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REVIEW ARTICLE

Endoscopy versus early surgery for the management of chronic pancreatitis: a systematic review and meta-analysis

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Abstract

Background and aim Endoscopic stone removal and stenting of pancreatic strictures are the initial treatment for treating chronic pancreatitis-related pain. Surgery is considered when endoscopic interventions fail to improve symptoms. In this meta-analysis, we have compared early surgery versus endoscopic interventions.

Methods The study was performed as per the PRISMA statement. The literature search was conducted on online databases to identify studies that compared endoscopy and surgery for the management of chronic pancreatitis symptoms. Primary outcomes of interest were pain relief, complications, and exocrine/endocrine insufficiency. Secondary outcomes were mean length of stay and mean number of procedures. Pooled odds ratio (OR) was calculated using random-effects model with 95% confidence interval (CI).

Results Of a total of 9880 articles that were screened, three randomized controlled trials and two retrospective studies with 602 patients (71.4% males) were found to be eligible. Endoscopic interventions were performed in 317 patients and 285 patients underwent early surgery. Early surgery provided significantly better pain relief compared to endoscopy (OR 0.46; 95%CI 0.27–0.80; $p=0.01$; $I^2=17.65\%$) and required less number of procedures (Mean difference 1.66; 95%CI 0.9–2.43; $p=0.00$; $I^2=96.46\%$). There was no significant difference in procedure-related complication (OR 0.91; 95%CI 0.51–1.61; $p=0.74$; $I^2=38.8\%$), endocrine (OR 1.18; 95%CI 0.63–2.20; $p=0.61$; $I^2=28.24\%$), or exocrine insufficiency (OR 1.78; 95%CI 0.66–4.79; $p=0.25$; $I^2=30.97\%$) or the length of stay (Mean difference 1.21; 95%CI −7.12 to 4.70; $p=0.69$).

Conclusion Compared to endoscopy, early surgery appears to be better in controlling chronic pancreatitis-related pain, with no significant difference in procedure-related complications. However, larger randomized controlled trials are needed to ascertain their efficacy.

Keywords Chronic pancreatitis · Pancreatic strictures · Pancreatic sphincterotomy · Extracorporeal shockwave lithotripsy · Pancreatectomy · Pancreatojejunostomy

Abbreviations

CI	Confidence interval
EUS	Endoscopic ultrasound
I^2	Inconsistency index
OR	Odds ratio
PICO	Patients, intervention, comparison, and outcomes
PRISMA	Preferred reporting items for systematic review and meta-analysis statement
ROBANs	Risk of Bias Assessment tool for Non-randomized studies

Chronic pancreatitis is characterized by a progressive fibro-inflammatory condition of the pancreatic parenchyma that usually results in scarring, progressive loss of exocrine and endocrine function resulting in chronic abdominal pain and steatorrhea [1–3]. Nearly 80–90% of the patients with chronic pancreatitis have episodic or continuous abdominal pain [2]. Chronic abdominal pain is responsible for impairment in quality of life, unemployment, and significant

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healthcare expenditure in patients with chronic pancreatitis [4].

In a prior large multicenter prospective study, patients with constant pain, regardless of the severity of the pain, were likely to have higher utilization of hospitalization, disability, pain medication use, and lower quality of life score as assessed by Short Form-36 score when compared to those who have intermittent pain [5]. The severity of pain in chronic pancreatitis varies widely during the course of the disease; nearly 60% of patients report constant pain, while 40% of patients report intermittent abdominal pain. Moreover, patients who report pain may have a history of anxiety and depression which add to the complexity of the pain mechanism in chronic pancreatitis [6]. In a cross-sectional study including 43 chronic pancreatitis (males 37/ mean age 47 7.9 ± 8.6) patients and 40 healthy volunteers, quality of life score was assessed using the Short-Form-36 questionnaire. Mean quality of life score was significantly lower in chronic pancreatitis patients compared to the control group, mainly affecting general health perception, physical functioning, role physical, and vitality scores [7]. Therefore, management of chronic pain in chronic pancreatitis is quintessential to reducing the psychological and financial adverse effects on patients [8].

The cause of pain is multifactorial in nature. The most common etiology is pancreatic duct obstruction from pancreatic stricture or pancreatic duct stones leading to increased intraparenchymal pressure and ischemia. Other causes of pain include neuropathic pain from recurrent scarring and fibrosis of pancreas and complications from chronic pancreatitis, such as pseudocysts, bile duct or duodenal obstruction, and secondary pancreatic malignancy.

Recent studies have suggested the presence of pancreatic neuropathy and neuroplasticity in both peripheral and central nervous systems leading to allodynia (a painful response to usually not painful stimuli) and hyperalgesia (increased pain response to usually less painful stimuli) in chronic pancreatitis patients [9]. While initially this can be intermittent, long term this can be more frequent and a constant feature. Based on this hypothesis, a randomized controlled trial evaluated pregabalin in pain associated with chronic pancreatitis and had shown benefit [10]. However, chronic pancreatitis-related pain is a complex entity that is driven by various factors, such as anatomical, psychosocial, and neurobiological factors. Therefore, pain management in chronic pancreatitis should address these factors for effective pain management.

