Total Pancreatectomy With Islet Autotransplantation for Chronic Pancreatitis in Adults: A Systematic Review

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Objectives: Chronic pancreatitis (CP) is a painful disease that can be refractory to multiple medical, endoscopic, and surgical interventions. Total pancreatectomy with islet autotransplantation (TPIAT) is a procedure that may be used to manage CP while potentially preserving endocrine pancreatic function. This study aims to ascertain the quality of life (QoL) and pain outcomes among CP patients after TPIAT through a systematic review of published literature.

Materials and Methods: A total of 22,691 studies published before May 2024 investigating TPIAT were collected from Scopus, Embase, Central, and PubMed databases. Title/abstract screening and full-text extraction were performed through a blinded, double review using Covidence; study quality was assessed using the MINORS criteria. Studies assessing adult patients undergoing TPIAT that reported pain or QoL outcomes using a validated scale were included. This study protocol has been registered to PROSPERO: CRD42024567887.

Results: Twelve studies matched our criteria, with 1333 patients receiving TPIAT for CP. MINORS scoring indicated a low risk of bias. In all, 80% (8/10) of studies reported a significant increase in at least one QoL outcome after TPIAT and 83% (5/6) reported a significant decrease in pain.

Conclusion: TPIAT improves QoL and pain outcomes in CP patients. Future studies should focus on identifying predictors of successful outcomes and exploring the impact of TPIAT on specific patient subgroups.

Key Words: TPIAT, quality of life, pain, chronic pancreatitis

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Chronic pancreatitis (CP) is a progressive fibroinflammatory disorder characterized by irreversible destruction of exocrine and endocrine pancreatic tissue caused by atrophy and fibrosis. The causes of chronic pancreatitis in adults are multifaceted, the most common being alcohol consumption, with genetic and environmental factors also playing a significant role in the pathogenesis of CP.[1] Recent epidemiological studies assessing patients of all ages in China and Denmark have reported the prevalence of CP ranging from 13.5 to 163 cases per 100,000 individuals, and an incidence range of 5–31.7 cases per 100,000 individuals.[2,3] There is an observed increasing trend in yearly incidence and overall CP hospitalization, highlighting the substantial health care burden of this disease.[2] However, CP can go undiagnosed for many years due to the progressive nature of the disease. Therefore, the true prevalence of CP may be greater than currently reported. The current survival rate for CP at 10 years is 70% and decreases to 45% at 20 years.[1]

Initial treatment for CP involves lifestyle changes, pancreatic enzyme replacement, and escalating pain medications as needed.[1] In cases of refractory/severe CP, more invasive management, including surgical resection, interventional radiology interventions (drainage and stent placement), celiac ganglion blockage, and endoscopy are utilized. Despite an increased level of involvement, these interventions are associated with their own morbidities, and often provide only transient improvements, with up to 50% having recurrent pain and progressive exocrine and endocrine failure.[4]

One of the most effective treatment options for CP is total pancreatectomy (TP), as it eliminates the pathology at its source. Due to the complete resection of pancreatic insulin-producing beta-cells, however, TP results in lifelong dependence on exogenous insulin use. To address this, total pancreatectomy with islet autotransplantation (TPIAT) has been used as a combination procedure to potentially mitigate diabetic complications and preserve secretory beta-cell function.[4] The procedure involves a total removal of the pancreas with subsequent isolation of pancreatic islets that are typically transplanted into the liver via the portal vein, but can also be transplanted elsewhere. The main indication for TPIAT is for patients with intractable CP pain who have failed medical, endoscopic, or surgical therapies.[5]

Abu-El-Haija et al[6] explain the indications for TPIAT as reported by the International Consensus Guidelines for CP; they assert that the main indication for this procedure is disabling pain, with the secondary benefit of preserving endocrine function. However, glycemic outcomes after TPIAT are variable, with factors such as CP progression and islet mass harvested/transplanted influencing postoperative glycemic control.[6] Most importantly, TPIAT is a surgical procedure that carries with it numerous risks, including but not limited to postoperative wound infection, anastomotic leaks, strictures, portal vein thrombosis, and bleeding, which is why multiple organizations and studies assert that careful evaluation by a multidisciplinary team is essential before recommending TPIAT.[5,6]

In terms of outcomes, a recent 2019 meta-analysis found that TPIAT decreased the need for opioids (0% and

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15% of patients opioid-free to 63% of patients opioid-free) and statistically improved quality of life scores, measured using the RAND Short Form surveys and Pain Disability Index and Depression Anxiety Stress scale, at follow-up periods ranging from 6 to 60 months.[7] Comparative studies to conventional surgical treatments are also challenging to compare, as candidates for TPIAT are patients who are not usually considered for other surgical or endoscopic procedures. This systematic review aims to analyze validated pain and quality of life outcomes after undergoing TPIAT for CP patients, and provide an updated understanding of the subjective benefits of this procedure. We hypothesize that TPIAT will result in improved postoperative quality of life and pain scores.

