MANAGEMENT OF REACTIVE HYPOGLYCAEMIA A SURGICAL PERSPECTIVE

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- Morphic Medical
- Trans.Duodenal.Concepts

LATE DUMPING - POST-OP HYPERINSULINEMIC HYPOGLYCEMIA (PHH)

POSTBARIATRIC HYPOGLYCEMIA

IINCIDENCE => WITH ORAL CARBOHYDRATE PROVOCATION (OGTT)

up to 75%

=> CLINICAL AWARENESS

up to 5-7%

Pre-OP T2DM => 25%

1. Runkel N et al (2011) Evidence-based German guidelines for surgery for obesity. Int J Colorectal Dis 26(4):397–404
2. Custer MD Jr, et al.1946) The so called dumping syndrome after subtotal gastrectomy.Ann Surg 123:410–418
3. Hertz AF (1913) The cause and treatment of certain unfavourable after-effects of gastro-enterostomy. Proc R Soc Med 6(Surg Sect):155–163
4. Tack J et al (2009) Pathophysiology, diagnosis and management of postoperative dumping syndrome. Nat Rev Gastroenterol Hepatol 6(10):583–590
5. Abell T, Minocha A (2006) Gastrointestinal complications of bariatric surgery: diagnosis and therapy.Am J Med Sci 331(4):214–218

- THE HORMONAL REGULATION (INCRETINS) OF DIGESTION IN THE SMALL INTESTINE
- IN THE CONTEXT OF ANATOMICAL BYPASS MODIFICATION (DUODENAL EXCLUSION)

⇒ MODIFICATION OF GLUCOSE METABOLISM

ANNALS OF SURGERY
Vol. 222, No. 3, 339–352

Who Would Have Thought It?

An Operation Proves to Be the Most Effective Therapy for Adult-Onset Diabetes Mellitus

Walter J. Pories, M.D., Melvin S. Swanson, Ph.D., Kenneth G. MacDonald, M.D., Stuart B. Long, B.S., Patricia G. Morris, B.S.N., Brenda M. Brown, M.R.A., Hisham A. Barakat, Ph.D., Richard A. deRamon, M.D., Gay Israel, Ed.D., Jeanette M. Dolezal, Ph.D., and Lynis Dohm, Ph.D.

From the Departments of Surgery and Biochemistry of the School of Medicine and the Human Performance Laboratory of East Carolina University, Greenville, North Carolina

Nat Rev Endocrinol. 2023 March ; 19(3): 164–176. doi:10.1038/s41574-022-00757-5.

Glucose metabolism after bariatric surgery: implications for T2DM remission and hypoglycaemia

Darleen A. Sandoval[1], **Mary Elizabeth Patti**[2]

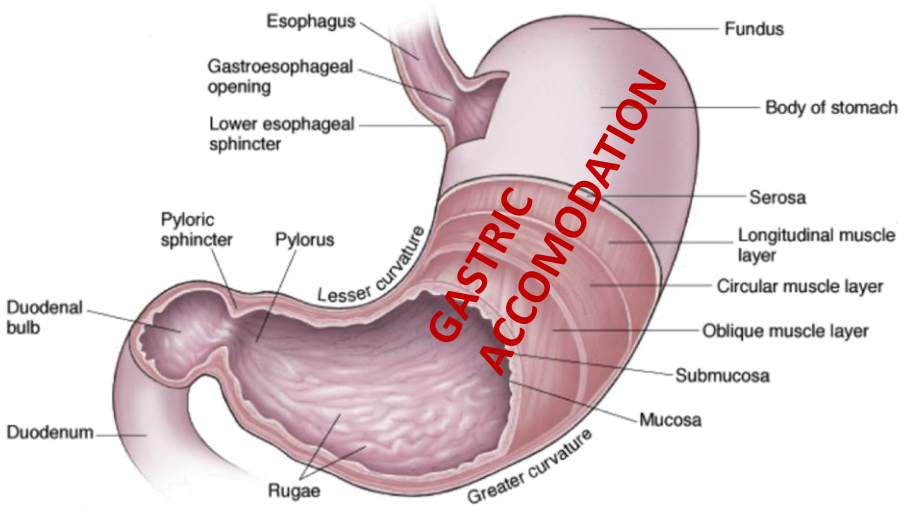
[1]Department of Paediatrics, Section of Nutrition, University of Colorado Anschutz Medical Campus, Aurora, CO, USA.

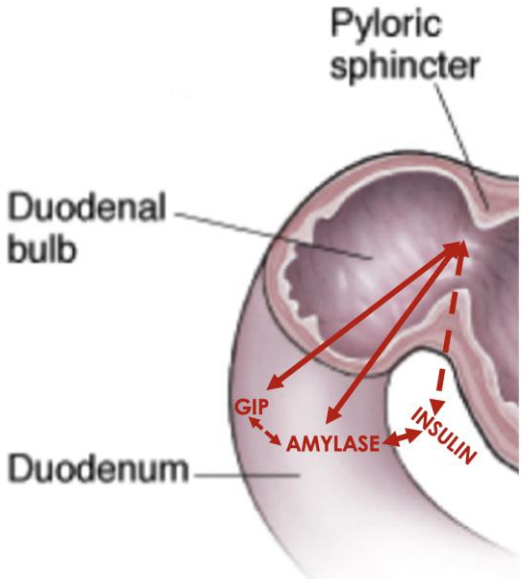
[2]Joslin Diabetes Center, Harvard Medical School, Boston, MA, USA.

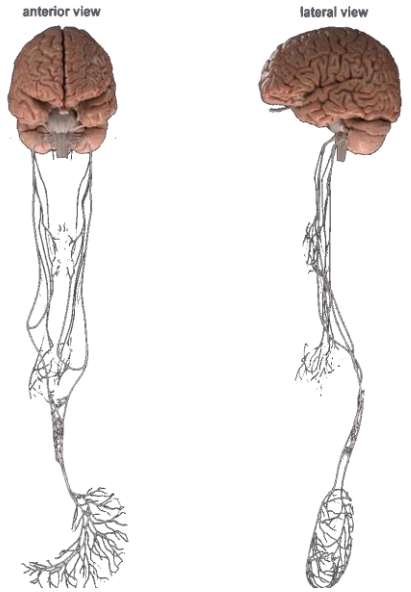
NATURAL ANATOMY

REGULATION OF GASTRIC DISTENTION AND GASTRIC EMPTYING

GASTRIC ACCOMODATION (FULLNESS) ⟷ **SPEED of GASTRIC EMPTYING: DUODENAL FEEDBACK** ⟷ **DISTENSABILITY of GASTRC WALL: VAGAL NERVE**