Currently, most patients with chronic pancreatitis pain are managed with analgesics such as opioids and endoscopic therapy as the first line of treatment. Endoscopic therapy can include pancreatic duct sphincterotomy with stone removal and/or stent placement to treat pancreatic duct stricture. However, when endoscopic measures fail to relieve the pain, surgery is considered the last resort to achieve pain relief. Approximately 35–75% of the patients with chronic pancreatitis will eventually undergo surgical intervention for pain management after several endoscopic interventions during the prolonged course of the disease [11]. Although previous studies have shown surgery to be effective in controlling the symptoms of chronic pancreatitis, a comparison between endoscopic intervention and early surgical intervention is lacking. The gastroenterology practice societies of North America and Europe recommend initial endoscopic intervention for the treatment of pain due to chronic pancreatitis and surgical intervention only after exhausting the endoscopic approaches as endoscopy is minimally invasive and surgery can be associated with high morbidity and mortality [12–14].

Currently, there is limited knowledge on surgical management of pain associated with chronic pancreatitis. Moreover, previous systematic reviews and meta-analysis by Cochrane reviews on early surgery and endoscopy for treatment of pain due to chronic pancreatitis included only two studies in the pooled estimates [15]. Another recent systematic review and meta-analysis that compared short-term and long-term effects of endoscopic and surgical interventions also suggested early surgery is superior to endoscopy [16]. However, this study also included only three studies with low power. Therefore, an updated systematic review and meta-analysis are needed to analyze the outcomes in the surgical and endoscopic groups. We have compared the efficacy of early surgical intervention and endoscopic therapies to relieve pain due to chronic pancreatitis in this systematic review and meta-analysis.

Methods and material

We followed Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) statement to perform this meta-analysis [17].

Patients, intervention, comparison, and outcomes (PICO) questions

Patients: Patients with abdominal pain due to chronic pancreatitis
Intervention: Endoscopic interventions
Comparison: Early surgical intervention
Outcome: Pain relief, complications, new-onset diabetes, and steatorrhea

Literature search strategy

We conducted a comprehensive literature search for articles that compared endoscopic and surgical interventions for the

treatment of chronic pancreatitis. An electronic database search on PubMed, Embase, Web of Science, and Cochrane library was performed looking for articles published in English from inception to November 2020. The following search words were used to identify the eligible articles: Chronic pancreatitis, pancreatic stricture, pancreatic duct stricture, surgical treatment for pancreatic stricture, and pancreatic stenting in various combinations of 'AND and OR.'

Selection of eligible studies

Clinical studies that reported data on the efficacy of early surgery and endoscopic interventions for the treatment of chronic pancreatitis were included. Early surgery included patients who underwent surgery for treatment of pain associated with chronic pancreatitis without any prior endoscopy treatment or those who underwent surgery when they were just initiated on opioid treatment for pain [6 months for weak opioids (codeine, tramadol, and hydrocodone) and two months for strong opioids (other opioids) with or without prior endoscopic treatment] [18]. The primary outcomes of interest were pain relief (partial or complete pain relief) and complication rate. We included studies that included adult patients only and published in the English language. We excluded abstracts, conference papers, meta-analyses, reviews, letters, correspondence, case reports, and animal studies. Studies that did not report data on both surgery and endoscopic interventions were excluded. We also reviewed the references to identify eligible studies that were not found during our initial screening.

Data collection

After the literature review, the data from included studies were collected by two authors independently (UB and CU). The data were initially tabulated on an excel sheet. Whenever there was no consensus on the inclusion of a study or data, a third experienced researcher (SS) reviewed the study independently and decided to include or exclude the study. The data extracted from studies included author, country of origin, year of publication, type of study, number of patients included in endoscopic and surgical interventions, patient gender, type of study, number of patients included in endoscopic and surgical interventions, patient gender, average age, cause of chronic pancreatitis, rate of pain relief, complications, and exocrine and endocrine insufficiency.

Outcome measures

Primary outcomes of interest for this meta-analysis were pooled odds ratio of pain relief and complication rates in endoscopic and surgical interventions for chronic pancreatitis. Leave one out sensitivity analysis was also performed to analyze the effect of individual studies on the pool estimates. Whenever there was a significant change in the pooled estimate, the same was reported. Secondary outcome measures were the rate of exocrine and endocrine insufficiency as well as the length of stay.

Quality assessment

The quality of included studies was evaluated using the risk of bias assessment tool for non-randomized controlled studies for observational studies, and the Cochrane risk of bias tool for randomized studies was used to assess randomized controlled trials.

Publication bias

To assess whether authors have selectively included studies, publication bias would be assessed using a funnel plot. Symmetry distribution of individual studies on the funnel plot by visual inspection was performed. Egger's test, which indicates whether there is a significant risk of small studies and publication bias, was also performed.

