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Characteristics of Patients Undergoing Endoscopic Retrograde Cholangiopancreatography for Sphincter of Oddi Disorders

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Conflicts of interest

The authors disclose no conflicts.

Supplementary Material

Note: To access the supplementary material accompanying this article, please click here.

Keywords

ERCP; Sphincter of Oddi Dysfunction; Functional GI Disorders; Sphincterotomy

The concept that sphincter of Oddi dysfunction (SOD) can cause attacks of biliary-type pain in postcholecystectomy patients and those with unexplained recurrent acute pancreatitis, and that endoscopic sphincterotomy can ameliorate symptoms, remains unproven. The Evaluating Predictors and Interventions in Sphincter of Oddi Dysfunction (EPISOD) study of patients without objective evidence for biliary obstruction showed no difference in outcomes between those who underwent sphincterotomy or sham treatment.[1] There are limited studies examining the characteristics or patients who are still being offered endoscopic retrograde cholangiopancreatography (ERCP) for SOD since the EPISOD publication, although the absolute number appears to have declined.[2]

The Results of ERCP for SPhincter of Oddi Disorders (RESPOnD) study is an ongoing, longitudinal cohort study whose overarching aims are to precisely estimate the benefit of ERCP with sphincterotomy when performed for SOD and to define characteristics associated with a favorable response. The aims of the present analyses were to define the baseline characteristics among individuals enrolled in RESPOnD and to measure differences in comparison with EPISOD.

Methods

This study compares patients from 2 prospective studies of ERCP performed for patients with suspected SOD. The reference population was patients randomized in the EPISOD trial, the enrollment criteria, methods, and results of which have been published.[1] The comparison population is the ongoing, longitudinal RESPOnD cohort (see Supplementary Table 1 for enrollment criteria). The key inclusion criterion for RESPOnD is the performance of an ERCP in a treatment-naïve patient for the indication of suspected SOD. For descriptive purposes and in keeping with the Rome IV definition of SOD, subjects in RESPOnD are dichotomized by those with and without the diagnosis of idiopathic recurrent acute pancreatitis (iRAP; or pancreatic SOD).[3] iRAP is defined by physician report and does not require 2 separate episodes meeting the revised Atlanta criteria or other expert criteria for recurrent acute pancreatitis.[4] See the Supplementary Methods for additional methodology.

Results

Between January 2018 and June 2020, the first 140 subjects enrolled in RESPOnD were compared with the randomized cohort from EPISOD (n = 214). Using Rome III definitions,[5] RESPOnD subtypes include biliary type I (n = 21), type II (n = 44), type III (n = 17), pancreatic (n = 48), and unknown (n = 10). Compared with EPISOD, subjects enrolled in RESPOnD are significantly older (Supplementary Table 2), and the majority (56%) of patients with biliary SOD had more than a 2-fold increase in at least 1 liver chemistry, with duct dilation less common (Table 1).

Using the Recurrent Abdominal Pain Interference and Disability instrument developed for EPISOD,[6] subjects in RESPOnD have fewer pain days in the past 90 days compared with EPISOD ($P < .0001$), with the lowest pain burden in RESPOnD iRAP. More patients in RESPOnD reported pain scores of 8 or higher on the 11-point visual analog scale (unadjusted $P = .0146$). Pain burden was similar between RESPOnD SOD and EPISOD ($P = .2584$), although it was lower when iRAP was included ($P < .0001$). Although depression was similar, more subjects in RESPOnD had a high likelihood of anxiety ($P = .0185$) and low mental health ($P = .0898$), especially when excluding RESPOnD iRAP. However, poor physical health was observed more frequently in EPISOD ($P = .0479$).

Discussion

The RESPOnD cohort confirms that the majority of patients being offered ERCP for suspected SOD have some degree of biochemical abnormality or duct dilation. Although low physical health was more common in EPISOD, more subjects in RESPOnD have a high likelihood of underlying anxiety and low mental health. In comparison with patients with other functional gastrointestinal disorders, the rate of depression in EPISOD and RESPOnD is lower, yet the rate of concomitant irritable bowel syndrome is higher than in the general population (9.0%).[7,8] There is a significantly lower rate of chronic pain in RESPOnD, which perhaps is an impact of the EPISOD publication. However, the high frequency of opioid use in both studies is a probable factor associated with response and baseline pain characteristics because it raises the concern for opioid-induced visceral hypersensitivity and duct dilation, central sensitization, and opioid-induced SOD.

The present study highlights some key differences in patients undergoing ERCP for SOD in current clinical practice compared with those enrolled in EPISOD: more underlying anxiety, greater use of neuromodulators, higher pain burden, and most (but not all) having some biochemical or duct abnormalities to suggest sphincter of Oddi disorder. These factors serve as important reminders of the complex pathophysiologic basis for functional abdominal pain disorders and the consequent challenges in clinical management. Finally, these observations further illustrate the impact of a sham-controlled clinical trial such as EPISOD on clinical practice at referral centers.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations used in this paper:

EPISOD	Evaluating Predictors & Interventions in Sphincter of Oddi Dysfunction

ERCP	endoscopic retrograde cholangiopancreatography
iRAP	idiopathic recurrent acute pancreatitis
RESPOnD	Results of endoscopic retrograde cholangiopancreatography for SPhincter of Oddi Disorders
SOD	sphincter of Oddi disorders

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Table 1.

