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Research article

Jejunal response to secretin is independent of the pancreatic response in secretin-enhanced magnetic resonance cholangiopancreatography☆

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ABSTRACT

Purpose: To investigate whether jejunal secretions are independent of the pancreatic response to secretin in secretin-enhanced Magnetic Resonance Cholangiopancreatography (s-MRCP) examination of subjects with and without chronic pancreatitis (CP).

Methods: Patients were identified through a search of s-MRCP examinations performed between 2014–2016 (n = 513) as well as the multidisciplinary pancreatitis clinic registry (n = 586). Fifty cases with CP (based on M-ANNHEIM criteria) and 50 matched controls were selected. Signal intensity changes after secretin administration (~1–5 min' post-secretin response) in three locations were assessed: second portion of the duodenum (D2), third/fourth portions of the duodenum (D3-4), and the jejunum. The post-secretin response was compared between (cases vs. controls) and within the study groups.

Results: There was a significantly lower 1–5 min' post-secretin response among CP patients in D2 (all p-values < 0.01). However, no significant difference in 1–5 min' post-secretin response was detected in the jejunum. Minute-by-minute analysis of the post-secretin response showed a significant increase up to the 5th minute only in D2 of the control group. The post-secretin response in the jejunum was significant after 1 min but was similar among patients with CP and controls. CP was a significant determinant of post-secretin response in D2 but not in the jejunum.

Conclusions: Early post-secretin response at jejunum is independent of the pancreatic response that can be detected at D2, and should not be misinterpreted as a rapid pancreatic response. Therefore, pancreatic function on s-MRCP should be assessed by the presence of fluid in D2 and not jejunum.

1. Introduction

Chronic pancreatitis (CP) is characterized by chronic inflammatory destruction of the pancreatic parenchyma and can result in functional deficiencies over time including diabetes and exocrine insufficiency [1,2]. Specific morphologic findings from imaging including computed tomography (CT), magnetic resonance imaging (MRI) and magnetic resonance cholangiopancreatography (MRCP) assist in diagnosis and management of CP [3]. Secretin-enhanced MRCP (s-MRCP) assesses pancreatic secretory capacity as secretin stimulates the pancreatic duct cell to produce a bicarbonate rich fluid. This improves the anatomic depiction of the pancreatic ductal system and is increasingly used to assess pancreatic secretory capacity. Pancreatic secretory capacity correlates with the presence and subsequent increase of duodenal fluid after secretin administration [4]. Increased signal and passage of fluid beyond the third and fourth portions of the duodenum (~ proximal small bowel) within 5–10 minutes is usually interpreted as evidence for sufficient secretory capacity [4,5].

Assessing and quantifying the amount of fluid signal in proximal jejunum is part of s-MRCP evaluation and interpretation [6–10]. While s-MRCP may not distinguish between different etiologies of CP, a reduced post-secretin response of the pancreas is a consistent feature of CP [6,7,11]. Although secretin has long been known to have a direct effect on postprandial proximal jejunal secretions [12–14], s-MRCP studies frequently report the presence of increased jejunal fluid 5–10 minutes post-secretin administration as a marker for normal pancreatic secretory capacity [8,7–10,15] and the timing of jejunal secretions in response to secretin administration has not been

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previously investigated.

The aim of our study was to demonstrate the presence of early jejunal secretions as a direct response to intravenous secretin administration during s-MRCP, independent of the pancreatic secretory capacity, in patients with and without CP.

2. Methods

2.1. Patient selection

This is an Institutional Review Board (IRB) approved, Health Insurance Portability and Accountability Act (HIPAA) compliant study. We performed a retrospective, case-control study. Participants were selected from two major databases. First, we evaluated all s-MRCP examinations performed at our institution from March 2014 to March 2016 (513 available records). Second, we examined the registry of subjects who were referred to our multi-disciplinary pancreatitis clinic (586 available records). Our inclusion criteria for CP cases consisted of fulfilling definite M-ANNHEIM diagnostic criteria [2], available s-MRCP examination (baseline, 1, 2, 3, 4, and 5 min' post-secretin images) and abdominal CT scan suggesting a diagnosis of CP (with or without calcifications). Controls were patients with non-obstructive branch duct IPMNs who underwent s-MRCP evaluation and did not have clinical or imaging (CT, MRI and/or s-MRCP) findings compatible with CP. A total of 58 cases and 161 controls met the inclusion criteria, from which 50 cases (including 30 cases with CT evidence of chronic calcific pancreatitis) and 50 controls (frequency matched age, gender, and race) were selected as the final sample. A flow diagram depicting the sample selection process is included as Fig. 1.

2.2. CT protocol

Contrast-enhanced CT is performed using pancreas protocol and in arterial (25–30 s) and venous phases (60 s), using multi-detector CT scanners at our institution. Images are acquired after bolus intravenous administration (4–5 mL/s) of 100 mL iodinated contrast (Visipaque 320 or Omnipaque 350, GE Healthcare, Waukesha WI, USA). Water was administered as negative oral contrast. Thin (0.75–1.5 mm) and thick (3–5 mm) axial slices along with sagittal and coronal reformatted images and 3D post-processing are prepared for most cases [16].