Statistical analysis

This meta-analysis was performed by calculating the pooled odds ratio for primary and secondary outcomes with a 95% confidence interval (CI). We used DerSimonian and Laird random-effects model or fixed-effects model when the heterogeneity among included studies was high or low, respectively. The heterogeneity among the included studies was assessed using the inconsistency index (I^2). Heterogeneity of 25% or less, 25–50%, and more than 50% was considered low, moderate, and substantial heterogeneity, respectively. Categorical variables were reported as percentages, and continuous variables were reported as means and standard deviations (SD). Statistical analysis was performed using STATA 16.1 (Stata Corp. 4905 Lakeway Drive, College Station, Texas 77845 USA).

Results

Search results and study characteristics

Initial electronic database search using above-mentioned keywords for articles on PubMed, Web of Science, and Embase revealed a total of 9880 studies. After duplicates, abstracts, reviews, notes, letters, and editorials, 5,657 unique articles remained for further screening. After screening the title and abstract, eight studies were included for a full-length article review. At the end of our thorough screening, five studies published as full-length articles were found

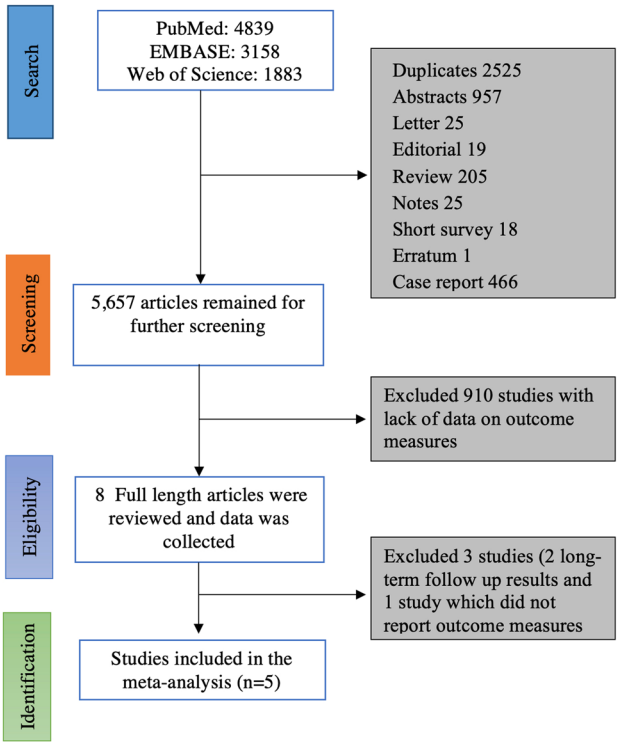

Fig. 1 PRISMA flowchart of selecting eligible studies for the meta-analysis

eligible for the meta-analysis as per inclusion and exclusion criteria [18–22]. The PRISMA flowchart for study selection is shown in Fig. 1. There were three randomized controlled trials [18–20] and two retrospective studies [21, 22]. Two studies were from the Netherlands, [18, 20] one study from China, the Czech Republic [19], and Austria [22] each. The baseline characteristics of the studies are listed in Table 1.

There were four single-center studies and one multicenter study. One of the studies by Dite et al. included a sub-group of patients who were randomized into endoscopy and early surgical groups. We used the entire study population and their results in the primary outcome analysis. Results from the randomized sub-group were included in the sub-group analysis for randomized controlled studies only.

Patient and procedure characteristics

There was a total of 602 patients from 5 studies that included 71.4% males and 28.6% females. Endoscopic interventions were performed in 317 patients and 285 patients underwent early surgery for the treatment of chronic pancreatitis. The average age of the patients in the endoscopy group was 51.65 ± 3.08 years, and the average age in the surgical group was 48.5 ± 1.68 years. Common endoscopic interventions performed in the endoscopy group were pancreatic sphincterotomy, pancreatic duct stenting, pancreatic duct stone extraction, and extracorporeal shock wave lithotripsy (ESWL). Common procedures performed in the surgical groups were duodenum-preserving pancreatic head resection (as described by Frey and Smith and Beger procedure) or surgical drainage of the entire length of the pancreatic duct by a lateral pancreaticojejunostomy (Puestow procedure) or pancreatoduodenectomy (Whipple's procedure) or distal pancreatectomy.