HORMONAL REGULATION OF CARBOHYDRAT DIGESTION IN THE SMALL INTESTINE

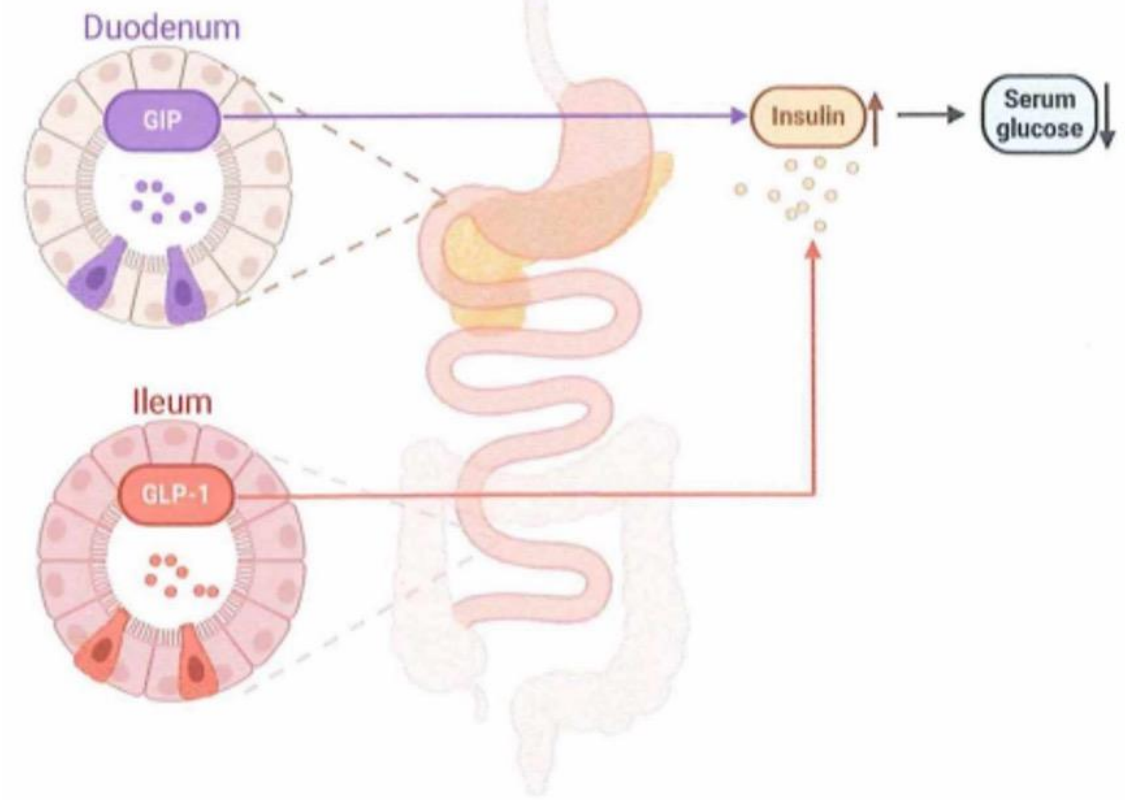
STARTING POINT
of carbohaydrate digestion
GIP HALF LIFE 4-7 MINUTES

K-cell

enterocytes

END POINT POINT
of carbohaydrate digestion
GLP-1 HALF LIFE 2 MINUTES

L-cell



BYPASS ANATOMY

DUMPING IS DEFINED AS THE RAPID PASSAGE OF FOOD FROM THE STOMACH INTO THE GUT (DUMP)

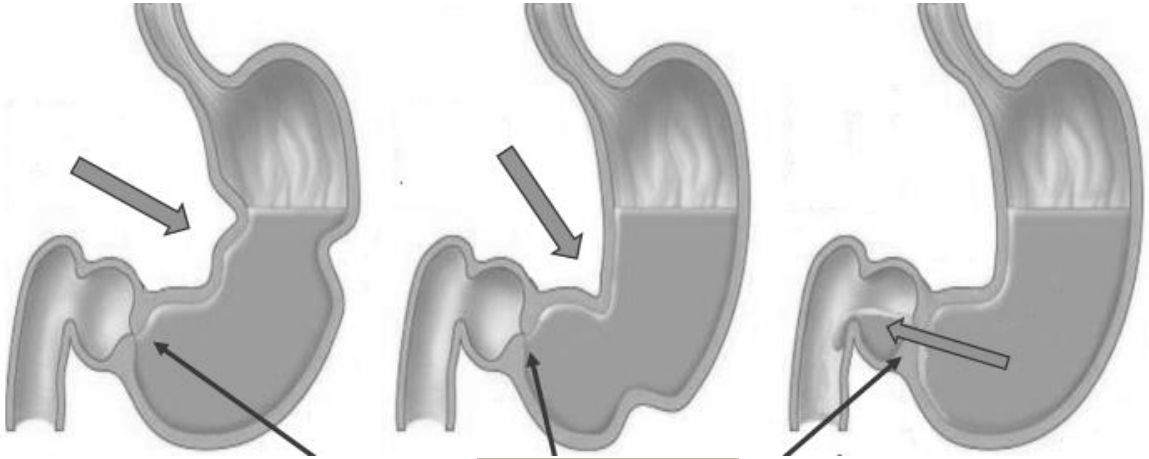
EARLY DUMPING

VASO-VAGAL

LATE DUMPING

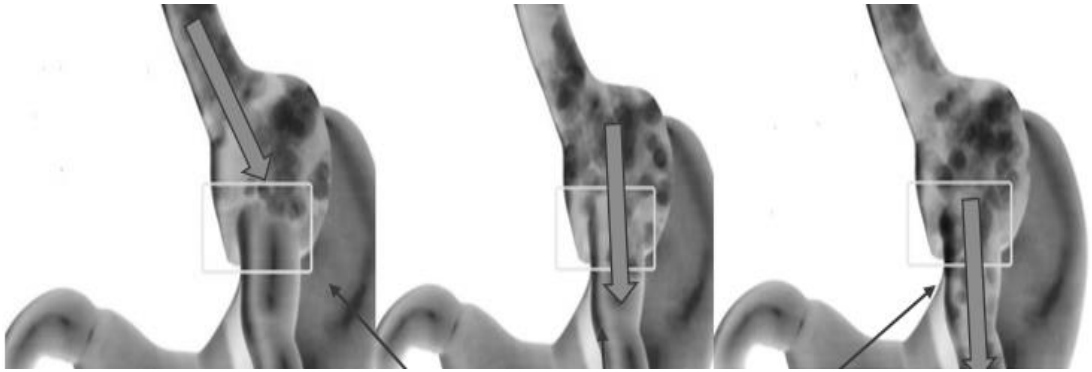
HYPERINSULINEMIC

REGULATION OF GASTRIC DISTENTION AND GASTRIC EMPTYING



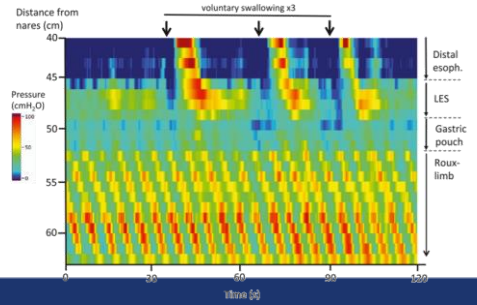
Pyloric Valve

DEMARCATION AND ALLOCATION FUNCTION OF THE PYLORUS.
Specified quantities are delivered to the duodenum



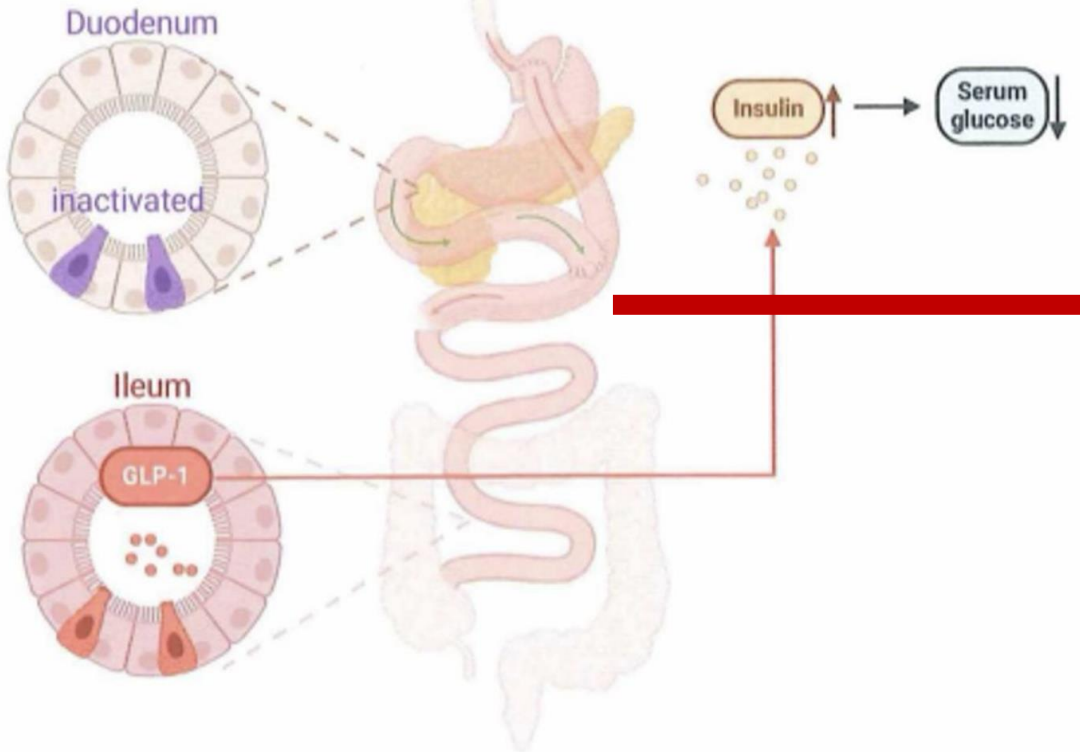
Poucho-Jejunostomy

NO DEMARCATION BETWEEN POUCH AND INTESTINE
The **diameter of the poucho-jejunostomy solely** determines the speed of gastric emptying. Pouch and intestine act as one systeme



Björklund P, Lönroth H, Fändriks L. **Manometry of the Upper Gut Following Roux-en-Y Gastric Bypass Indicates That the Gastric Pouch and Roux Limb Act as a Common Cavity**. Obes Surg. 2015 Oct;25(10):1833-41. doi: 10.1007/s11695-015-1639-1. PMID: 25736230.