2.3. MRI and s-MRCP protocol

At our institution, abdominal MRI is performed with standardized MRI and MRCP protocols using 1.5 T or 3 T MR scanners (Siemens Avanto and GE Signa HDx) before and after administration of intravenous contrast agent (Gadopentetate 0.1 mmol/kg; Magnevist, Bayer, Wayne, NJ, USA). A phased array torso coil is used and pre- and post-gadolinium images (arterial phase: 20 s, venous phase: 70 s, delayed phase: 3 min) are obtained. Transverse and coronal T2 weighted single-shot fast spin echo (SE) sections are obtained (repetition time msec/echo time msec: 4500/ 92; field of view: 320 mm; matrix: 256 9 180; section thickness: 6 mm; slice gap: 1.2 mm; receiver bandwidth: 543 Hz/pixel; flip angle: 150). Coronal and reconstructed maximum intensity projections are used for viewing the MRCP images. Multiplanar images are obtained by T1-weighted fat-suppressed spoiled gradient-echo imaging (repetition time/echo time (milliseconds): 5.77/ 2.77; field of view: 320–400 mm; matrix: 192 9 160; section thickness: 2.5 mm; receiver bandwidth: 496 Hz/pixel; flip angle: 10).

s-MRCP examinations at our institution includes axial fat-saturated T2 images (4–6 mm, TR 4000–6000, TE 90–100), with 6 thick slab (40–50 mm, TR 4500, TE 500–700) T2 weighted MRCP images. Human synthetic secretin (0.2 g/kg; ChiRhoClin, Inc, Burtonsville, MD) is administered intravenously, and MRCP images are obtained in the coronal plane, before and every one minute afterward (up to the 5th minute). The sequence is repeated in the coronal oblique planes and thin section (1–3 mm; TE 150–200; overlap 0–50%) respiratory triggered or navigator coronal 3D FS TSE images are also obtained.

2.4. Image analysis

Image analysis was performed by a radiology research fellow and was reviewed and revised by an abdominal radiologist with ten years of experience reading abdominal MRIs. CT findings including pancreatic calcification, atrophy and calculi were evaluated based on our previous study [17] and were extracted from standardized radiology reports. Similarly, information on the main pancreatic ducts' size and grading of the exocrine function was obtained from the standardized radiology reports. An elliptical region of interest measuring 10 mm^2 was drawn on the T1 weighted pre- and post-gadolinium injection MRI to measure the pancreatic signal intensity in the head, body, and tail. This was

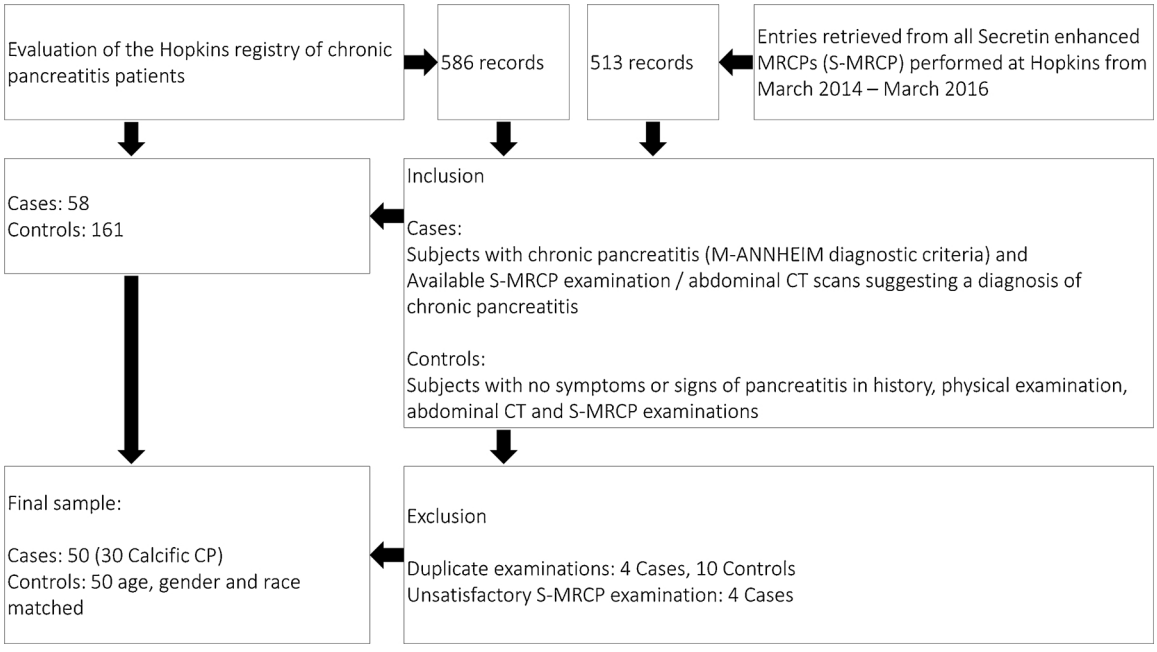

Fig. 1. Flow diagram demonstrating selection of the study samples.