In the endoscopy group, the most common cause of chronic pancreatitis was alcohol ($n = 147$, 58%). Idiopathic chronic pancreatitis was seen in 70 patients (27.7%), pancreatic ductal stone in 10 patients (4%), pancreatic divisum in two patients, hereditary chronic pancreatitis in two patients, and eight patients had other causes of chronic pancreatitis

Table 1 Basic characteristics of studies included in the meta-analysis

Author—Year	Country	Type of study	Follow-up in months	Endoscopy n	Endoscopy Males	Endoscopy Age	Surgery n	Surgery males	Surgery age
Jiang 2018	China	Retrospective study—Single center	63.5	40	23	47.3	46	36	50.5
Issa 2020	The Netherlands	Multicenter RCT	18	44	34	56 ± 9	44	33	49 ± 10
Cahen 2007	The Netherlands	Single-center RCT	24	19	11	52 ± 9	20	15	46 ± 12
Dite 2003	The Czech Republic	Prospective cohort study—single center	60	64	NA	NA	76	NA	NA
Rutter 2010	Austria	Single-center retrospective study	33.3/ 98.1	150	105	51.3 ± 12.7	99	73	49.5 ± 13

as reported by four studies. Dite et al. did not report data on gender distribution or etiology of chronic pancreatitis. Similarly, causes of chronic pancreatitis in the surgery group were alcohol in 96 patients ($n=96$; 46%), idiopathic in 85 (40.7%) patients, and 10 (5%) patients had pancreatic ductal stone, hereditary chronic pancreatitis in 2 patients, and 11 had other causes. Commonly reported complications in endoscopic interventions included acute pancreatitis, bleeding episodes, pancreatic abscess, pancreatic stent occlusion, and pancreatic duct rupture leading to leak and intra-abdominal fluid collections. Similarly, commonly reported complications included after surgical intervention were acute pancreatitis, bleeding, bowel injury, sepsis, postoperative ileus, anastomotic leakage, cholangitis, new-onset diabetes mellitus, and steatorrhea.

Primary outcomes

Pooled proportions and odds ratio for pain resolution

The pain resolution was higher in the surgery group (76%; 95% CI 69% −82%) when compared to the endoscopy group (60%; 95% CI 52% −67.4%). Pooled estimates also suggested surgery is superior to endoscopic interventions for chronic pancreatitis (OR 0.46; 95%CI 0.27–0.80; $p=0.01$). There was low heterogeneity among the included studies ($I^2=17.65\%$) Fig. 2. A sub-group analysis of randomized controlled trials only showed early surgical intervention is significantly better in pain relief compared to endoscopic interventions (OR 0.32; 95%CI 0.16–0.65; $p=0.00$; $I^2=0\%$) Supplementary Figure 1.

Pooled proportions and odds ratio for complications rates

The rate of complications in the endoscopic group was 24.6% (95% CI 20–29.7%), and it was 24.21 (95%CI 19–29.6%) in the surgery groups. Pooled estimates showed no significant difference in complication rate between endoscopy and surgery groups (OR 0.91; 95%CI 0.51–1.61; $p=0.74$; $I^2=38.8\%$) Fig. 2.

Pooled proportions and odds ratio for new-onset endocrine insufficiency

There were 16% ($n=50$; 95%CI 23–37.5%) patients in the endoscopy group and 28% ($n=52$; 95%CI 22–35%) patients in the surgery group with new-onset endocrine insufficiency manifesting as pancreatogenic diabetes. Pooled estimates did not show significant difference between the two groups (OR 1.18; 95%CI 0.63–2.20; $p=0.61$; $I^2=28.24\%$) Fig. 3.

Pooled proportions and odds ratio for exocrine pancreatic insufficiency

Exocrine pancreatic insufficiency manifested as new-onset steatorrhea was noted in 30% ($n=50$; 95%CI 22–35%) of the patients who underwent endoscopic intervention and 23% ($n=43$; 95%CI 17–30%) of the patients who underwent surgical interventions. The pooled estimates showed no significant difference between the two procedures (OR 1.78; 95%CI 0.66–4.79; $p=0.25$; $I^2=30.97\%$) Fig. 3.

Secondary outcomes

Length of stay

The mean duration of hospital stays for patients who underwent endoscopic interventions was 21.2±12.9 days and 19.5±6.12 days for those who underwent surgical interventions. The pooled mean difference showed no significant difference in the length of stay between the two procedures (Mean difference 1.21; 95%CI −7.12 to 4.70; $p=0.69$) Fig. 4.

The mean number of procedures

The mean number of procedures in the endoscopy group was 4.33, and the mean number of procedures in the surgical group was 1.67.

The Pooled mean difference showed the number of procedures needed was significantly lower in the surgical group compared to the endoscopy group (Mean difference 1.66; 95%CI 0.9–2.43; $p=0.00$; $I^2=96.46\%$) Fig. 4.

Quality assessment and publication bias

The quality of randomized controlled trials was assessed using the Cochrane risk of bias tool for randomized studies, and quality assessment of non-randomized studies was performed using the Risk of Bias Assessment Tool for Non-randomized Studies (RoBANS). The quality assessment results are shown in Supplementary Tables 1 and 2. The publication bias was not performed since the total number of studies included in the meta-analysis was less than 10.