MATERIALS AND METHODS

Search Strategy

We utilized the Guidelines established by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) to perform a systematic search in 4 databases: Scopus, Embase, Central, and PubMed. The keywords used to perform the systematic review are located in Appendix A. Studies published before May 2024 were eligible for inclusion in this review.

The PICOT (Patient, Intervention, Comparison, Outcome, Time) method was utilized to guide our search strategy. Chronic pancreatic patients identified within the patient population were defined as having irreversible destruction of the pancreas over a prolonged period, regardless of the underlying cause. The intervention included the patient population that received a total pancreatectomy with islet autotransplantation (TPIAT). Patient-reported outcomes (PROs) of postoperative pain and QoL were assessed using validated scales such as the Visual Analog Scale, SF-12, SF-36, etc. Studies with any follow-up period were included. Inclusion criteria were adult patients who underwent a total pancreatectomy with autologous islet cell transplantation for chronic pancreatitis, and studies that included a pain scale measurement and/or a validated QoL assessment tool. Exclusion criteria consisted of studies that did not include a pain or QoL scale, studies including pediatric patients, cadaveric articles, reviews, technique studies, expert opinions, non-English studies, and studies without reported outcomes.

Each article included in this study was reviewed by 2 independent reviewers; conflicts were resolved by a third independent reviewer. A reference search was performed for all included studies to seek additional publications for review. This protocol is registered to PROSPERO: CRD42024567887.[8]

Quality Assessment

To assess for quality, the Methodological Index for Nonrandomized Studies (MINORS) criteria was utilized to evaluate the quality of included studies.[9] MINORS scores range from 0 (not reported), 1 (reported but inadequate), or 2 (reported and adequate) across 8 (noncomparative) or 12 (comparative) categories, with a maximum score of 16 or 24, respectively. Quality assessment was performed independently by 2 authors, and a third author provided consensus for conflicts. Scores of 1 and 2 for seven or more categories (11 or more for comparative studies) are considered low risk of bias, in 5–6 sections (9–10 for comparative studies) are at moderate risk of bias, and 4 or fewer sections (8 or less for comparative studies) indicate a high risk of bias.

Data Extraction and Statistical Analysis

Study variables evaluated in this systematic review include title, publication date, study year, number of patients, mean age ranges, mean follow-up time ranges, as well as preoperative/postoperative PROs, including pain and QOL. Extracted data were collected and analyzed using Google Sheets (Google Drive; Google, Mountain View, CA). If applicable and available, descriptive statistics such as mean, percentage, standard deviations, and ranges were reported. Due to significant heterogeneity among the included studies, a meta-analysis was not performed, although originally planned.

RESULTS

Literature Selection

Using Scopus, Embase, PubMed, and CENTRAL, the initial search yielded 22,691 studies, of which 4318 were identified automatically or manually as duplicates. The remaining 18,373 studies were screened based on the abstract and title, of which 154 studies were selected for full-text screening. In the final screening process, 12 studies published between 2013 and 2023 assessing 1333 patients were included in the systematic review. Follow-up periods ranged from 1 month to 11.5 years postoperatively. Of the 12 studies that were analyzed, statistically significant improvements in pain and QoL outcomes after TPIAT were seen in 5/6 studies and 8/12 studies, respectively.[10–21] All studies analyzed included a standardized scaled score of either pain or QoL outcomes. These were further subdivided based on the specific scales that were used in each study. The PRISMA flow chart highlights the selection of studies included in the systematic review (Fig. 1). The mean MINORS score for comparative ($n = 4$) and noncomparative studies ($n = 8$) was 17.25 and 11.75, respectively, indicating a low risk of bias (Tables 1–3).

Pain Outcomes

Six studies, totaling 423 patients, assessed pain outcomes in CP patients after TPIAT. Of note, Georgiev et al[13] measured pain outcomes using both the Visual Analog Scale (VAS) and the McGill Pain Questionnaire in 60 patients, and Takaki et al[21] measured outcomes using both the VAS and the Izbicki pain score. A meta-analysis on pain outcomes was not feasible, given the variations in pain assessment tools and follow-up periods.