Table 1
Baseline characteristics of the study population.

	Controls	Chronic Pancreatitis (All)	*p*-value	Chronic Calcific Pancreatitis	*p*-value
Number	50	50		30	
Age (years)	58.84 ± 13.73	58.28 ± 14.46	0.843	60.23 ± 13.74	0.662
Gender (% Female)	58 %	58 %	1.000	67 %	0.447
Race (% White)	84 %	84 %	1.000	90 %	0.457
- **CT**					
Calcification	0 %	60 %	< 0.001	100 %	< 0.001
Intraductal calculi	0 %	9 %	0.044	14 %	0.043
Atrophy	0 %	39 %	< 0.001	48 %	< 0.001
- **MRI-MRCP**					
MPD dilation	N/A	32 %	N/A	45 %	N/A
MPD stricture	N/A	19 %	N/A	24 %	N/A
Abnormal side branches	N/A	32 %	N/A	31 %	N/A
Cysts	N/A	36 %	N/A	41 %	N/A
- **s-MRCP: MPD diameter**					
Pre-secretin	2.65 ± 1.01	3.77 ± 2.66	0.014	4.25 ± 3.22	0.028
Post-secretin at 1 min	3.41 ± 1.21	4.27 ± 2.65	0.014	6.63 ± 3.11	0.035
Post-secretin at 2 min	3.11 ± 1.20	4.27 ± 2.69	0.013	4.65 ± 3.12	0.030
Post-secretin at 3 min	3.07 ± 1.21	4.24 ± 2.70	0.013	4.51 ± 3.20	0.047
Post-secretin at 4 min	3.00 ± 1.12	4.32 ± 2.74	0.006	4.65 ± 3.21	0.024
Post-secretin at 5 min	2.92 ± 1.17	4.23 ± 2.77	0.007	4.57 ± 3.22	0.025
Grade	2.98 ± 0.14	2.81 ± 0.46	0.038	2.84 ± 0.37	0.135

All diameters are in millimeters (mm). s-MRCP: Secretin-enhanced Magnetic Resonance Cholangiopancreatography. MPD: Main pancreatic duct. N/A: Not Applicable. Chronic pancreatitis cases (with and without calcification) are compared to the controls.

compared to that of the spleen on the pre-contrast T1 weighted fat saturated images as reference (after iron deposition was ruled out by absence of loss of signal on the increased TE images on the chemical shift imaging) [18]. The pre- and post-secretin MRCP images were used to assess the signal intensity at the second portion of the duodenum (D2), third/fourth portion of the duodenum (D3-4) and jejunum (J). The bowel loops with the highest signal intensity at D2, D3-4 and J were selected, and signal intensities were measured and recorded by free hand drawing of a 10 mm^2 region of interest, in each of the three locations.

2.5. Statistical analysis

Subjects' age, gender, race, as well as specific CT (calcification, calculi, and atrophy), and s-MRCP (main duct diameter at pre- and 1-5-minute post-secretin images) findings were extracted. Baseline characteristics of cases and controls were compared using student's *t*-test for continuous, and Chi-square test for categorical variables. Changes in the pancreatic signal intensity ratios were measured at head, body, and tail (in pre-gadolinium, arterial, venous and delayed phases; Signal intensity ratio: Pancreas SI/Spleen SI). Next, signal intensity ratios were compared between cases and controls. In s-MRCP examinations, the post-secretin response was calculated as the percent change in MR signal intensity (at D2, D3-4, and jejunum) compared to the pre-secretin image in each subject.

The analytic approach consisted of three sets of comparisons as below:

1 Between groups analysis: Comparing cases and controls' response to secretin

For the between-group analysis and with pre-secretin images as the reference point, post-secretin response at 1, 2, 3, 4 and 5 (1–5) minutes was calculated and compared between cases and controls at D2, D3-4 and jejunum. Student's *t*-test was used to compare the mean response values at every time point (1–5 minutes) and at different locations (D2, D3-4, J), between cases and controls.

2 Within group analysis: Comparing baseline and post-secretin images at 1, 2, 3,4, and 5 min

For the within-group analysis, minute by minute change in post-secretin response was calculated for cases and controls, separately. The *p*-values were extracted by comparing the average amount of minute by minute change in the D2, D3-4, and jejunal response. Cases were not compared with controls in this analysis and instead, were compared across different time points within the same group.