HORMONAL REGULATION OF CARBOHYDRAT DIGESTION IN THE SMALL INTESTINE



Reduced to suspended GIP output

⇒ **NO INCRETIN EFFECT**
⇒ **Reduced insulin output**

Bypassed segment **(supraconfluent => PHASE 1 INSULINE RELEASE)**

Common Channel **(infraconfluent => PHASE 2 INSULINE RELEASE))**

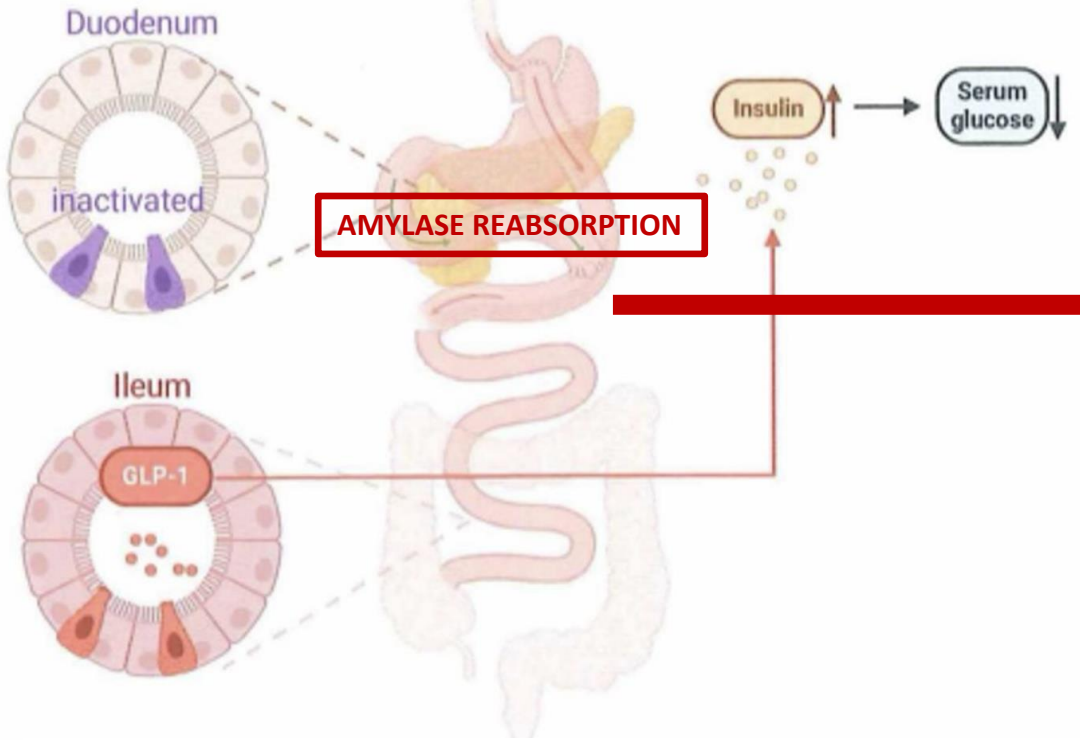
Massive GLP-1 output

⇒ **MASSIVE INCRETIN EFFECT**
⇒ **Massive insulin output**

Green arrow: amylase (exocrine pancreas encymes) and bile transport

Red arrow: food transport

HORMONAL REGULATION OF CARBOHYDRAT DIGESTION IN THE SMALL INTESTINE



Reduced to suspended GIP output

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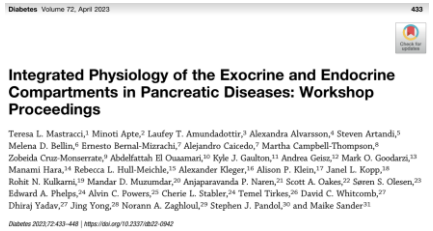
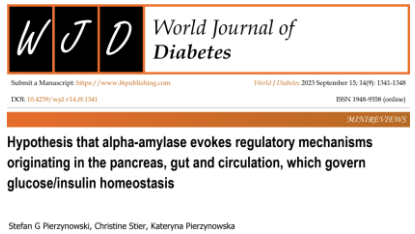

Diabetes Volume 72, April 2023 433

Integrated Physiology of the Exocrine and Endocrine Compartments in Pancreatic Diseases: Workshop Proceedings


World Journal of Diabetes

Hypothesis that alpha-amylase evokes regulatory mechanisms originating in the pancreas, gut and circulation, which govern glucose/insulin homeostasis

Stefan G Pierzynowski, Christine Stier, Kateryna Pierzynowska

Bypassed segment (supraconfluent => PHASE 1 INSULINE RELEASE)

Common Channel (infraconfluent => PHASE 2 INSULINE RELEASE))