Discussion

The results from our meta-analysis suggest that early surgical intervention for chronic pancreatitis may result in substantially higher relief from pain from chronic pancreatitis when compared to endoscopic interventions (OR 0.46; 95%CI 0.27–0.80; $p=0.01$; $I^2=17.65\%$). Sub-group analysis of randomized controlled trials only also revealed

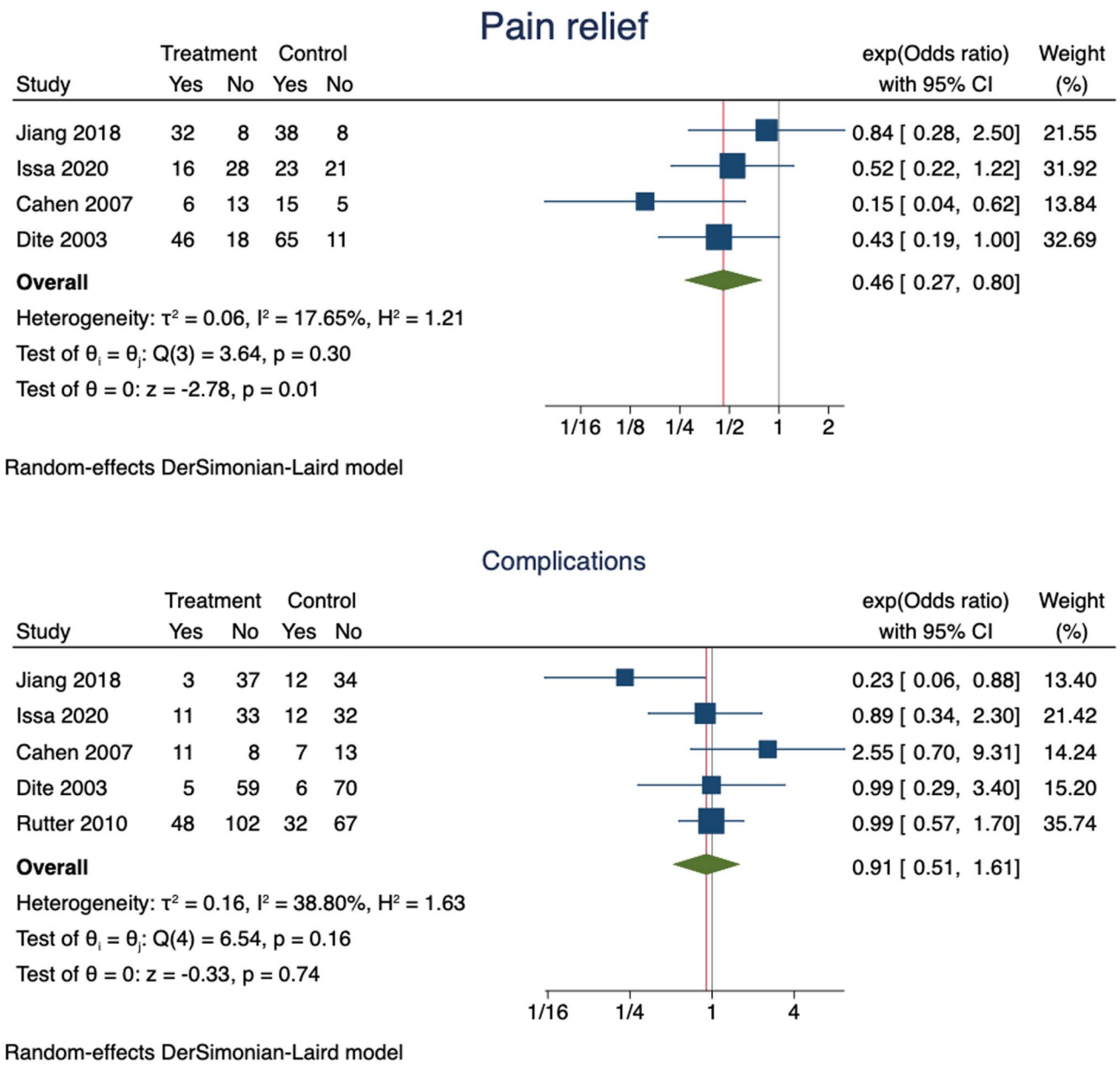

Fig. 2 Forest plot for pooled estimation of pain relief and complication rates

similar findings suggesting early surgical intervention may lead to better pain relief from chronic pancreatitis compared to endoscopic intervention (OR 0.32; 95%CI 0.16–0.65; $p = 0.00$; $I^2 = 0\%$). However, there was no significant difference in procedure-related complication rates (OR 0.91; 95%CI 0.51–1.61; $p = 0.74$; $I^2 = 38.8\%$), endocrine (OR 1.18; 95%CI 0.63–2.20; $p = 0.61$; $I^2 = 28.24\%$) or exocrine insufficiency resulting from chronic pancreatitis between the two groups (OR 1.78; 95%CI 0.66–4.79; $p = 0.25$; $I^2 = 30.97\%$). Pooled estimates also showed no significant difference in the duration of hospital stay due to surgical or endoscopic therapy for the treatment of chronic pancreatitis. However, the number of interventions required to achieve pain relief from chronic pancreatitis was significantly lower in patients who underwent surgery when compared to patients treated with endoscopic interventions. Among the study populations included in the meta-analysis, alcohol was the most common cause of chronic pancreatitis in both endoscopy and surgical groups (58% vs. 46%). Other common etiologies were idiopathic (27% vs 40%) and pancreatic duct stones (4% vs. 5%). A small percentage of patients may have hereditary pancreatitis (1%) and pancreatic divisum (1%). Also, the majority of the patients with chronic pancreatitis were males.