3 CP status as a predictor of response to secretin at D2, D3-4, and jejunum

Finally, the association between CP status (case vs. control) and post-secretin response (after 1–5 minutes and at D2, D3-4, and jejunum) was assessed using generalized estimating equations (GEE) with linear functions and by defining the case/control pairs as the units of analysis. Covariate adjustment was performed for age, gender, and race. The adjusted beta coefficients were extracted and recorded. Data handling and analysis were performed using PASW (v.18, Chicago, IL) and Stata (v12. College Station, TX).

3. Results

A total of 50 cases with CP and 50 age, gender, and race matched controls were included in our analysis. There was no significant difference in age (58.84 ± 13.73 years, cases vs. 58.28 ± 14.46 years, controls), gender (58% female) and race (84% Caucasian) between cases and controls. Abdominal CT revealed calcifications in 60%, atrophy in 39%, and intra-ductal calculi in 9% of patients with CP. On MRI, main pancreatic duct dilation, stricture, and abnormal side branches were found in 32%, 19%, and 32% of the patients with CP, respectively. None of the controls had signs of CP on CT or MRI. The main pancreatic duct diameters were significantly larger among CP patients in pre- and 1-5-minute post-secretin images (Table 1).

The signal intensity ratio (pancreas to spleen ratio) was significantly lower among cases with CP on pre-gadolinium T1-weighted fat saturated (average among controls 1.22 ± 0.28 vs. 1.01 ± 0.35 among cases; *p*-value 0.002) and arterial phase (average among controls 2.16 ± 0.63 vs. 1.87 ± 0.71 among cases; *p*-value 0.042) images. In both the venous (average among cases 2.05 ± 0.51 vs. 1.90 ± 0.71; *p*-value 0.275) and the delayed (average among cases 1.89 ± 0.44 vs. 1.79 ± 0.63; *p*-value 0.407) phases, no statistically significant difference in pancreatic signal intensity was observed. Supplementary

Table 2
Post-secretin response at D2, D3-4, and Jejunum: ***between-group analysis comparing cases with controls***.

	Controls	Chronic Pancreatitis	*p*-value	Chronic Calcific Pancreatitis	*p*-value
Pre-secretin	Reference	Reference		Reference	
Post-secretin at 1 minute					
- **D2**	**63 ± 140**	**−7 ± 62**	**0.002**	**−11 ± 51**	**0.001**
- D3-4	48 ± 96	77 ± 251	0.448	111 ± 305	0.279
- J	221 ± 303	197 ± 526	0.773	180 ± 430	0.613
Post-secretin at 2 minute					
- **D2**	**118 ± 240**	**22 ± 93**	**0.010**	**12 ± 77**	**0.005**
- D3-4	85 ± 151	57 ± 172	0.383	92 ± 211	0.878
- J	250 ± 375	252 ± 810	0.987	172 ± 390	0.379
Post-secretin at 3 minute					
- **D2**	**155 ± 272**	**36 ± 94**	**0.005**	**27 ± 89**	**0.003**
- D3-4	107 ± 222	46 ± 138	0.098	66 ± 163	0.377
- J	293 ± 445	246 ± 673	0.680	186 ± 330	0.256
Post-secretin at 4 minute					
- **D2**	**193 ± 297**	**64 ± 118**	**0.006**	**54 ± 107**	**0.004**
- D3-4	158 ± 322	47 ± 118	0.031	69 ± 181	0.169
- J	295 ± 497	247 ± 558	0.653	214 ± 427	0.461
Post-secretin at 5 minute					
- **D2**	**238 ± 319**	**82 ± 141**	**0.002**	**75 ± 131**	**0.002**
- D3-4	195 ± 374	138 ± 330	0.422	179 ± 364	0.852
- J	332 ± 504	204 ± 413	0.170	225 ± 493	0.361

The post-secretin response was calculated as percent changes in MR signal intensity compared to the pre-secretin image. D2: Second portion of the duodenum. D3, 4: Third and fourth portion of the duodenum. J: Jejunum. Chronic pancreatitis cases (with and without calcification) are compared to the controls.

Table 1 demonstrates the signal intensity ratios among cases and controls before and after gadolinium injection.

Post-secretin response after 1, 2, 3, 4 and 5 min at D2 (but not at D3-4 or jejunum) was significantly lower among CP cases (Table 2). Since the fluid secretions are dynamic we compared signal intensity at each level compared to the one previous minute (Within group analysis). Minute by minute change in the post-secretin response at D2 was statistically significant up to the 5th minute among the controls. Fig. 2 demonstrates the amount of secretory response at duodenum and jejunum at 1–5 min post secretin administration. Figs. 3 and 4 show representative s-MRCP images from patients with CP and controls respectively. Post-secretin response at jejunum did not show any significant change after 1 min post secretin administration among cases or controls (Table 3). GEE analysis showed that CP status (cases vs. controls) were inversely associated with post-secretin response at D2. Nevertheless, there was no significant association between CP status and post-secretin response at jejunum in multivariable analysis (Table 4).