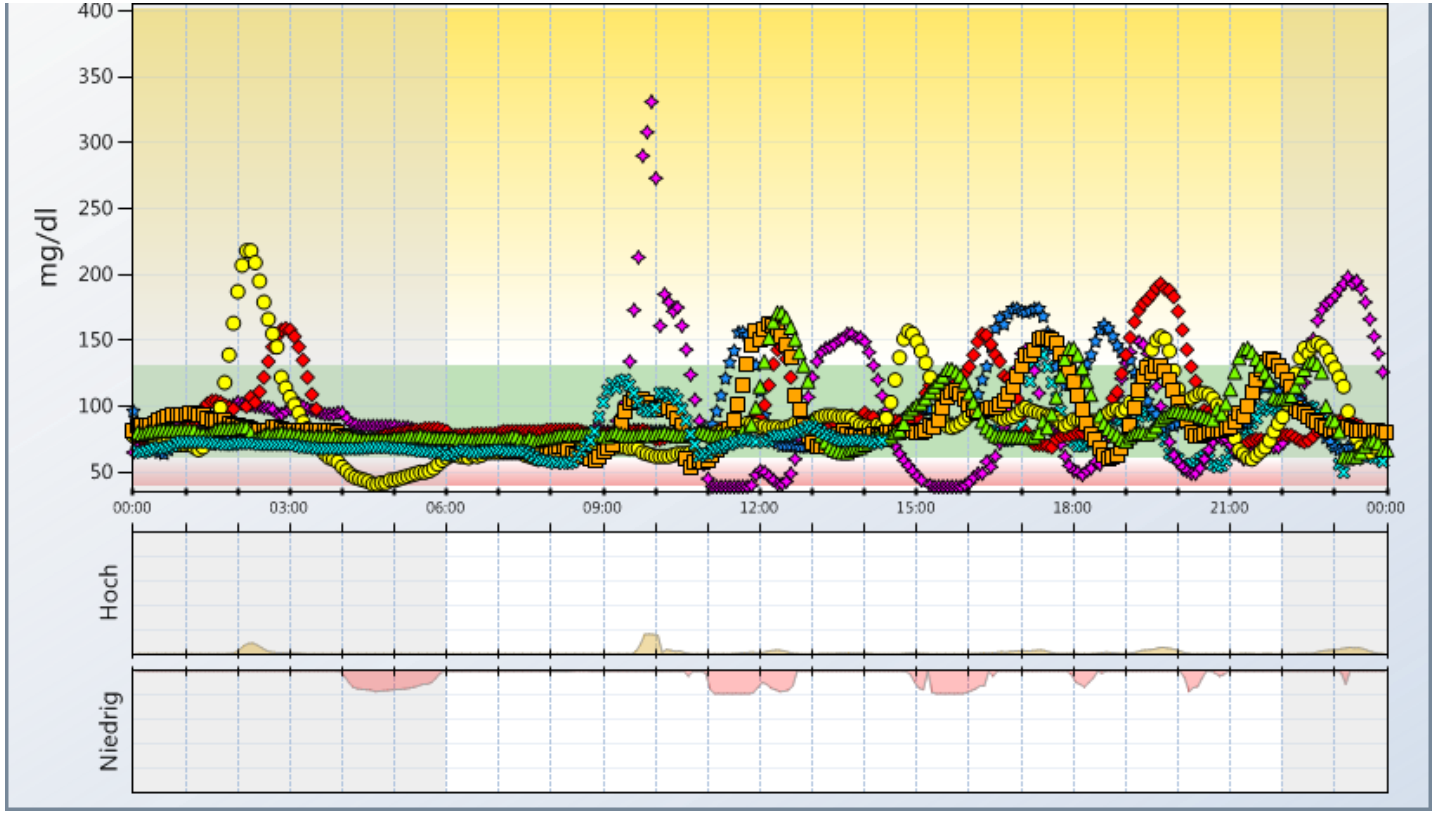
Massive GLP-1 output

⇒ MASSIVE INCRETIN EFFECT
⇒ Massive insulin output

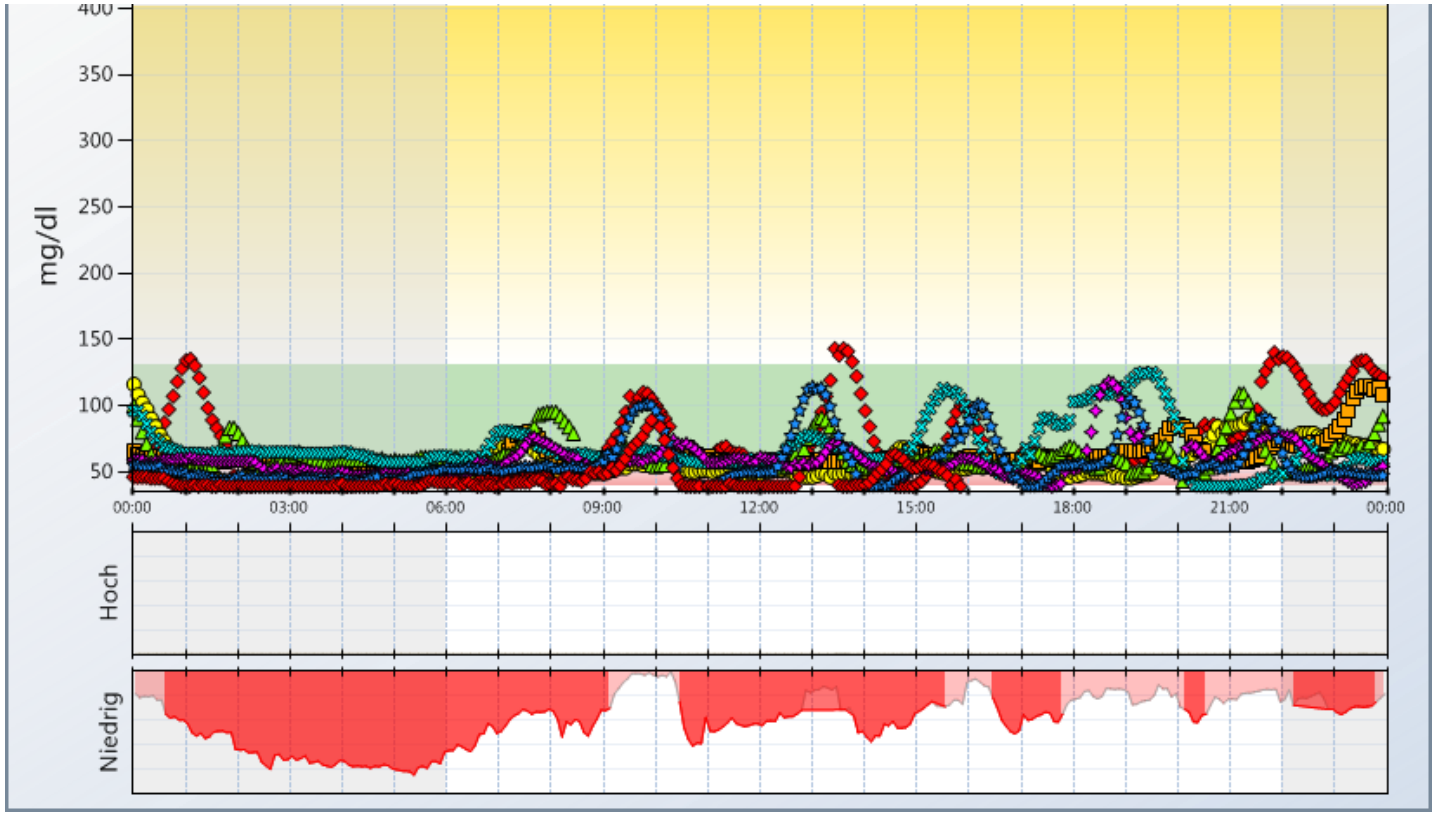
Mastracci TL, et al. **Integrated Physiology of the Exocrine and Endocrine Compartments in Pancreatic Diseases: Workshop Proceedings.** Diabetes. 2023 Apr 1;72(4):433-448. doi: 10.2337/db22-0942. Erratum in: Diabetes. 2023 Aug 1;72(8):1173. doi: 10.2337/db23-er08. PMID: 36940317; PMCID: PMC10033248.

Pierzynowski SG, Stier C, Pierzynowska K. **Hypothesis that alpha-amylase evokes regulatory mechanisms originating in the pancreas, gut and circulation, which govern glucose/insulin homeostasis.** World J Diabetes. 2023 Sep 15;14(9):1341-1348.