McGill Pain Questionnaire

The McGill Pain Questionnaire was used in 2 studies (144 patients).[13,18] Georgiev and colleagues found that the Pain Rating Index was lower in all time periods measured up to 12 months postoperatively ($P < 0.001$). Present Pain Intensity scores had declined up to 12 months postoperatively ($P < 0.001$).[13] Dunderdale and colleagues assessed pain by comparing alcoholic and nonalcoholic chronic pancreatitis. They found that after 2 years postoperatively, those with nonalcoholic pancreatitis had a significant improvement in pain ($P < 0.01$) with no difference in those with alcoholic pancreatitis ($P = 0.19$).[18]

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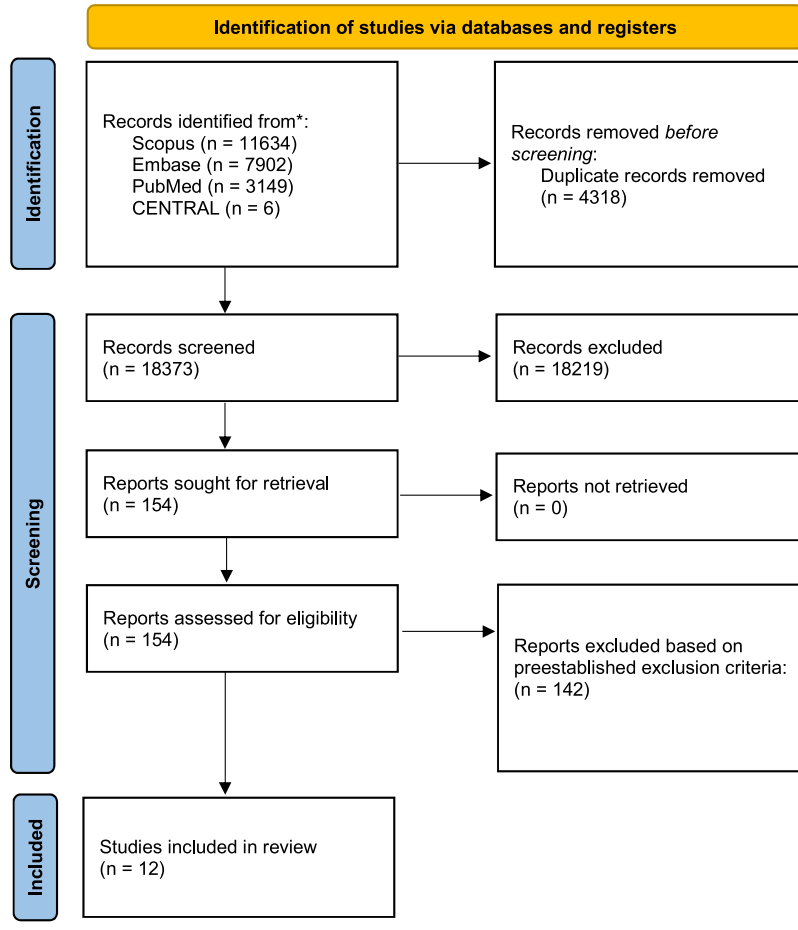

FIGURE 1. PRISMA flow chart summarizing the selection process of finalized studies.

Visual Analog Scale

Four studies (271 patients) reported pain using the Visual Analog Scale.[13,16,20,21] Georgiev et al[13] reported that patients had lower pain scores 1, 6, and 12 months postoperatively ($P < 0.001$, < 0.001, < 0.005, respectively). Coluzzi et al[20] had similar findings with pain scores decreasing up to 3 years postoperatively ($P < 0.001$). Garcea et al[16] compared 2 populations of TPIAT and non-TPIAT patients and found that the median VAS score significantly dropped in TPIAT patients ($P < 0.001$), with a median follow-up of 11.5 years for the islet group. Takaki et al,[21] found significant improvements in VAS scores among all 5 patients that they studied for 1 year after TPIAT ($P = 0.03125$).

Other Scales

The Izbicki pain score is a validated assessment for CP-related pain and is measured from 0 to 100, with higher scores indicating increased pain severity. One study, Takaki et al,[21] assessed patients using this measure and found significant improvements in pain 1 year after TPIAT ($P = 0.03125$); the mean score before surgery was 79.6, and reduced to 18 after TPIAT. Gruessner et al[11] measured pain scores in 61 patients using the SF-36 and found that at 1 year postoperatively, ~71% of the patients were pain-free and no longer required the use of analgesics.

Quality of Life Outcomes

12-Item Short Form Survey (SF-12)

Three studies, totaling 302 patients, reported QoL based on the RAND SF-12 surveys, which aggregate QoL scores into the physical component score (PCS) and mental component score (MCS); higher scores in the MCS and PCS subsections indicate improved functioning, with a range between 0 and 100 and the average score being 50.[12,17,19] Previous studies have utilized the SF-12 for the assessment of QoL in chronic pancreatitis, with a comparative study finding the SF-12 to be a valid alternative to the SF-36 for QoL assessment.[22]

In Dorlon and colleagues, patient PCS and MCS scores were recorded at up to 2 years postoperatively. They reported that the average PCS scores had incrementally increased by each follow-up until 2 years postoperatively ($P < 0.05$). The average MCS scores had increased 2 years postoperatively ($P < 0.05$).[12] John et al[19] reported increases in PCS and MCS up to 2 years postoperatively, but the authors did not report any significance with these results.