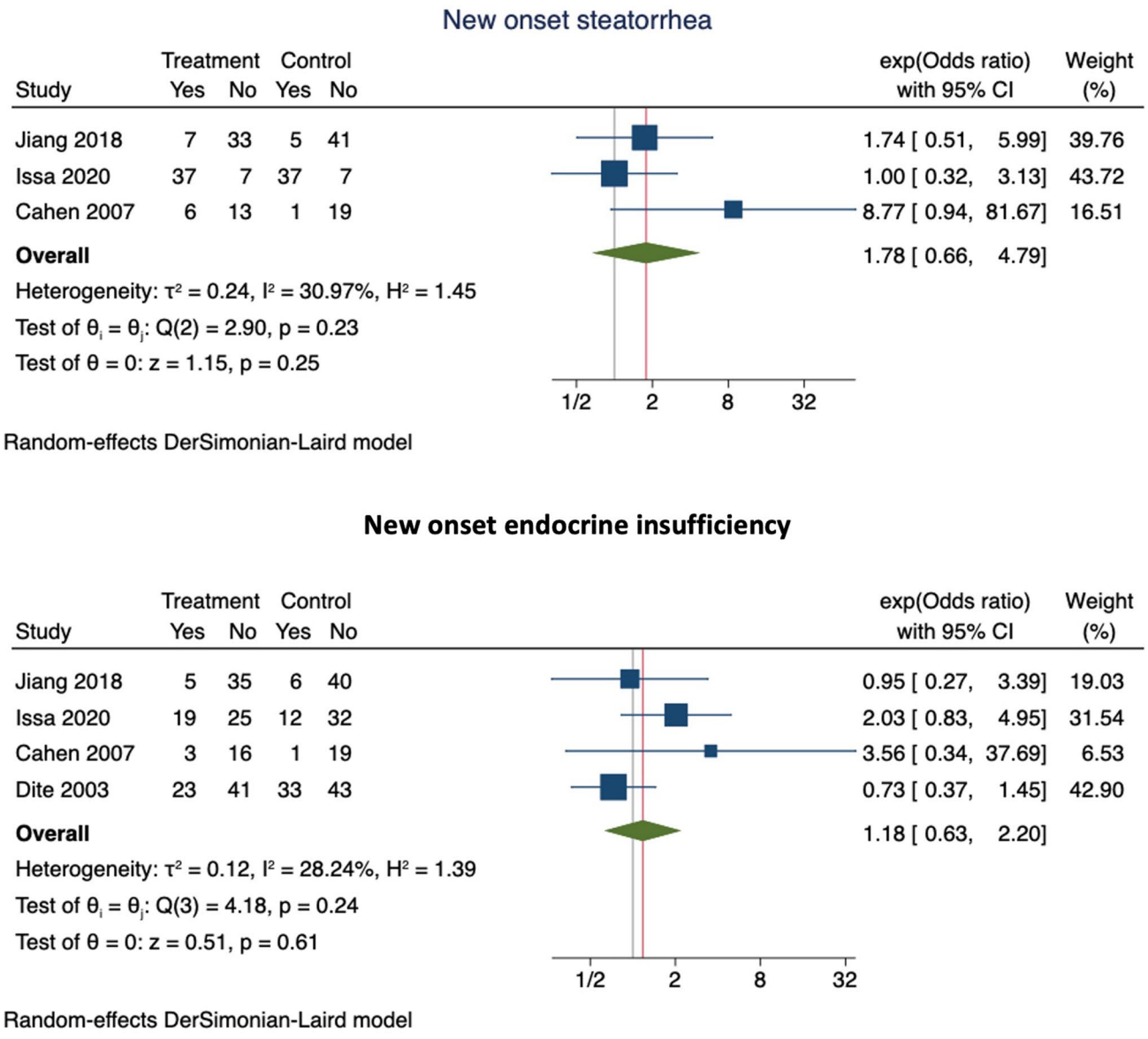

Fig. 3 Forest plot for pooled estimation of exocrine and endocrine insufficiency

Pain due to chronic pancreatitis is complex and heterogeneous, driven by anatomical, neurobiological, inflammatory, and psychosocial conditions. Although causes of pain in chronic pancreatitis can be due to various etiologies (pancreatic or peripancreatic strictures, parenchymal inflammation, or local complication of chronic pancreatitis), recent studies have suggested the presence of central sensitization of pain in up to 50% of patients with chronic pancreatitis [23, 24]. Fibrotic replacement of pancreatic parenchyma in chronic pancreatitis causes pancreatic neuropathy due to an increase in nerve fiber diameter and neurogenic inflammation [9]. Damage to peripheral nerve fibers due to pancreatitis causes an initial barrage of painful stimuli that sensitizes the peripheral nerve endings pain. Similarly, changes in the central nervous system also lead to hyperalgesia. Moreover, the prolonged time between diagnosis of chronic pancreatitis and surgical treatment might be associated with more crucial histological changes not only in the pancreas itself but also in the central nervous system.