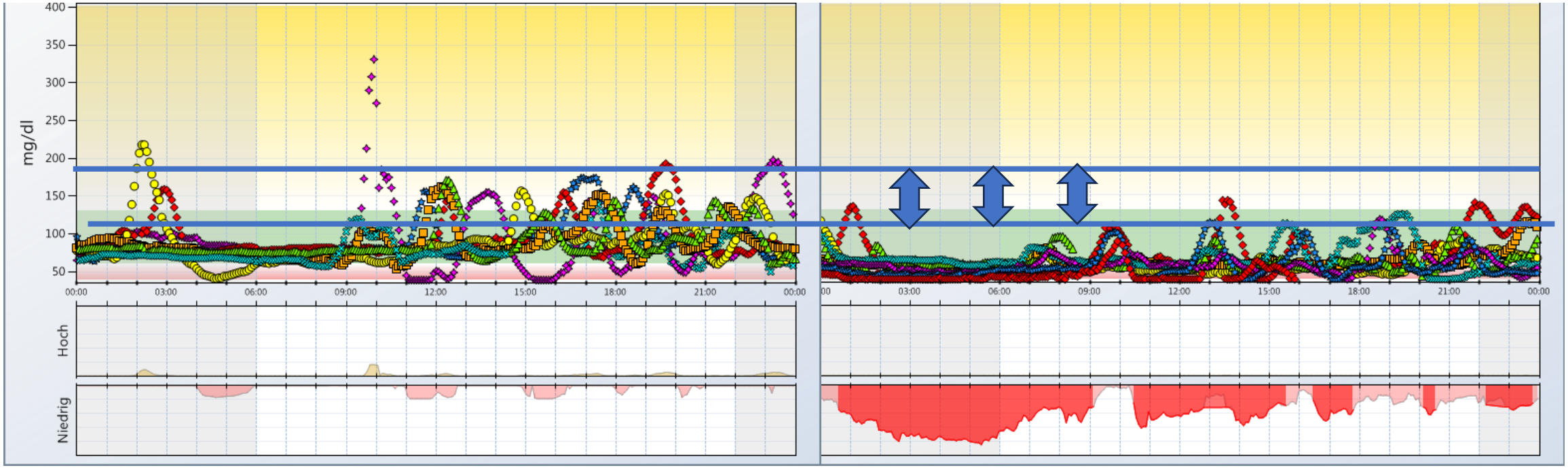
PREOPERATIVE TYPE 2 DIABETES MELLITUS



PREOPERATIVE NO TYPE 2 DIABETES MELLITUS, BUT DUMPING SYNDROME



COMPARISION OF BOTH ENTITIES

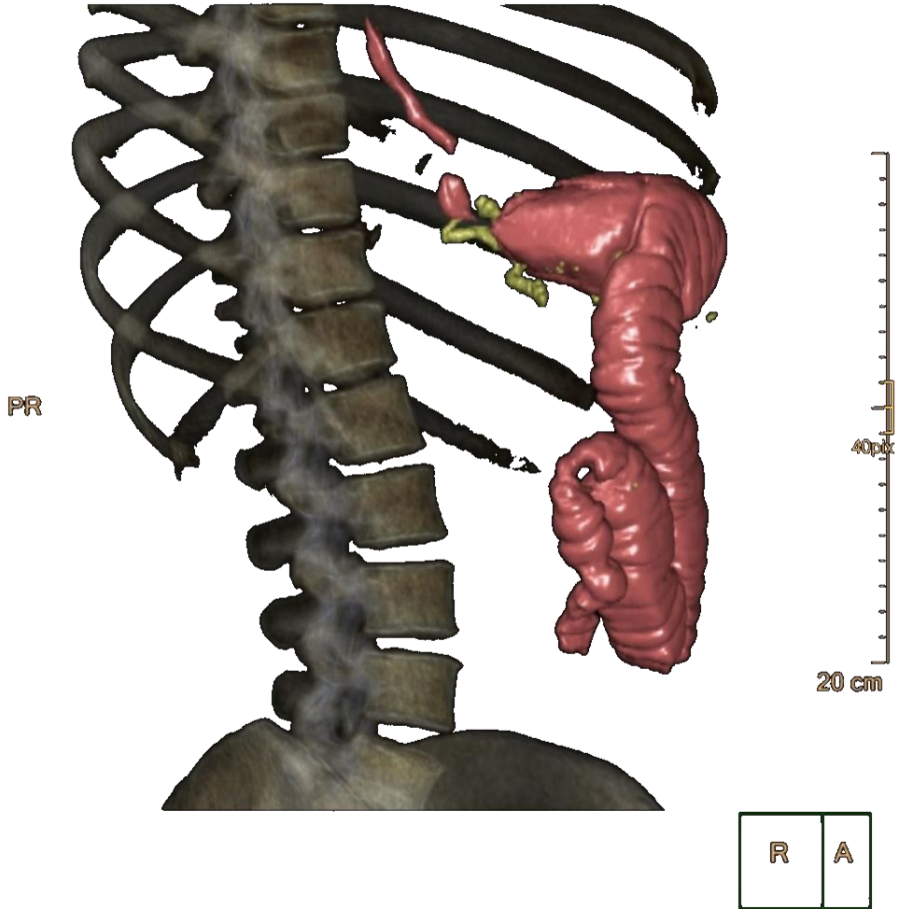


INCRETIN LEVELS PRE- AND POST-OP

	Time (minutes)	Preoperative	Postoperative	p
GLP-1 curve (ng/ml)	-15	3.4±0.5	3.3±3	0.853
	0	3.7±0.5	3.2±3	0.674
	15	3.8±0.5	11.2±13.7	0.077
	30	4.2±0.7	13±17.8	0.107
	45	3.6±0.5	7.1±5.4	0.048
	60	3.9±0.7	5.9±5.9	0.297
	90	3.8±0.6	4.2±2.6	0.703
	120	4±0.6	3.9±2.1	0.866
	150	3.7±0.6	3.8±2	0.616
	180	4±0.7	3.3±1.8	0.455
GLP-2 curve(ng/ml)	-15	4.6±3.4	4.5±0.9	0.941
	0	4.7±2.8	4±0.8	0.582
	15	4.8±3	13.9±1.4	<0.0001
	30	5±2.6	14.8±1.7	<0.0001
	45	5±2.7	12.9±1.7	<0.0001
	60	5±2.4	11.5±1.3	<0.0001
	90	5.1±2.8	9.7±1.1	0.002
	120	4.6±2.3	9.1±1	0.001
	150	4.3±2.1	6.9±0.9	0.031
	180	4.6±2.5	7±0.9	0.044
GLP-1 AUC		709.6±320.4	1026±714.3	0.543
GLP-1 IAUC		79.4±108.3	438.2±889	0.1414
GLP-2 AUC		945.3±449.1	1787.9±602.7	0.0037
GLP-2 IAUC		44±306.1	947.5±604	0.0003

DIAGNOSTICS

- **PATIENT's HISTORY**
- **SIGSTAD SCORE** / ARTs Score
- OGTT/ **CONTINIOUS GLUCOSE MONITORING**
- Scintigraphy of pouch emptying (study condition)
- Hunger Test (exclusion of an autonomous insolinoma
- **UPPER ENDOSCOPY**
- **FLUOROSCOPY**



DUMPING SCORING SYSTEMS

Sigstad score	
Shock	+5
Fainting, syncope, unconsciousness	+4
Desire to lie or sit down	+4
Breathlessness, dyspnea	+3
Weakness, exhaustion	+3
Sleepiness, drowsiness, apathy, falling asleep	+3
Palpitation	+3
Restlessness	+2
Dizziness	+2
Headaches	+1
Feeling of warmth, sweating, pallor, clammy skin	+1
Nausea	+1
Abdominal fullness, meteorism	+1
Borborygmus	+1
Eructation	−1
Vomiting	−4

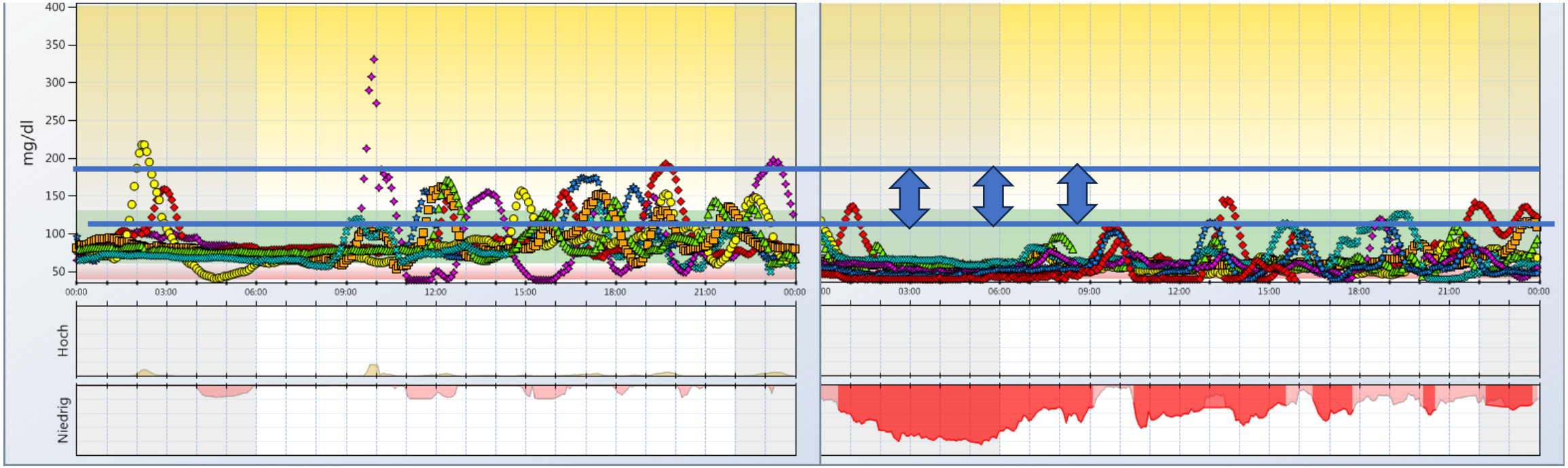
Arts Dumping Score Questionaire	
Early dumping syndrome symptoms	Late dumping syndrome symptoms
Sweating	Sweating
Flushing	Palpitations
Dizziness	Hunger
Palpitations	Drowsiness and/or unconsciousness
Abdominal pain	Tremor
Diarrhea	Irritability
Bloating	
Nausea	

