile pressurization and was quantified using the absolute mean intraluminal pressure minus the nadir-level of the pressure oscillations during the HAC. Mean values within or between two groups were compared by two-tailed Student's t test. In a case of more than two groups, one-way ANOVA was used. Differences between categorical variables were determined by the help of chisquared test. p value  $\leq 0.05$  was considered as significant. All statistical analyses were performed using GraphPad Prism version 7.02 for Windows, GraphPad Software, La Jolla, CA, USA, www.graphpad.com.

## Results

## Manometry in Patients with Severe Abdominal Symptoms After RYGBP

Sixteen patients with severe gastrointestinal symptoms after RYGBP were referred to manometry of the gastric pouch and Roux limb. One patient was impossible to intubate (narrowness in the nose with pain) so the number of successful manometries was fifteen. Fourteen were female, 9/15 had prescribed opioid analgesics and the median number of reoperations due to abdominal symptoms was 4.5 (range 0 to 11). Quality of life estimated by EQ5D on average was 37 (21.1) and mean pain score was 6.25 (1.9) and pain had on average 5.2 (2.9) points influence on general activity. The average score for GSRS items were as follows: 3.7 (1.9) for

diarrhoea, 4.0 (1.8) for indigestion, 3.0 (1.3) for constipation, 4.8 (0.9) for pain and 2.4 (2.0) for the reflux. During manometry, median investigation time was 195 min (range 145 to 220) with median of 4 HAC (range 1 to 6). Median cycle duration was 44 min (range 9 to 82) and the median propagating velocity of phase III-like HAC was 2.7 cm/min (range 0.4 to 26). All HAC started in the proximal Roux limb.

Table 1 shows the results divided according to the manometric findings in the Roux limb. Five patients had normal manometries. In 6 cases, phase II activity was abnormal, and in 4 study persons, we found distal pacemaker activity with distinct retrograde propulsion. Only 1 out of the examined 15 patients had symptoms that correlated to manometry findings during the investigation (not shown). In the 'normal manometry' group, the patients had higher quality of life (EQ5D VAS) and less pain (BPI Pain) than patients with 'retrograde propulsion in the Roux limb' (Table 1). Figures 1 and 2 show examples from two study persons with distal contractions concomitant with the onset of phase III-like HAC and retrograde contraction waves at the end of HAC.

#### **Roux Limb Motility After Morphine Infusion**

Two groups of RYGBP patients were compared with regard to MMC phase III-like high activity complexes (HAC) in the Roux limb. As a rule, the analysis of motor activity was related to the first two HAC occurring in the study period. One group (n = 11) served as untreated controls, thus with no interference between the first and second HAC (HAC1 and HAC2, respectively). In the other group (n = 9), a morphine infusion (rate 40 µg/kg/h) was initiated after the first observed HAC and HAC2 was therefore recorded in the presence of circulating morphine.

There were no significant differences between the groups regarding duration, contraction frequency or propagation velocity of neither the first nor the second HAC (Table 3). Pressurization due to contractions (see the "Material and Methods" section) did not differ between HAC1 and HAC2 in either group. Mean Roux limb pressure of HAC1 and HAC2 did not differ in the untreated time control group. In contrast, the mean limb pressures associated with HAC2s in the morphine-receiving group were significantly higher than the corresponding HAC1. Also, when comparing delta pressure between groups, a significant difference was noted with a muscular tone step-up of  $\approx$  7 mmHg in response to the morphine infusion (Table 3).