4. Discussion

s-MRCP provides a non-invasive imaging test to assess both structural and functional changes of the pancreas associated with CP. Decreased response to secretin has been seen in patients with advanced CP as shown in multiple prior studies [19–21]. However, increased signal observed within jejunum can confound the assessment of the passage of pancreatic fluid by demonstrating a falsely increased rate of flow of pancreatic juices to the jejunum. In this study, we aimed to improve our understanding of the dynamics of jejunal response to secretin administration on s-MRCP examination by comparing response to secretin on s-MRCP in patients with CP to age, gender and race matched controls without CP. The 1–5 minute response to secretin administration in D2 was significantly lower in patients with CP and the minute by minute increase in post-secretin response at D2 was significantly higher among the controls (Table 3). This is in concordance with previous studies quantifying pancreatic secretions among CP cases and controls [19,20]. Bian et al. reported a significant difference in pancreatic flow rate by comparing 17 healthy subjects with 36 patients with CP. They found the peak flow time to be at 5.76 ± 1.71 min post secretin administration in healthy controls and as late as 12.33 ± 1.55 min for cases with advanced CP [19]. Likewise, Manfredi et al. used T2-weigthed rapid acquisition with relaxation enhancement (RARE) MRCP images of duodenal filling 10 min post secretin administration to show how it correlates with pancreatic function in patients with CP or acute recurrent pancreatitis [20].

The most important clinical implication of our findings is regarding radiologists' interpretation of s-MRCP examinations. Pancreatic response to secretin is graded (0–3) based on the amount and extent of secretion. Grade 0 refers to no filling while grades 1 and 2 are assigned to filling of the duodenal bulb and up to genu, respectively. Grade 3 pancreatic response is when the fluid filling in the duodenum goes beyond the caudal flexure and continues to the proximal section of jejunum [22]. Our study is the first of its kind to show that the jejunal response to secretin was independent of the CP status (Tables 2–4), and was the highest at 1 min after the administration of intravenous secretin (Table 4). Therefore, an early increase (1 min post-secretin administration) of fluid and signal intensity at proximal jejunum should not be considered as evidence for pancreatic response to secretin. Of note, most of the previous studies that have elaborated on the association between jejunal secretions on s-MRCP and CP status, have focused on later increase in jejunal secretions (in terms of signal intensity that is observable at > 10 min post-secretin administration) [8,15,23,24]. For example, an increase in the signal intensity at proximal jejunum occurring after 13 min as a continuation of duodenal secretions has been shown to be a compelling sign of pancreatic response [8]. However, early jejunal response at 1 min post-secretin administration would falsely increase the fluid signal in the jejunum confounding the estimation of total pancreatic secretion in response to secretin on more delayed imaging. Thus, such an early increase in jejunal fluid cannot be attributed to the pancreatic function when grading and predicting pancreatic exocrine function using s-MRCP examination.

We also evaluated the morphological differences in CT and MRI findings of cases and controls in our study (Table 1 and supplementary Table 1). Our control group was devoid of findings consistent with CP including calcifications, main duct dilation, stricture, and abnormal side branches (Table 1). We assessed pre-gadolinium pancreas to spleen SI ratio as an ancillary baseline evaluation to have a more precise assessment of the disease extent in our CP group and to corroborate the findings seen on s-MRCP. The ratio was significantly lower among cases with CP (vs. controls) and is consistent with prior descriptive studies demonstrating imaging features of CP [25]. Our study has several limitations. First, although we tried to find controls with matching basic demographic variables, matching was not performed for CP risk factors [2]. Factors other than CP can lead to a decreased secretin response in control patients (advanced age, smoking, alcohol use, obesity) that were not assessed in our analysis. Second, the retrospective nature of our comparisons limits the outreach of our conclusions. Third, inter-subjects and minute by minute variations could reduce the repeatability of our findings. Finding the proximal jejunal loop with the highest signal intensity in every post-secretin image is operator dependent. We tried to address this issue by re-evaluating and confirming our initial measurements by a second observer with extensive experience in