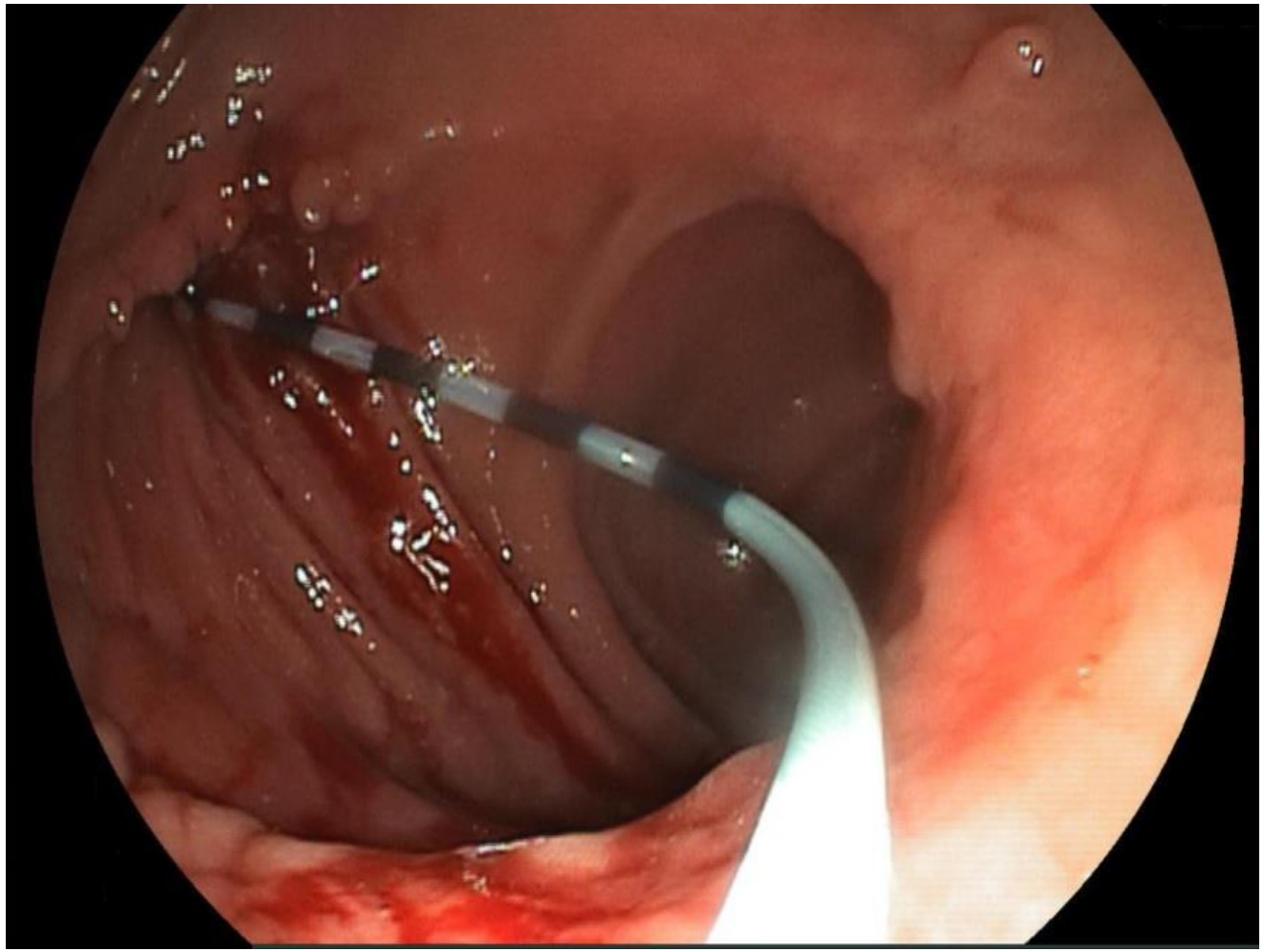
For each symptom: 0 = absent, 1 = mild, 2 = relevant, and 3 = severe

Sigstad H. **A clinical diagnostic index in the diagnosis of the dumping syndrome. Changes in plasma volume and blood sugar after a test meal.** Acta Med Scand. 1970 Dec;188(6):479-86.

Scarpellini et al. **International consensus on the diagnosis and management of dumping syndrome**. Nat Rev Endocrinol. 2020 Aug;16(8):448-466.