## Discussion

Motor activity of the Roux limb has been evaluated after total and sub-total gastrectomy and demonstrated various abnormal motility patterns [16–22]. However, the Roux limb motor activity of RYGBP patients with longstanding symptoms has so

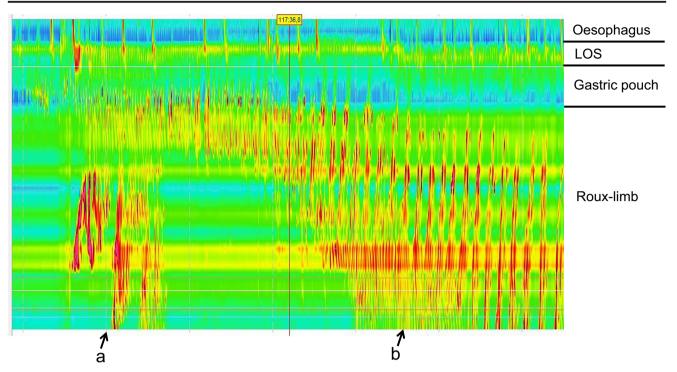


Fig. 1 High-resolution manometry (study subject 15, woman 56 years). Note the powerful contractions in the distal Roux limb at onset of phase-III-like high activity complex (a) and retrograde direction of the contractions at the end of the activity complex (b)

far not been reported. In the symptomatic patients of our retrospective case series, the median investigation time was 195 min, during which the patients had a median of

4 HACs giving an estimated frequency of roughly 1.2 HAC per hour in the Roux limb. The presented HAC's in this study was consistent with the findings of other

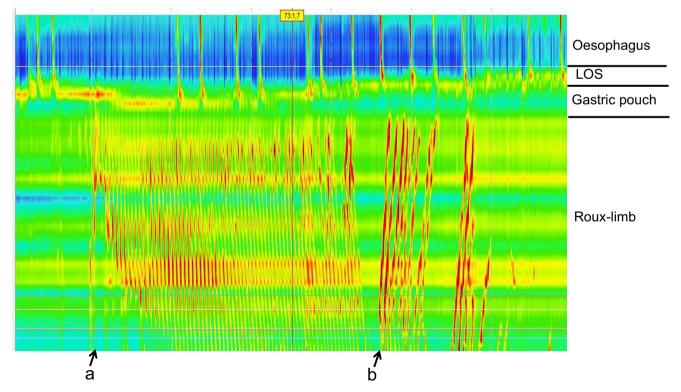


Fig. 2 High-resolution manometry (study subject 16, woman 43 years). Note the contractions in the distal Roux limb at onset of phase-III-like high activity complex (a) and retrograde direction of the contractions at the end of the activity complex (b)

	Untreated time controls $(n = 11)$	trols ( $n = 11$ )			Morphine i.v. after HAC1 $(n = 9)$	HAC1 $(n=9)$			Betwe	Between groups
	HAC1	HAC2	Diff	Diff Paired t test test	HAC1	HAC2	Diff	Paired t test	Diff	Diff Paired t test Diff Unpaired t test
Duration of HAC (seconds)	502.9 (327–1118)	531.2 (308–1324) 28.3 <i>p</i> = 0.4756	28.3	p = 0.4756	356.1 (222–505)	356.1 (222-505)  572.3 (333-1183)  216  p = 0.097	216		188	188 $p = 0.1101$
Contraction frequency (number/min)	10.8 (10-12)	10.9 (10-12)	I	I	10.7 (9–12)	10.4 (9–12)	I	I	I	I
Propagation velocity (cm/min)	3.4 (1.9-4.8)	3.8 (2.2–7.0)	0.4	p = 0.3641	2.9 (1.7-4.0)	3.2 (2.0–7.0)	0.3	p = 0.5139	0.1	p = 0.8748
Mean Roux limb pressure (mmHg)	11.0 (1.6–22.6)	9.7 (3.6–17.3)	1.3	p = 0.3435	22.9 (11.4-34.1)	28.6 (8.0-43.3)	5.7	p = 0.0384	7	p = 0.0129
Contractile pressurization (mmHg)	13.6 (9.3–18.3)	12.7 (9.2–17.3)	0.9	p = 0.1223	17.4 (13.8–26.4)	17.4 (13.8–26.4) 17.7 (13.9–23.4)	0.3	p = 0.8052	1.2	p = 0.369
Data are given as mean (min-max). HACI and HAC2 refer to the first and second recorded phase III high activity complex (HAC), respectively	ACI and HAC2 refer	to the first and second	recorde	d phase III high activ	vity complex (HAC)	, respectively				
Morphine (40 µg/kg/h) was infused intravenously immediately after HAC1 in one group	itravenously immediat	ely after HAC1 in one	group							
Mean luminal pressure is the Roux limb pressure minus the mean intraesophageal pressure during the same period of time	ab pressure minus the	mean intraesophageal	pressure	the same be	riod of time					