Morgan and colleagues found that MCS and PCS scores increased at 1, 2, and 5 years postoperatively ($P < 0.05$). Specifically in patients with genetic pancreatitis, they found similar increases in MCS and PCS scores at 1 and 2 years postoperatively ($P < 0.02$, < 0.003).[17]

TABLE 1. Outcomes Within Studies Included in This Systematic Review

References	Population description (mean age ± SEM)	Causes of chronic pancreatitis	Pain/QoL scales used (time points of administration)	Pain outcome	QoL outcome
Chinnakotla et al[15]	484 patients with hereditary and nonhereditary chronic pancreatitis receiving TP-IAT. (Hereditary: 21.9 y ± 1.3) (nonhereditary: 37.9 y ± 0.6)	Hereditary: PRSS1: 38 (48%) SPINK1: 9 (11%) CFTR: 14 (18%) Familial: 19 (24%) Nonhereditary: Alcohol: 34 (8%) Idiopathic: 266 (66%) Pancreas divisum: 56 (14%) Other: 48 (12%)	RAND 36-Item Short Form (Baseline, 3, 6, 12, and 24 mo postoperatively)	NA	Significant improvements were found in PCS and MCS scores post-op in both hereditary and nonhereditary groups ($P < 0.001$)
Coluzzi et al[20]	116 patients diagnosed with chronic pancreatitis receiving TP-IAT. (41 y)	Alcoholic: 9 (8%) Autoimmune: 7 (6%) Hereditary: 19 (16%) Idiopathic: 55 (47%) Other: 26 (22%)	QLQ-C30 QLQ-PAN26 VAS (Baseline, 1, 2, and 3 y postoperatively)	Pain scores evaluated with VAS decreased after TPIAT ($P < 0.001$).	QLQ-30: Global health QoL, physical, role, emotional, cognitive, and social functioning significantly increased over 2 years post-TPIAT ($P < 0.001$, < 0.001, < 0.001, < 0.001, $= 0.007$, and < 0.001, respectively). QLQ-30: Fatigue, nausea and vomiting, pain, insomnia, appetite loss, and constipation were significantly reduced post-TPIAT ($P < 0.001$, < 0.001, < 0.001, < 0.001, $= 0.001$, and < 0.001, respectively). QLQ-PAN26: Pancreatic pain, bloating, digestive symptoms, taste, indigestion, weight loss, body image, and future worries had a statistically significant trend of reduction over time ($P < 0.001$, < 0.001, < 0.001, $= 0.009$, $= 0.001$, < 0.001, $= 0.003$, and $= 0.009$, respectively)
Dorlon et al[12]	74 patients diagnosed with chronic pancreatitis (42 y)	Sphincter of Oddi Disease: 33 (45%) Idiopathic: 16 (22%) Pancreatic divisum: 11 (15%) Alcohol abuse: 6 (8%) Familial: 5 (7%) Unknown: 2 (3%) Hypertriglyceridemia: 1 (1%)	SF-12 (Baseline, 6 mo, 1 y, and 2 y postoperatively)	NA	The mean PCS score had significantly improved at 6 and 12 mo postop ($P < 0.001$, $P < 0.05$) The mean MCS score had seen similar improvements postop at 6 and 12 mo ($P < 0.05$)
Dunderdale et al[18]	91 patients diagnosed with chronic pancreatitis receiving TP-IAT		McGill Pain Questionnaire SF-36 Form	Those with NAP had improvement in pain	It was shown that although all patients have improved QOL,