COMPARISION OF BOTH ENTITIES



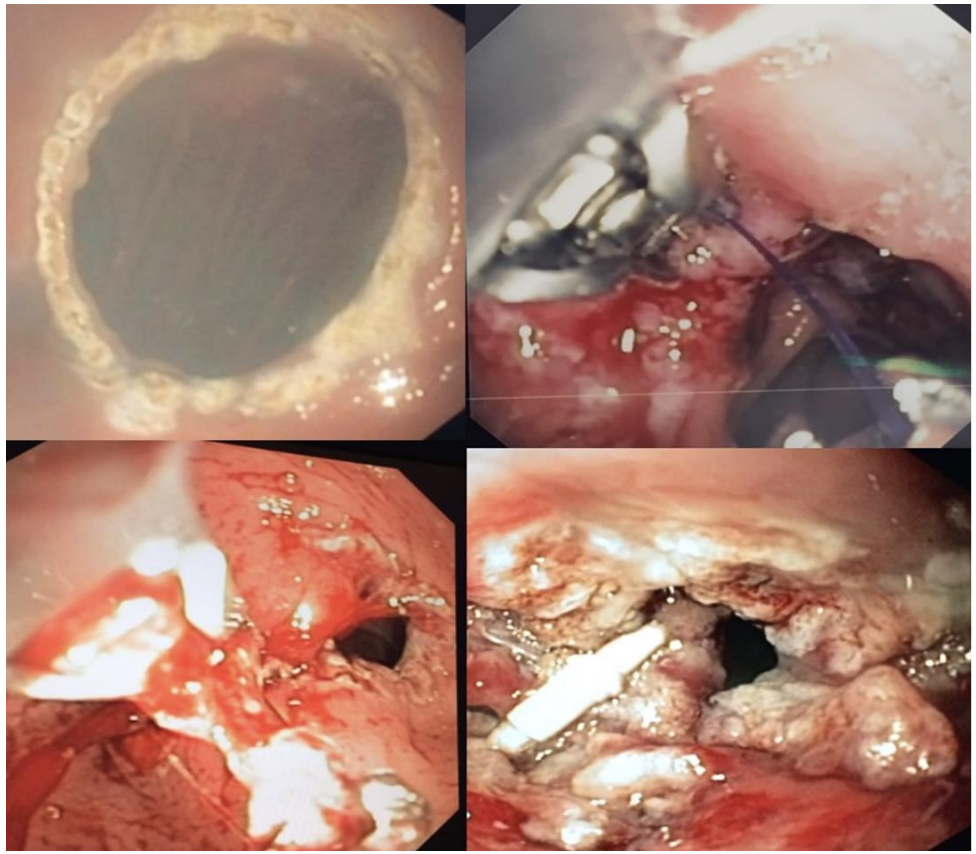


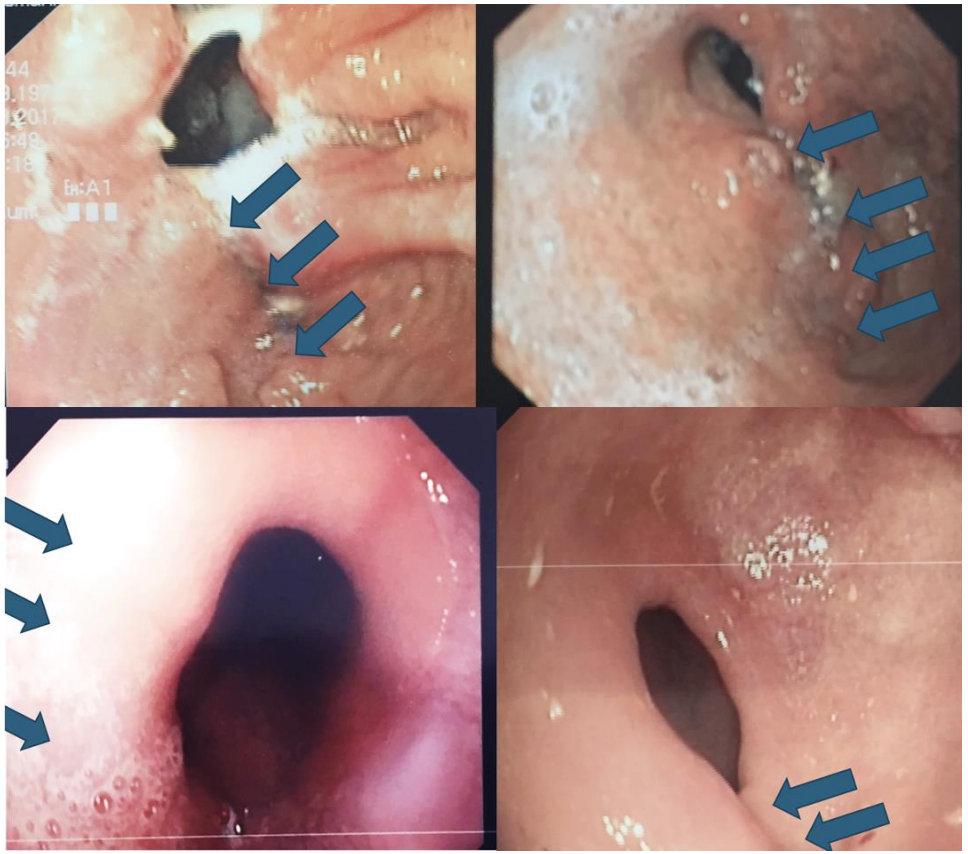
INDICATION TO ENDOLUMINAL REVISION OF THE OUTLET

Two applicable suturing systems:

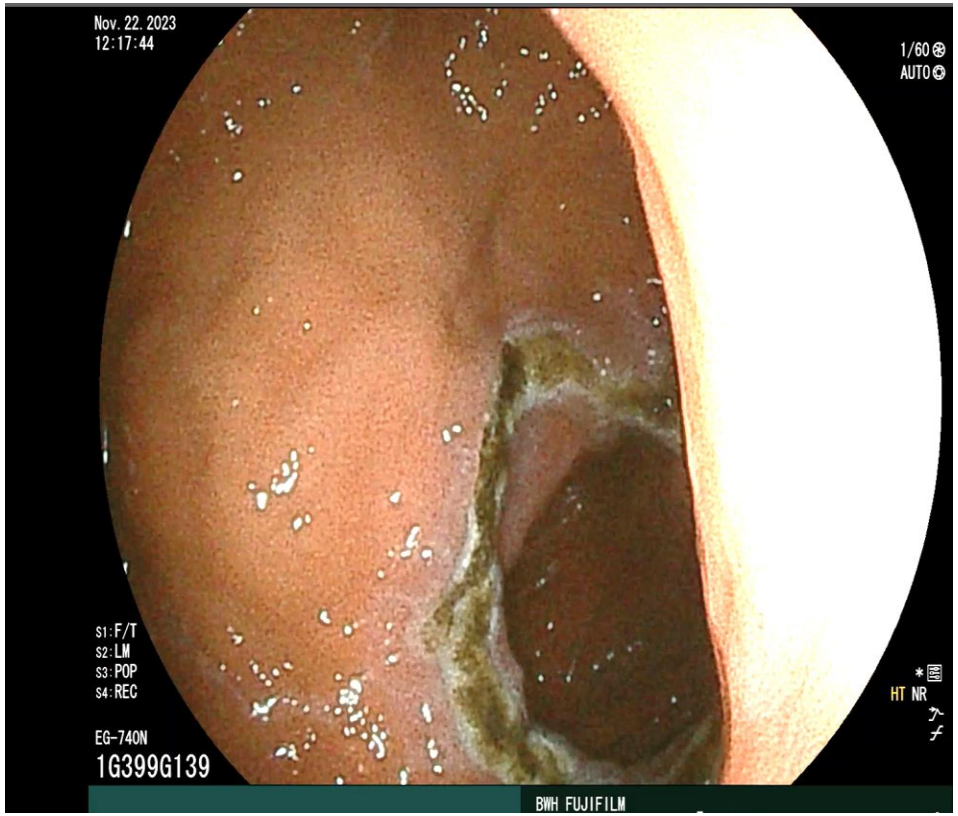
- TORe with the Overstitch system
- ROSE with the IOP

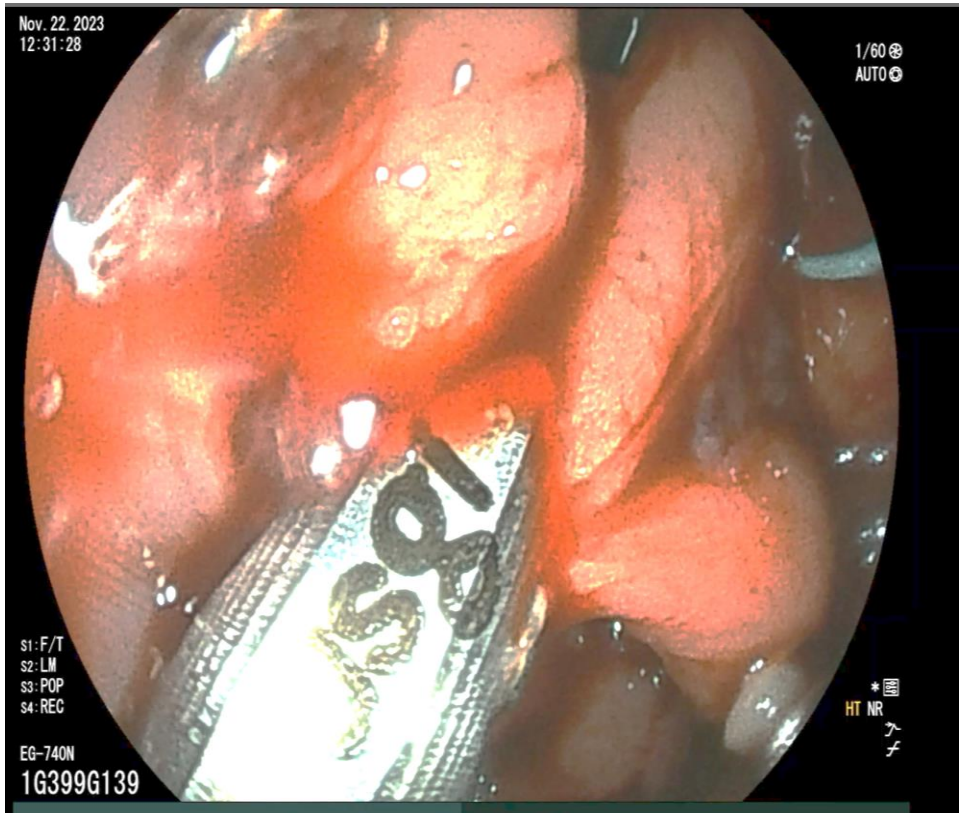
TORe. Transoral Outlet Repair endoscopically