Manometry of the Roux limb: interdigestive high activity complexes (HAC)

Table 3

Contractile pressurization; mean luminal pressure minus the nadir value level of pressure oscillations

3865

authors [19, 21]. Even though we noted several abnormal motility events, very few of them correlated with patient-reported symptoms during the examination.

Fourteen of the 15 patients referred to manometry were females. This overrepresentation of females is in concordance with Høgestøl et al. who reported an odds ratio of 2.64 for female gender in chronic abdominal pain at 5-year follow-up [9], as well as with Gribsholt et al. who reported an adjusted prevalence ratio of 1.14 in females self-reporting symptoms associated with bariatric surgery [7]. Because manometry was not routinely performed on all cases of chronic abdominal pain at our clinic, the 15 patients should probably be viewed as the 'worst cases' in our patient flow. It follows that we cannot conclude that the gender imbalance in the present study is representative for a larger cohort of gastric bypass patients with abdominal pain; still the female dominance could be a starting point for future pathophysiologic research. Another feature of potential importance is that many patients (14 out of 15) had undergone several bariatric reoperations (median 4.5, range 0–11) before manometry. In a majority of these patients (10 out of the 15), the first reoperation was due to a primary surgical complication, e.g., postoperative bleeding or internal herniation, suggesting that such an event can trigger a vicious circle leading to chronic abdominal pain.

Even though the questionnaires used in the present study originally were evaluated for larger cohorts, we used them for indicative purposes. In general, we found that EQ5D (quality of life) was scored with a mean of 37 that could be regarded as rather low. GSRS showed that diarrhoea and indigestion were scored well above what could be expected in a normal population. According to the manometry findings, we divided out patients into 3 groups: normal manometry, phase II abnormalities and pacemaker in Roux limb with retrograde propulsion. The EQ5D quality of life in the normal manometry was higher (means 53) compared with the patients who had retrograde propulsive activity (means 20). A similar figure was apparent for the pain where the participants with normal manometry scored 5.4 whereas retrospective propulsivity was scored 7.9 (of a maximal 10 pain score).

Although we found distal pacemaker activity in some participants, no strong support for that RSS was present. Another phenomenon instead caught our interest: a substantial number of the patients used prescribed opioid-based analgesics. Moreover, when one patient with distal pacemaker activity in Roux limb discontinued opiates, manometric findings have completely normalised. We hypothesised that opioid use, via induction of dys-coordinated Roux limb motility, could be one pathophysiologic link to chronic abdominal symptoms occurring in some gastric bypass patients. A chronic need for opioid analgesics after surgical interventions has during recent years been highlighted as a growing problem [23, 24].

In a retrospective cohort study, Raebel et al. report that 4% of patients that were not chronic opioid users became chronic

opioid users after bariatric surgery [25]. Opioids are well known for causing symptom-generating gastrointestinal dysmotility that, in turn, can cause a demand for continued prescription, but now with focus on the abdominal discomfort. Therefore, in the prospective part of the present study, we investigated if acute opiate administration influences Roux limb motility in asymptomatic and morphine-naïve gastric bypass patients.