	divided between alcoholic and nonalcoholic cases (Alcoholic: 46.3 ± 7.2) (Nonalcoholic: 43.7 ± 13.7)	Alcoholic pancreatitis (AP): 23 (25%) Nonalcoholic pancreatitis (NAP): 68 (75%)	(baseline, 6 mo, 1 y, and 2 y postoperatively)	during follow-up, persisting for more than 2 y ($P < 0.01$). No difference in pain was found among those with AP ($P = 0.19$).	the benefits seen after resection with IAT in patients with NAP are more significant than those in patients with AP
Garcea et al[16]	97 total patients (60 receiving TP-IAT) diagnosed with chronic pancreatitis (TPIAT: 43 y) (non-TPIAT: 45 y)	TP-IAT Alcohol: 19 (32%) Gallstones: 5 (8%) Other: 5 (8%) Unknown: 31 (52%) non-TPIAT alcohol: 17 (46%) Gallstones: 8 (22%) Other: 1 (3%) Unknown: 11 (30%)	VAS (Baseline, postop, median follow-up 11.5 y for islet group)	Median VAS scores for pain and quality of life had significantly improved for TP-IAT patients postop ($P < 0.001$)	NA
Georgiev et al[13]	53 patients diagnosed with chronic pancreatitis (47 y ± 1.4)	Idiopathic: 29 (54%) Hereditary: 8 (15%) Alcohol: 7 (13%) Pancreas divisum: 5 (9%) Other: 4 (8%)	McGill Pain Questionnaire Visual Analog Scores (VAS) SF-36 Form (baseline, 1 mo, 6 mo, and 12 mo postoperatively)	McGill Pain Rating Index scores were reported lower in all intervals ($P < 0.001$) McGill Present Pain Intensity scores declined in the 1 mo ($P < 0.001$), 6 mo ($P < 0.005$), and 1-y ($P < 0.001$) surveys. Patients reported lower VAS scores in 1, 6, and 12 mo postop ($P < 0.001$, < 0.001, < 0.005)	The increase in the PCS score was evident in 6 mo and 1 y postop ($P < 0.0001$). MCS scores also increased significantly in the 1-mo ($P < 0.005$), 6-mo ($P < 0.05$) and 12-mo ($P < 0.05$) after the procedure
Gruessner et al[11]	61 patients diagnosed with chronic pancreatitis (42.2 y ± 1.6)	Idiopathic: 45 (73%) Hereditary: 10 (16%) Alcohol: 7 (11%)	SF-36 Pain Score (baseline, 1, 6, and 12 mo postoperatively)	By 12 mo after surgery, 71% of patients were pain free and no longer required analgesics	NA
John et al[19]	33 patients diagnosed with chronic pancreatitis receiving TP-IAT (42 y)	Idiopathic: 17 (52%), Genetic: 10 (30%), Alcoholic: 3 (9%) Alcohol & Genetic: 1 (3%) Necrotizing (3%) Post-trauma: 1 (3%)	SF-12 Form (Baseline, < 6 mo, 6 mo–1 y, > 2 y postoperatively, mean follow-up: 344 d)	NA	PCS increased near healthy individuals at 6 mo–1 y and > 2 y time points. Patients post-TP-IAT at < 6 mo and 6 mo–1 y had an MCS close to or better than healthy individuals (no *P*-value reported)
Morgan et al[17]	195 patients diagnosed with chronic pancreatitis receiving TP-IAT (40.3 y)	Alcohol:11 (6%) Pancreas divisum: 30 (15%) Papillary stenosis: 58 (30%) Hereditary: 46 (24%) Other (idiopathic, triglyceride, etc): 50 (25%)	SF-12 Form (Baseline, 1, 2, and 5 y postoperatively)	NA	MCS and PCS increased at 1, 2, and 5 y postop ($P < 0.05$). In patients with genetic pancreatitis, MCS and PCS significantly increased at 1 and 2 y postop ($P < 0.02$, $P < 0.003$)
Takaki et al[21]	5 patients with pancreatitis receiving TP-IAT (34 y)	Alcohol: 2 (40%) Genetic: 2 (40%) Idiopathic: 1 (20%)	Izbicki Pain Score VAS Score SF-36 Form EORTC QLQ-C30	Izbicki Pain Score improved significantly 12 mo postop ($P = 0.03125$) VAS significantly improved 12 mo postop ($P = 0.03125$)	Significant improvements in SF-36 role-physical ($P = 0.03125$), general health perception ($P = 0.0077$), and vitality ($P = 0.035$). Improved QLQ-C30 global health/QoL

TABLE 1. (*continued*)

References	Population description (mean age ± SEM)	Causes of chronic pancreatitis	Pain/QoL scales used (time points of administration)	Pain outcome	QoL outcome
					scores, but this was a nonsignificant increase
Waage et al[10]	60 patients diagnosed with chronic pancreatitis (50 y)	Alcoholic: 18 (30%) Nonalcoholic: 42 (70%) Hereditary: 5 (8%) Idiopathic: 20 (33%) Other: 18 (30%)	EORTC QLQ-C30 (Baseline, once at follow-up with an average time of 20 mo)	NA	Global health was significantly increased postoperatively. For symptomatic and functional scores, improvement was obtained in all but 3 domains (financial difficulties, diarrhea, dyspnea). Pain, nausea, and appetite revealed the largest improvements in scores between assessments
Wilson et al[14]	64 patients diagnosed with chronic pancreatitis receiving TP-IAT (38 y)	Idiopathic: 42 (66%) Genetic: 6 (9%) Divisum (6%) Alcohol: 5 (8%) Other: 7 (11%)	SF-36 Form (mean follow-up: 49 mo)	NA	Improvements in all fields of variables reported in the SF-36 form ($P < 0.001$)