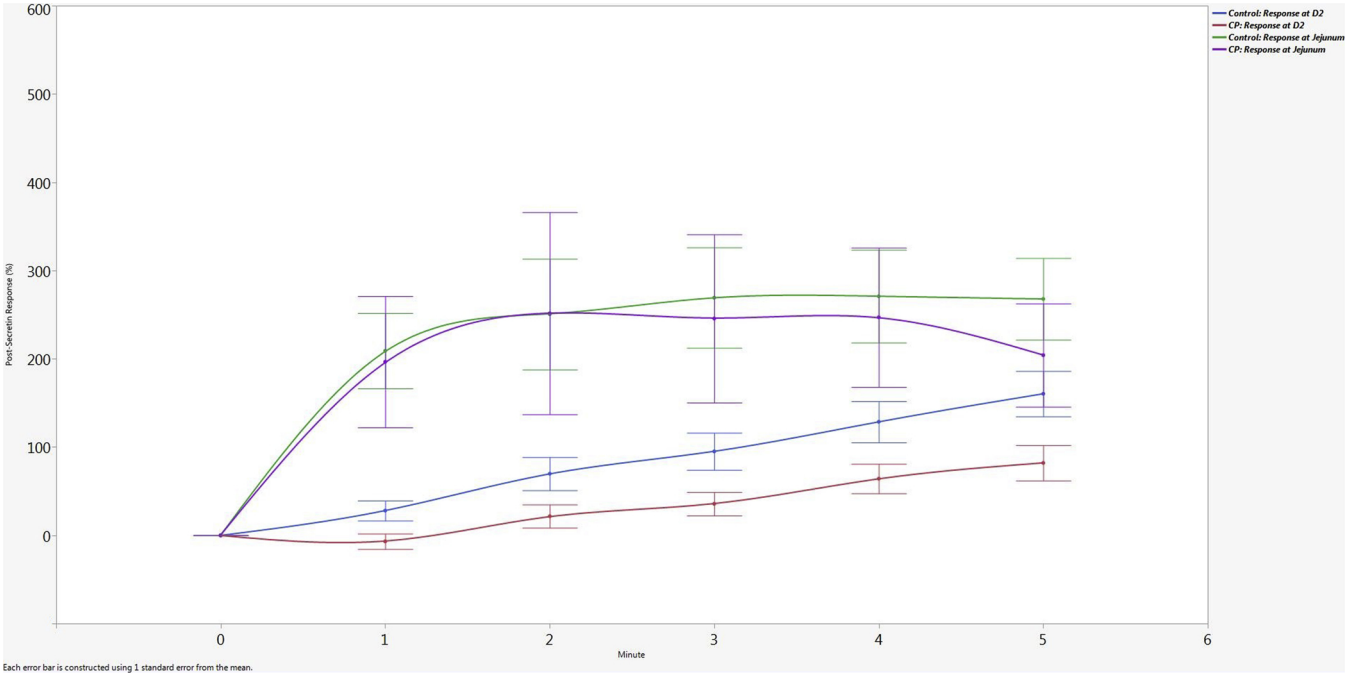

Fig. 2. (a) Post-secretin response at D2, D3-4 and Jejunum among case and controls. (b) Foot note: Post-secretin response (percent changes in MR signal intensity compared to the pre-secretin image) is plotted against post-secretin minutes. Means and standard errors are shown as points and intervals. Blue line: Control response at D2. Red line: CP response at D2. Green line: Control response at jejunum. Purple: CP response at jejunum.

interpretation of these studies. Fourth, we do not routinely use negative oral contrast as part of the s-MRCP protocol in our institution. As part of our analysis (the within group analysis; Table 3), we specifically observed the minute by minute change within the duodenal fluid present at baseline after the administration of secretin (evaluating real time trend) to make sure the observed effect represents the amount of change after secretin administration rather than the absolute amount of intraluminal fluid). Finally, though our study highlights independent jejunal response to secretin administration, it does not elucidate the mechanism behind it. Previous studies have proposed a central nervous