ROSE. Revisional Obesity Surgery endoscopically

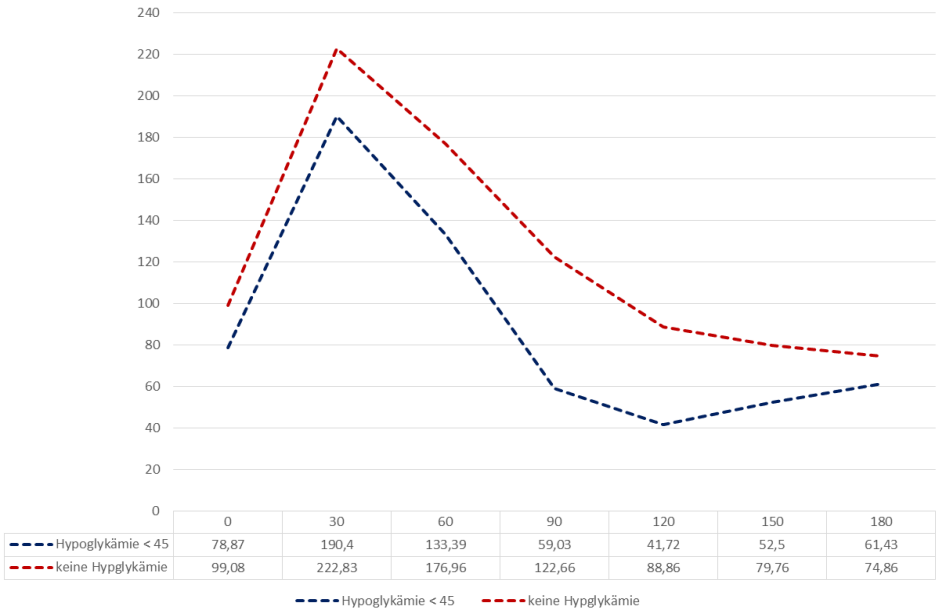


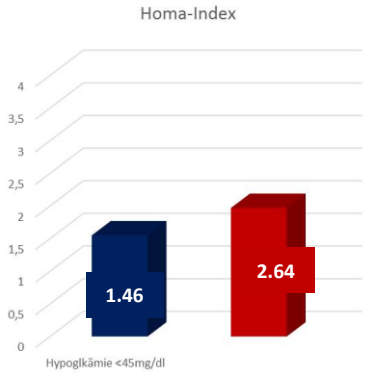


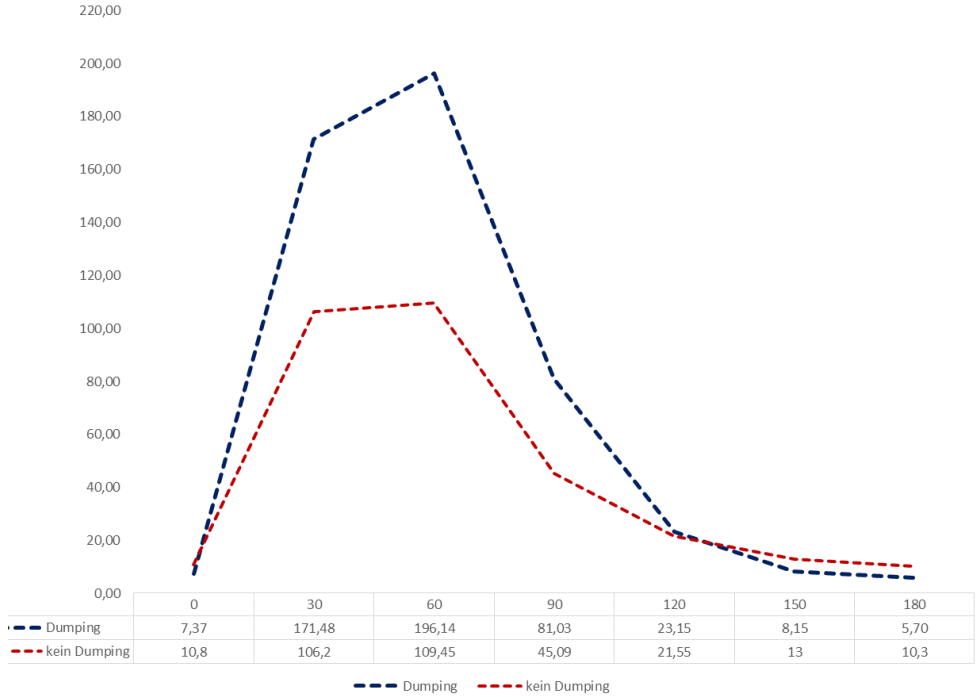
ORIPH trial: n=135; PHH n=84; No PHH n=51

	Total Cohort	glucose level < 45 mg/dL ≙ < 2.5 mmol/L	glucose level > 45 mg/dL ≙ > 2.5 mmol/L	p-value (GOI/RG) (Confidence %)
Number	135	84	51	
Female	116	71	45	
Male	19	13	6	
Age	45 ± 9.65	43.68 ± 10.51	46.45 ± 7.63	
Total Body Weight Loss (TBWL) %	42.49 ± 10.75	45.81 ± 9.30	36.99 ± 11.17	P < 0.01 (100%)*
HOMA-IR	1.88 ± 3.32	1.46 ± 0.96	2.64 ± 5.64	P = 0.03 (97%)*
History of T2DM %	5.92	0.00	15,69	P < 0.01 (99.79%)*

ORIPH trial: n=135; PHH n=84; No PHH n=51







NEW CONCEPT

Endoluminal Revision (OverStitch™, Apollo Endosurgery) of the Dilated Gastroenterostomy in Patients with Late Dumping Syndrome After Proximal Roux-en-Y Gastric Bypass

Christine Stier[1] · Sonja Chiappetta[1]

	14 patients 2M/12F Age	*Time elapse from RYGB to endoluminal revision*	*Weight at RYGB*	*Weight at endoluminal revision*	*Weight 6 months post-overstitch*	*Sigstad Score pre-revision*	*Sigstad Score 4 weeks post-revision*	*Score of visual pain scale (0-10)*	*C-reactive protein at 2. Post-OP day*
Median	**39,50**	**55,29**	**144,04**	**91,90**	**80,75**	**12**	**2,50**	**0,46**	**< 5**
SD	**11,17**	**30,48**	**32,95**	**30,40**	**22,90**	**4,18**	**2,06**	**1,13**	

Endoscopic management of dumping syndrome after Roux-en-Y gastric bypass: a large international series and proposed management strategy

Eric J. Vargas, MD,[1] Barham K. Abu Dayyeh, MD, MPH,[1] Andrew C. Storm, MD,[1] Fateh Bazerbachi, MD,[2] Reem Matar, BSc,[1] Adrian Vella, MD,[3] Todd Kellogg, MD,[4] Christine Stier, MD[5]

Rochester, Minnesota; Boston, Massachusetts, USA; Würzburg, Germany

Results: One hundred fifteen patients across 2 large academic centers in Germany and the United States underwent TORe for dumping syndrome. Patient age was mean 8.9 ± 1.1 years from their initial RYGB with an average percent total body weight loss of 31% ± 10.6% at the time of endoscopy. Three months postprocedure, the Sigstad score improved from a mean of 17 ± 6.1 to 2.6 ± 1.9 (paired *t* test $P = .0001$) with only 2% of patients (n = 2) experiencing weight gain. Mean weight loss and percentage of total body weight loss 3 months post-TORe were 9.47 ± 3.6 kg and 9.47% ± 2.5%, respectively. Six patients (5%) failed initial endoscopic therapy, with 50% (n = 3) successfully treated with a repeat TORe. Three patients underwent surgical reversal, indicating an overall 97% endoscopic success rate.

TABLE 2. Baseline characteristics

Variable	Value
Age, y	44.9 ± 9.2
Weight, kg	98.4 ± 22.7
Female, %	84
Baseline weight at time of Roux-en-Y gastric bypass, kg	143.5 ± 26.8
Weight at intervention, kg	98.2 ± 22.6
Baseline Sigstad score	17.02 ± 6.1

Values are mean ± standard deviation unless otherwise defined.

TABLE 3. Postintervention results

Variable	At 3 months	Mean difference	*P* value
Sigstad score	2.55 ± 1.87	−14.5 ± 5.5	<.0001
Weight, kg	89.4 ± 1.96	−9.3 ± 3.8	<.0001

Values are mean ± standard deviation.

TAKE HOME.

ENDOSCOPIC RE-INTERVENTIONS PRESERVE THE BARIATRIC ANATOMY (POUCH LENGTH)

ENDOSCOPIC RE-INTERVENTIONS ARE MINIMAL INVASIVE AND SAFE

THEY CAN BE APPLICATED WITHIN AN ESCALATING TREATMENT ALGORITHM

RESEARCH CONCERNING ENDOSCOPIC RE-INTERVENTION IS PROMISING, AND ONGOING STUDIES WILL FURTHER SUBSTANTIATE THEIR UTILITY AND BENEFICIALS.

THANK YOU FOR YOUR KIND ATTENTION

christine.stier@umm.de