36-Item Short Form Survey (SF-36)

The SF-36 survey is an assessment of QoL that has been validated in prior studies, such as the ESCAPE clinical trial, for use in chronic pancreatitis.[23] Georgiev et al[13] (53 patients) found a significant improvement in SF-36 PCS ($P < 0.0001$) and MCS ($P < 0.05$) scores 1 year after TPIAT. Takaki and colleagues observed an increase in average physical, mental, or social component summaries in the 5 patients they studied 1 year after TPIAT, but these increases were not found to be statistically significant. The authors did observe significant improvements in role-physical ($P = 0.03125$), general health perception ($P = 0.0077$), and vitality ($P = 0.035$), which are included among the 8 multi-item dimensions of health assessed in this survey.[21]

Two studies reported QoL outcomes with a 2-year follow-up period after TPIAT.[15,18] In Chinnakotla and colleagues, significant improvements in both PCS and MCS scores persisted 2 years after TPIAT in the 120 patients they studied ($P < 0.001$). Interestingly, they did not find significant differences in MCS or PCS scores between patients with hereditary and nonhereditary/genetic causes of CP.[15] Dunderdale and colleagues compared QoL improvements in 69 patients, comparing post-TPIAT outcomes in patients with alcoholic and nonalcoholic CP. Among all patients, PCS significantly improved postoperatively at 2 years follow-up ($P < 0.01$), but MCS improvement was not significant. When patients with alcoholic pancreatitis were analyzed separately, significant improvement was only seen in the bodily pain section of the SF-12 ($P < 0.01$), without significant improvements in PCS or MCS. The authors found that QoL improvements in patients with nonalcoholic etiologies of CP were more significant than those with alcoholic chronic pancreatitis ($P < 0.01$).[18] Wilson et al[14] found that, in the 17 patients who completed the SF-36 with a mean follow-up period of 49 months, all QoL subscales significantly improved ($P < 0.001$).

European Organisation for Research and Treatment of Cancer Core Quality of Life Questionnaire (EORTC QLQ-C30)

Three studies, totaling 181 patients, reported QoL using the EORTC QLQ-C30, which outputs a global health/QoL score, and also divides QoL into functional and symptomatic scales.[10,20,21] This tool has previously been used to assess QoL in CP patients undergoing endoscopic procedures.[24] Coluzzi and colleagues assessed 116 patients at baseline and up to 3 years postoperatively and found statistically significant improvements in physical, role, emotional, and social functioning scales ($P < 0.001$); similar improvements were observed in cognitive functioning ($P < 0.007$). Considering symptomatic scales, statistically significant improvements were seen in fatigue, nausea and vomiting, pain, insomnia, appetite loss, and constipation ($P < 0.001$).[20]

Waage and colleagues had a median follow-up time of 19.5 months for the 60 patients they studied; compared with baseline characteristics, global health was reported to have significantly increased, with pain, nausea, and appetite loss having the greatest reported improvements ($P < 0.05$). All other domains included in the assessment (fatigue, insomnia, and constipation) similarly improved, in addition to physical, role, emotional, cognitive, and social functioning scales ($P < 0.05$).[10]

Takaki et al[21] assessed 5 patients using the QLQ-C30 and found no significant improvement in global health

TABLE 2. Patient Outcomes Across Various Scales Used to Analyze Pain and QoL Improvement

Scale used (number of studies)	Patient outcomes ($P < 0.05^*$, $P < 0.001^\dagger$)
Rand SF-36 (6 studies)	Physical component summary†
	Bodily pain†
	Role physical†
	Mental component summary†
Rand SF-12 (3 studies)	Physical component summary†
	Mental component summary*
QLQ-C30/QLQ-PAN 26 (4 studies)	Global health†
	Functional scales
	Physical functioning†
	Role functioning†
	Emotional functioning†
	Cognitive functioning†
	Social functioning†
	Symptom scales
	Pancreatic pain†
	Fatigue, nausea, vomiting†
McGill Pain Questionnaire (2 studies)	Pain†
Visual Analog Scale (4 studies)	Pain†
Izbicki Pain Score (1 study)	Pain*

*$P < 0.05$.
†$P < 0.001$.

status/QoL scores, although the averages did increase 1 year after TPIAT. The authors also observed increases in the average scores of the functional scales, including role, cognitive, emotional, and social functioning; these improvements were not significant.