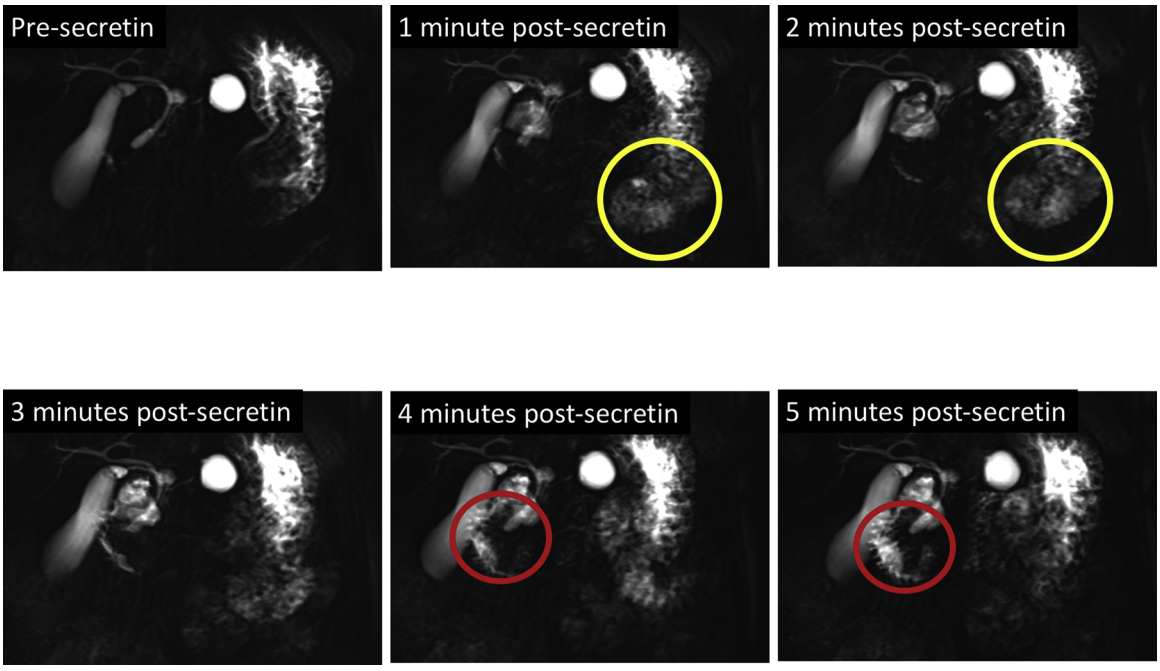

Fig. 3. A 60-year-old woman with history of chronic pancreatitis. Pre-secretin diameter of the main pancreatic duct was 3 mm and did not show any significant change after secretin administration. Yellow circles show prominent jejunal response 1 and 2 min after secretin administration, independent from duodenal secretions. Pancreatic secretions at duodenum are visualized only after 4 and 5 min post-secretin administration (red circles) and are not continued to the jejunum.

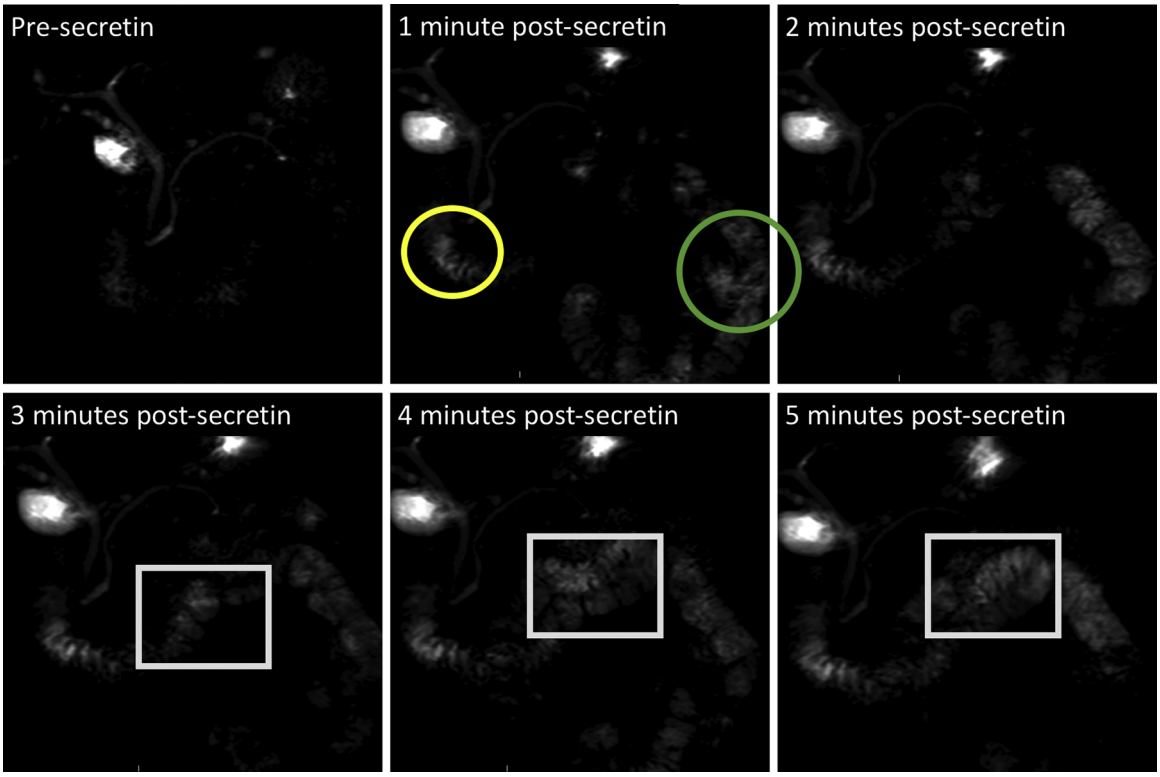

Fig. 4. A 68-year-old man with no history of chronic pancreatitis. Yellow circle shows increased secretions in duodenum 1 min after secretin administration. Green circle shows jejunal response 1 min after secretin administration which is not in continuation of duodenal secretions. Continuation of duodenal secretions to jejunum is visible after 3–5 minutes post secretin administration (white boxes).

Table 3
Trends of post-secretin response at D2, D3-4, and Jejunum: ***within-group analysis comparing every time point to its predecessor***.