In general, surgical interventions are invasive in nature and are expected to have higher complications such as bleeding, infections, bowel injury, and endoscopy should have a lower risk. Therefore, current guidelines from the American College of Gastroenterology recommend a step-up strategy in selecting patients with chronic pancreatitis for surgical intervention once endoscopic measures fail to treat pain effectively. However, our study showed no significant difference in the rate of complications between early surgery

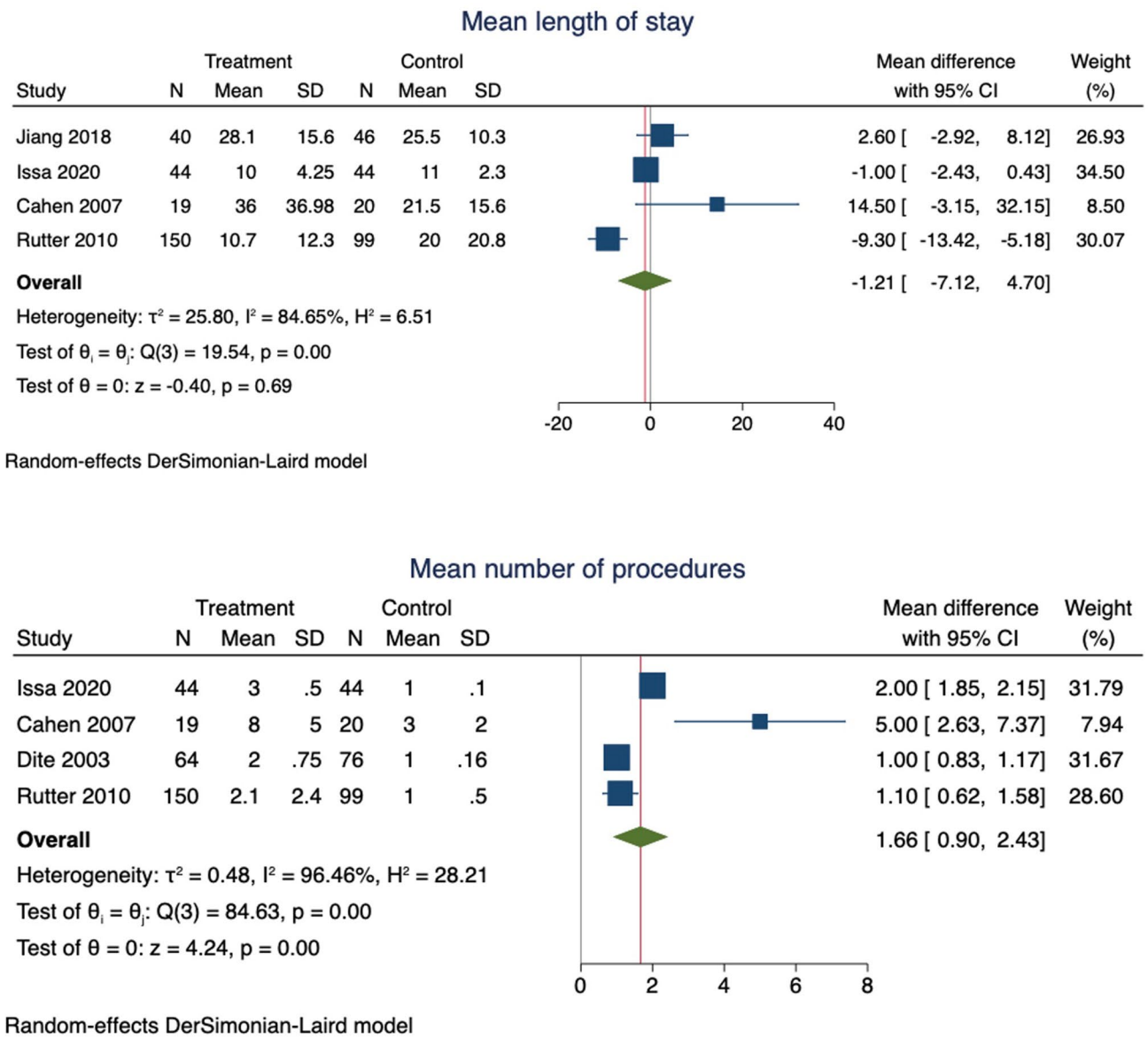

Fig. 4 Forest plot for pooled estimation of mean length of hospital stay and mean number of procedures

and endoscopy groups. This is possible because patients who undergo early surgery are less frail, unlike patients who have long-standing chronic pancreatitis with a prolonged course of pain and opioids. It should be noted that patients who undergo endoscopic interventions will likely need repeated procedures. The need for repeat procedures in the endoscopy group increases the risk of complications from endoscopy and anesthesia even though the endoscopic procedures are considered less invasive. Similarly, although endoscopic procedures can be performed as an outpatient procedure, the total duration of hospital stay could be higher as several of the patients who undergo these procedures can have worsening pain from hyperalgesia due to stricture manipulation by dilation or stent placement leading to frequent, prolonged hospitalizations as noted in our study with no significant difference for the length of hospital stay between those who undergo endoscopy and surgery for treatment of chronic pancreatitis.