European Organisation For Research And Treatment Of Cancer Core Quality of Life Questionnaire Pancreatic Cancer Module (QLQ-PAN 26)

The EORTC QLQ-PAN 26 and QLQ-C30 were both found to be reliable and valid assessments for QoL in CP patients, with patients across four countries endorsing their suitability.[25] The QLQ-PAN 26 functions as a symptom scale, in which lower scores indicate a better QoL. One study, totaling 116 patients, reported QoL outcomes using the QLQ-PAN 26.[20] Values were measured up to 3 years postoperatively. Statistically significant improvements ($P < 0.001$) were seen in pancreatic pain, bloating, digestive symptoms, indigestion, weight loss, future worries, and sexuality. Improvements were also seen in taste ($P = 0.009$), body image ($P = 0.004$), planning of activities ($P = 0.03$), and satisfaction with health care ($P = 0.004$).[20]

DISCUSSION

Chronic pancreatitis is a painful disease that can be refractory to multiple medical, endoscopic, and surgical interventions. TPIAT is a surgical intervention that may be used to manage CP definitively while transplanting islets to minimize long-term dependence on exogenous insulin. This study aimed to systematically review 12 articles investigating 1333 adult CP patients who underwent TPIAT for postoperative improvements in pain and QoL. We found significant improvements in QoL outcomes in 80% (8/10) of studies that assessed QoL, and significant reductions in pain in 83% (5/6) of studies that assessed pain outcomes.

A previous systematic review and meta-analysis published by Kempeeners et al[7] observed similar improvements in QoL outcomes after TPIAT; 5 studies utilizing the SF-12 (1 study) and SF-36 (4 studies) scales found significant improvements in physical and mental component summaries. Another recently published study by Barthold et al[26] also observed an improvement in QoL (PCS and MCS) after TPIAT, but postoperative scores were still lower than those of the average healthy adult in the United States. At the time of the systematic literature search, this study was not yet published, and therefore was not included in this systematic review. John and colleagues found that SF-12 physical component scores in CP patients were close to those of healthy individuals between 6 months and 1 year and more than 2 years after TPIAT; interestingly, mental component scores were close to or better than those of healthy patients at <6 months and between 6 months and 1 year after TPIAT, which differs from the findings of Barthold et al (2024).[19,26] However, it is important to clarify that John and colleagues did not report significance with these findings.

Takaki et al[21] observed no significant changes in symptom scales or global health/QoL within the EORTC QLQ-C30 questionnaire. They specify a decrease in digestive functioning, and no change or improvement in nausea, vomiting, or dyspnea symptom scores. The authors speculate that the decrease in digestive functioning may be a sequela of pancreatic resection or more frequent stools due to increased appetite after TPIAT.[21] Coluzzi and colleagues and Waage and colleagues both utilized the QLQ-C30 to assess postoperative outcomes, and both found significant improvements in global health/QoL and symptomatic scales, findings that differ from Takaki and colleagues. One possible explanation for this discrepancy in results is the small sample size within the Takaki et al[21] study; the authors only studied 5 patients over a 1-year follow-up period, while Coluzzi et al[20] and Waage et al[10] studied 116 and 60 patients over a 3-year and 20-month follow-up period, respectively.

In terms of pain control after TPIAT, our current analysis observed significant overall pain reduction in 83% of studies that assessed pain outcomes using the VAS, McGill Pain Questionnaire, and Izbicki pain score. Conversely, Zhang et al[27] report narcotic independence, a

TABLE 3. MINORS Risk of Bias Assessment for Included Studies

References	Clearly stated aim	Inclusion of consecutive patients	Prospective data collection	Endpoints appropriate to study aim	Unbiased assessment of study endpoint	Follow-up period appropriate to study aim	< 5% Lost to follow-up	Prospective calculation of study size	Adequate control group	Contemporary groups	Baseline equivalence of groups	Adequate statistical analysis	Total score
Chinnakotla et al[15]	2	2	2	2	1	2	2	0	2	1	1	2	18
Coluzzi et al[20]	2	2	2	2	1	2	2	0					13
Dorlon et al[12]	2	2	2	2	1	2	1	0					12
Dunderdale et al[18]	2	2	2	2	1	2	1	0	2	1	1	2	18
Garcea et al[16]	2	2	1	2	1	2	1	0	2	1	1	1	15
Georgiev et al[13]	2	2	2	2	1	1	1	0					11
Gruessner et al[11]	2	2	1	2	1	2	2	0	2	2	1	1	18
John et al[19]	2	2	1	2	1	1	1	0					11
Morgan et al[17]	2	2	2	2	1	2	0	0					11
Takaki et al[21]	2	2	2	2	1	2	2	0					13
Waage et al[10]	2	2	2	2	1	2	1	0					12
Wilson et al[14]	2	2	2	2	1	1	1	0					11

different tool for assessing pain, between 14% and 100% in their systematic review of 1024 patients. The authors explain the heterogeneity of narcotic independence in their review as possibly being due to differences in pain sensitivity across patients.[27] Given that CP is a painful disease that often requires long-term use of narcotics pre-TPIAT, patient sensitivity to pain is wildly variable, particularly across large populations. As such, they assert that narcotic independence may not be the most accurate reflection of pain post-TPIAT.[27] Our review, for this reason, only included and analyzed pain outcomes from studies in which a validated scale such as the VAS was used.