	Post-secretin at 1 minute	Post-secretin at 2 minute	Post-secretin at 3 minute	Post-secretin at 4 minute	Post-secretin at 5 minute	Significant increase from baseline up to
D2						
- Controls	**63 ± 140**	**55 ± 146**	**37 ± 110**	**38 ± 89**	**46 ± 108**	**5 minutes**
	***p*: 0.003**	***p*: 0.010**	***p*: 0.023**	***p*: 0.004**	***p*: 0.004**	
- CP	−7 ± 62	28 ± 69	14 ± 61	29 ± 61	18 ± 93	N/A
	P: 0.440	P: 0.005	P: 0.107	P: 0.002	P:0.184	
- CCP	−11 ± 51	23 ± 62	15 ± 50	27 ± 56	22 ± 76	N/A
	P: 0.249	P: 0.053	P: 0.106	P: 0.015	P: 0.131	
D3-4						
- Controls	**48 ± 95**	**37 ± 110**	22 ± 129	51 ± 153	37 ± 119	2 minutes
	***p*: 0.001**	***p*: 0.019**	p: 0.233	*p*: 0.023	*p*: 0.033	
- CP	**77 ± 251**	−20 ± 166	−11 ± 116	1 ± 131	91 ± 223	1 minute
	***p*: 0.035**	*p*: 0.399	*p*: 0.494	p: 0.949	p: 0.006	
- CCP	111 ± 305	−19 ± 202	−26 ± 140	3 ± 157	110 ± 243	N/A
	p: 0.056	*p*: 0.603	*p*: 0.319	*p*: 0.916	*p*: 0.019	
J						
- Controls	**221 ± 303**	28 ± 234	43 ± 188	2 ± 170	37 ± 149	**1 minute**
	***p*: < 0.001**	*p*: 0.400	*p*: 0.110	*p*: 0.937	*p*: 0.086	
- CP	**197 ± 526**	55 ± 362	−6 ± 182	1 ± 219	−43 ± 354	**1 minute**
	***p*: 0.011**	*p*: 0.288	*p*: 0.819	*p*: 0.965	*p*: 0.396	
- CCP	**180 ± 430**	−8 ± 115	14 ± 153	29 ± 148	12 ± 125	**1 minute**
	***p*: 0.029**	*p*: 0.702	*p*: 0.621	*p*: 0.303	*p*: 0.614	

The post-secretin response was calculated as percent changes in MR signal intensity compared to the pre-secretin image. Each point estimate is compared to its predecessor (˜ 5th minute is compared to 4th minute, 4th minute is compared with 3rd minute, 3rd minute is compared with 2nd minute, 2nd minute is compared with 1st minute, and the 1-minute post-secretin exam is compared with the pre-secretin image). D2: Second portion of the duodenum. D3, 4: Third and fourth portion of the duodenum. *J*: Jejunum.

system control for intestinal secretions [26]. Secretin can influence ion and fluid absorption and secretion in jejunum [13]. Enteric nervous system release of neurotransmitters and neuropeptides may further regulate the intestinal secretions [26].

4.1. Conclusions

A significant increase in jejunal secretions can be detected 1 min after secretin administration with no difference between CP cases and

Table 4
Post-secretin response in association with chronic pancreatitis and chronic calcific pancreatitis.

	Post-secretin at 1 minute	Post-secretin at 2 minute	Post-secretin at 3 minute	Post-secretin at 4 minute	Post-secretin at 5 minute
D2					
CP vs. Control	**−70 ± 22**	**−97 ± 37**	**−120 ± 41**	**−130 ± 47**	**−157 ± 50**
	***p*: 0.001**	***p*: 0.008**	***p*: 0.004**	***p*: 0.005**	***p*: 0.002**
CCP vs. Control	**−55 ± 25**	**−88 ± 41**	**−99 ± 47**	**−107 ± 52**	**−128 ± 57**
	***p*: 0.028**	***p*: 0.033**	***p*: 0.034**	***p*: 0.038**	***p*: 0.024**
D3-4					
CP vs. Control	30 ± 38	−29 ± 33	−62 ± 37	**−112 ± 51**	−57 ± 72
	p: 0.441	*p*: 0.382	*p*: 0.097	***p*: 0.028**	*p*: 0.425
CCP vs. Control	70 ± 42	29 ± 37	−21 ± 42	−53 ± 58	14 ± 80
	p: 0.096	*p*: 0.423	*p*: 0.620	*p*: 0.362	*p*: 0.859
J					
CP vs. Control	−23 ± 87	5 ± 127	−45 ± 115	−46 ± 107	−126 ± 93
	p: 0.792	*p*: 0.971	*p*: 0.697	*p*: 0.668	*p*: 0.175
CCP vs. Control	−51 ± 96	−115 ± 141	−124 ± 127	−96 ± 118	−80 ± 104
	p: 0.598	*p*: 0.414	*p*: 0.330	*p*: 0.417	*p*: 0.439

Reported numbers are adjusted beta values from generalized estimating equations with linear functions in the prediction of post-secretin response. The post-secretin response was calculated as percent changes in MR signal intensity compared to the pre-secretin image. Adjustments were made for age, gender, and race.

controls. Post-secretin response at jejunum is independent of the pancreatic response that can be detected at D2, and should not be misinterpreted as a rapid pancreatic response.

Conflicts of interest

Vikesh Singh is a consultant to Abbvie, Ariel Precision Medicine and Akcea Therapeutics. Other authors have no disclosures.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.ejrad.2018.12.024.

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