Food intake during nasointestinal intubation is cumbersome for the patient and the amount of de facto swallowed food is generally small thereby reducing the sensitivity of the method to reflect luminal distension [21]. Attention in the current study was put on the features of the propagating phase III-like HAC that are suitable for quantification and interindividual comparison. We assessed the effect of a low rate morphine infusion on the fasting HAC in uncomplicated RYGBP patients without long-term exposure to opiate analgesics. No differences in duration, contraction frequency or propagation velocity of the MMC phase III-like HAC were observed. However, the mean Roux limb pressure of the HAC was significantly higher during morphine infusion indicating an induction of a tonic contraction in the wall musculature. Similarly, Lewis demonstrated that intravenous infusion of morphine induced duodenal phase III-like activity [26]. In a review from 2012, Brock et al. state that opioids via µ-receptors, mainly located on enteric nerve plexa, induce an increased tone in the circular muscle layer. The enhanced rhythmic contractions in the small intestine and the occasional occurrence of high-amplitude, non-propulsive phasic contractions resulting in increased segmental contraction and decreased propulsive peristalsis [27]. The pathophysiological relevance of opiate induced increase muscular tone in the Roux limb remains to be investigated in detail. It can be speculated that the elevated muscle tonus induces a 'relative narrowness' with reduced compliance to distension. Theoretically, such a 'pre-tension' in the wall musculature facilitates activation of tension-sensitive pain receptors in response to a luminal volume expansion after food intake, thereby eliciting an abdominal pain sensation. The generation of symptoms due to a changed mechano-sensitivity of the Roux limb can be facilitated by type of intestinal contents, e.g. lipids, or conditions like irritable bowel syndrome [28, 29]. It would be interesting to investigate the Roux limb basal muscular tonus and effect of morphine in patients with chronic abdominal pain and longstanding opioid usage, and preferably also after drug detoxification. We however found it unethical to further expose this patient group to opioids; it would also become a challenge to standardise test doses, taking into account the patients standing medication.

An obvious weakness of the present study was the qualitative and exploratory character of retrospective observations made on the case series. The number of included patients was low and the representativity to the RYGBP-operated patient community is uncertain. The results must, therefore, be regarded mainly as hypothesis-generating for future systematic research on the same subject. There are also technical aspects that must be taken into consideration. Initially, the examinations were carried out using a 22 channel multi-lumen fluid-perfused manometry. This method is sensitive to body movement and body positioning reducing its usefulness when comparing absolute values of pressure between individuals. The Manoscan system is not sensitive to body position but has two types of inborne errors due to temperature changes. The 'thermal effect' is an immediate change in pressure reading, while the 'thermal drift' is a linear change, i.e. drift in the pressure baseline which becomes a problem in prolonged studies [30-32]. To avoid these problems, we have not reported pressure values in absolute terms but instead as relative values. The mean Roux limb pressure was related to the basal pressure of the distal, non-spincteric part of the oesophagus being a region not sensitive to morphine exposure [33, 34]. Furthermore, the thermo-sensitivity of the Manoscan catheter made meal provocations with heated food impossible. Instead of warm food, as used with the water-perfused technique, the participants were asked to eat small portions of white bread during the Manoscan examinations. This change of stimulus impaired the analysis of food-induced motor activity. Furthermore, the clinical manometry protocol lacked a prolonged recording after food intake making analysis of the switch to fed state motor activity impossible. However, it is our impression that further research on Roux limb motility during and after food intake should employ methods not demanding intubation. Thus, more research concerning opioids, intestinal motility and chronic symptoms have to be performed. The conclusion of the present study is that opioids to bariatric patients should be prescribed with great caution.

In summary, the retrospective analysis of RYGBP patients with chronic pain revealed a disturbed Roux limb fasting motility, as well as a high prevalence of prescribed opioid analgesics. In an experimental setting on opiate-naïve RYGBP patients, acute morphine intravenously increased the muscular tone of the Roux limb. These findings underline the fact that morphine might be a cause, as well as a cure for abdominal pain after RYGBP. More systematic research is warranted regarding intestinal motility, opioid consumption and chronic abdominal pain after RYGBP surgery.

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## **Compliance with Ethical Standards**

**Conflict of Interest** The authors declare that they have no conflict of interest.

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