Initial management for chronic pancreatitis-associated pain includes pain medications like opioids, neuromodulators, and endoscopic interventions. Neuromodulator medications (e.g., Tricyclic antidepressants (TCA), Serotonin and norepinephrine reuptake inhibitors (SNRI), and Atypical antipsychotics) have been used in the treatment of chronic pancreatitis by decreasing central sensitization to modify the brain-gut axis and to reduce the dose of opioid pain medication for effective pain control [10]. However, with time, chronic use of opioids in the treatment of

chronic pancreatitis can cause significant adverse effects, including opioid dependency, opioid-induced hyperalgesia, worsening of gastroparesis, and constipation leading to more pain [25]. Long-term pain can cause a change in the central nervous system pain pathways leading to adverse alteration in the brain-gut axis that is less dependent on local pancreatic inflammation, and this, in turn, may play a role in worsening chronic pancreatitis-related pain wherein now patients have both peripheral and central pain.

Currently, there are no guidelines to identify which patients would benefit from early surgical interventions. Previous studies suggest that patients with chronic pancreatitis due to toxic etiologies such as alcohol have better outcomes with surgery than hereditary and idiopathic etiologies [26]. Perception of pain and tolerance to pain are highly variable and subjective, leading to significant heterogeneity in presentation. Although one would expect the pain would be severe in patients with ductal stone and ductal dilation, our clinical practice suggests the morphological features alone would not predict the severity of pain. This is because the peripheral pain from chronic pancreatitis can be due to ductal hypertension from stones and stricture in the pancreatic duct and may also be due to concurrent peri-neural inflammation from long-term fibrosis associated with chronic pancreatitis. While the pain originating from ductal hypertension only may respond well to endoscopic therapy but those with concurrent peri-neural inflammation pain may not respond well from just endoscopic therapy and may need additional intervention, like surgery. Therefore, it is challenging to predict the outcomes of endoscopic interventions. One of the significant side effects of conservative management is opioid dependence and permanent alteration to central pain. If early surgery offers significant pain relief before peripheral pain from chronic pancreatitis progresses to central pain and avoids opioid dependency, it could significantly change how we treat chronic pancreatitis. Only two studies reported mortality data, with one death in the endoscopy group and five deaths in the surgical groups during the follow-up period. Pooled analysis to evaluate its significance was not performed since there were only two studies reporting mortality. Besides, conversion to surgery in the endoscopy group was required in 77 patients (of the 317 patients) during the follow-up period due to no response from endoscopic interventions suggesting that nearly 25% of the patients did not have a response to endoscopic therapy [18, 22]. Therefore, while it is reasonable to treat pain from chronic pancreatitis initially with the endoscopic therapy, those with pain despite endoscopic therapy should be referred early for consideration of surgery than subjecting patients with repeated endoscopy procedures over a prolonged period of time.

Limitations

Our study has a few limitations that should be noted. This study has a small number of studies with a small patient sample. It should also be noted that one study had a subset of patients randomized and not the entire study population. The study also excluded patients with increased pancreatic head size [19]. Two of the studies were retrospective studies and therefore, this increases the risk of inclusion bias. However, it does have three high-quality randomized controlled trials, which adds weightage to the study. The study looked at the efficacy of pain relief from chronic pancreatitis but not the long-term durability of pain relief from both surgery and endoscopic therapy. The measurement of pain using different pain scores might strongly vary between the different studies and, therefore, can cause significant heterogeneity in the results and increase the risk of bias. Studies included in this meta-analysis were conducted outside of the USA. Therefore, the applicability of these results to the US population is debatable. Nonetheless, this study can be considered to look at the practice patterns in the USA by both surgeons and endoscopists and help us to tailor the management of pain associated with chronic pancreatitis.

In conclusion, our study shows that early surgical interventions in chronic pancreatitis are better than a step-up strategy with prolonged medical therapy and endoscopy. Careful selection criteria for surgical intervention could lead to better outcomes for chronic pancreatitis. Larger randomized controlled trials are needed to make further recommendations on early surgery versus endoscopy for the management of pain associated with chronic pancreatitis.

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Declarations

Disclosures Dr. Umesha Boregowda, Dr. Juan Echavarria, Dr. Chandraprakash Umapathy, Dr. Laura Rosenkranz, Dr. Hari Sayana, Dr. Sandeep Patel, and Dr. Shreyas Saligram have no conflicts of interest or financial ties to disclose.

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