Biochemical and Psychosocial Characteristics

Patient characteristic	RESPOnD SOD only	RESPOnD iRAP	RESPOnD total	EPISOD	RESPOnD vs EPISOD, *P* value	RESPOnD SOD only vs EPISOD, *P* value
Bile duct diameter, *mm,* median (IQR)	10 (7–14)	7 (5–10)	9 (6–12)	7 (5–8)		
Bile duct diameter ≥10 mm, n (%)	34 (45.9)	8 (21.1)	42 (37.5)	5 (2.4)		
Pancreatic duct diameter, *mm,* median (IQR)	2.7 (2–4)	2 (1.5–4)	2.3 (2–4)	N/A		
Biliary laboratory results						
AST range, n (%)						
Normal	28 (35.4)	25 (55.6)	53 (42.7)	195 (97)		
1–2× ULN	12 (15.2)	5 (11.1)	17 (13.7)	6 (3)		
>2× ULN	39 (49.4)	15 (33.3)	54 (43.5)	0 (0)		
ALT range, n (%)						
Normal	24 (39.3)	27 (69.2)	51 (51)	193 (95.1)		
1–2× ULN	14 (23)	7 (17.9)	21 (21)	10 (4.9)		
>2× ULN	23 (37.7)	5 (12.8)	28 (28)	0 (0)		
AP range, n (%)						
Normal	39 (49.4)	29 (64.4)	68 (54.8)	197 (98)		
1–2× ULN	31 (39.2)	12 (26.7)	43 (34.7)	4 (2)		
>2× ULN	9 (11.4)	4 (8.9)	13 (10.5)	0 (0)		
AST, ALT, or AP >2× ULN, n (%)	44 (55.7)	16 (35.6)	60 (48.4)	0 (0)		
Pancreatic laboratory results						
Lipase range, n (%)						
Normal	49 (81.7)	11 (26.8)	60 (59.4)	192 (95)		
1–3× ULN	4 (6.7)	9 (22)	13 (12.9)	10 (5)		
>3× ULN	7 (11.7)	21 (51.2)	28 (27.7)	0 (0)		
Amylase range, n (%)						
Normal	17 (85)	10 (55.6)	27 (71.1)	199 (98.5)		
1–3× ULN	0 (0)	3 (16.7)	3 (7.9)	3 (1.5)		
>3× ULN	3 (15)	5 (27.8)	8 (21.1)	0 (0)		

Patient characteristic	RESPOnD SOD only	RESPOnD iRAP	RESPOnD total	EPISOD	RESPOnD vs EPISOD, *P* value	RESPOnD SOD only vs EPISOD, *P* value
Lipase or amylase >3× ULN, n (%)	9 (14.8)	22 (52.4)	31 (30.1)	0 (0)		
Pain characteristic						
Days of pain episodes in past 90 days, median (IQR)	61.5 (10–90)	18 (6–45)	30 (10–90)	85 (48–90)	<.0001	.1893
Pain intensity (0–10) in past 90 days, median (IQR)	7 (6–9)	7.5 (6–10)	7 (6–9)	7 (5–8)	.4101	1.000
Pain burden (frequency × intensity product) in past 90 days, median (IQR)	360 (72–630)	150 (56–320)	210 (70–540)	450 (300–630)	<.0001	.2584
Psychosocial characteristic						
High likelihood of depression,[a] n (%)	8 (12.3)	3 (7.9)	11 (10.7)	11 (5.1)	1.000	1.000
High likelihood of anxiety[b] n (%)	16 (24.6)	6 (15.8)	22 (21.4)	17 (7.9)	.0185	.0075
Low physical health, [c] n (%)	27 (42.2)	10 (26.3)	37 (36.3)	118 (55.1)	.0479	1.000
Low mental health[d] n (%)	27 (42.2)	8 (21.1)	35 (34.3)	41 (19.2)	.0898	.0048

NOTE. All *P* values were adjusted using Bonferroni correction for multiple comparisons. Comparative statistics are not included for duct and oratory characteristics given differences in study enrollment criteria.

AP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BSI, Brief Symptom Inventory; EPISOD, Evaluating Predictors and Interventions in Sphincter of Oddi Dysfunction; HADS, Hospital Anxiety and Depression Scale; IQR, interquartile range; iRAP, idiopathic recurrent acute pancreatitis; PROMIS-29, Patient-Reported Outcomes Measurement Information System 29; RESPOnD, Results of Endoscopic retrograde cholangiopancreatography for SPhincter of Oddi Disorders; SOD, sphincter of Oddi dysfunction; ULN, upper limit of normal.

[a] High likelihood of depression was defined by a BSI-18 T score ≥65 in EPISOD and Beck Depression Inventory II >18 in EPISOD.

[b] High likelihood of anxiety was defined by a HADS Anxiety score ≥11 in EPISOD and a BSI-18 Anxiety T score ≥65 in RESPOnD.

[c] Low physical health was defined as a Short Form-36 Physical Component T Score ≤40 in EPISOD and a PROMIS-29 Physical Health Summary T score ≤40 in RESPOnD.

[d] Low mental health was defined as a Short Form-36 Mental Component T Score ≤40 in EPISOD and a PROMIS-29 Mental Health Summary T score ≤40 in RESPOnD.

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