Beyond TPIAT, other interventions for painful CP exist; D'Haese et al[28] explain that celiac ganglion nerve blocks, performed using anesthetics or steroids, may be used to decrease pancreatic pain. However, the authors assert that continued pain relief was only achieved in 10% of patients at 24-week follow-up.[28] Our review found much more promising results, with significant pain reduction in the analyzed patient populations after at least a 1-year follow-up. In terms of QoL improvement, pancreatic enzyme replacement therapy (PERT) is a method of restoring exocrine pancreatic function in patients with insufficiency, such as CP patients, and TPIAT patients are placed on PERT to supplement exocrine pancreatic enzymes.[29] de la Iglesia-García et al,[29] in their systematic review, found significant improvement in QoL after PERT in CP; however, the maximum period of follow-up was 2 months, indicating the need for future studies to assess for long-term efficacy. Within our review, TPIAT improved QoL significantly, with at least 1 year of follow-up across included studies, indicating that the combination of these interventions may be more efficacious over longer follow-up periods.

This study must be considered in light of the following limitations. The main limitation within this review is the level of heterogeneity across included studies; given the differences in methodology, particularly in terms of the type of pain/QoL scale used to assess outcomes or follow-up periods, we were unable to perform a meta-analysis on included data. Further, none of the included studies were randomized controlled trials (RCTs), and there is a risk of bias in the interpretation of our findings. The above limitations should be considered when interpreting our results; however, this study provides an updated and informative insight into the ongoing research surrounding TPIAT for CP, with validated measures of pain and QoL used to assess the efficacy of this procedure. Although our review indicates that TPIAT is efficacious in improving pain/QoL in CP patients, TPIAT cannot be recommended as a first-line standard of care for CP, given its high-risk profile and need for a multidisciplinary approach with careful patient evaluation. Future systematic reviews investigating TPIAT and CP should assess predictors of successful outcomes, such as islet mass harvested/transplanted, as well as explore the efficacy of TPIAT across different patient subgroups, including those with different etiologies of CP or varying degrees of pancreatic dysfunction.

CONCLUSION

TPIAT is a promising procedure that has been shown to potentially mitigate diabetic complications and preserve secretory beta-cell function, while improving pain and QoL in CP patients. Our findings suggest that TPIAT significantly improves pain and physical/mental quality of life outcomes for CP patients. We found improvement in postoperative QoL outcomes in 80% of the included studies and significant overall pain reduction in 83% of the studies. Although we were able to provide evidence for significant QoL and pain improvement after TPIAT, future studies should investigate how specific etiologies of CP and different patient populations may benefit most from TPIAT.

Appendix A

Pubmed: 05/08/2024 - 3,147 results

((pancreatectomy OR "pancreatectomy acute pancreatitis" OR "partial pancreatectomy" OR "total pancreatectomy" OR pancreatitis OR "chronic pancreatitis" OR pancreas OR "pancreatic tumor") AND (autoislet OR "autoislet transplant" OR "autoislet transplantation" OR "islet transplant" OR islet)) AND ("Pain"[MeSH Terms] OR "Quality of Life"[MeSH Terms] OR "postoperative pain" OR "quality of life" OR pain OR "pain scores" OR "Health-Related Quality Of Life" OR "Health Related Quality Of Life" OR "functional outcomes" OR outcomes)

Embase: 05/08/2024 - 7,902 results

(pancreatectomy OR "pancreatectomy acute pancreatitis" OR "partial pancreatectomy" OR "total pancreatectomy" OR pancreatitis OR "chronic pancreatitis" OR pancreas OR "pancreatic tumor") AND (autoislet OR "autoislet transplant" OR "autoislet transplantation" OR "islet transplant" OR islet) AND ("postoperative pain" OR "quality of life" OR pain OR "pain scores" OR "Health-Related Quality Of Life" OR "Health Related Quality Of Life" OR "functional outcomes" OR outcomes)

Cochrane Central Register of Controlled Trials (CENTRAL): 05/08/2024 - 6 results

(pancreatectomy OR pancreatectomy acute pancreatitis OR partial pancreatectomy OR total pancreatectomy OR pancreatitis OR chronic pancreatitis OR pancreas OR pancreatic tumor) AND (autoislet OR autoislet transplant OR autoislet transplantation OR islet transplant OR islet) AND (postoperative pain OR quality of life OR pain OR pain scores OR Health-Related Quality Of Life OR Health Related Quality Of Life OR functional outcomes OR outcomes)

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