

Cystectomy for Patients With Hunner-Type Interstitial Cystitis at a Tertiary Referral Center in Japan

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Abstract

Cystectomy is an ultimate treatment option for patients with end-stage Hunner-type interstitial cystitis (HIC). However, pertinent information regarding this procedure such as optimal candidate selection, surgical procedures, possible complications, and treatment prognosis, is limited owing to its extremely low prevalence. We report outcomes of 17 cystectomies for end-stage HIC patients at a tertiary referral center in Japan over a period of 20 years, including partial cystectomy with augmentation ileocystoplasty (PC–CP, 4) and total cystectomy with ileal conduit (TC–IC, 13). Postoperative events including changes in symptoms and quality of life (QOL), related complications, and overall satisfaction were examined. Pain persisted in three PC–CP patients while completely resolved in all TC–IC patients. QOL improved significantly in TC–IC but not in PC–CP patients. Two PC–CP patients required clean intermittent catheterization due to voiding dysfunction. Two TC–IC patients developed stricture of ureteroileal anastomosis, resulting in permanent placement of a ureteral stent or nephrostomy. Satisfaction rate was significantly higher in TC–IC than in PC–CP patients (76.9% vs 25.0%, $p < 0.05$). Despite the limited number of cases, this study demonstrates that TC–IC provides highly reliable pain relief and improves QOL in end-stage HIC patients.

Introduction

Hunner-type interstitial cystitis (HIC) is a chronic inflammatory disease of the urinary bladder of unknown etiology, clinically characterized by persistent pelvic pain and lower urinary tract symptoms such as urinary frequency and urgency.¹ The progressive nature of this disease in some patients can result in severe bladder contraction, leading to incredibly increased urinary frequency and/or urinary leakage. Associated vesicoureteral reflux (VUR) may cause hydronephrosis, recurring pyelonephritis, or irreversible renal dysfunction. Cystectomy may be the ultimate treatment for patients with end-stage HIC, as described in clinical guidelines for patients with interstitial cystitis/bladder pain syndrome (IC/BPS).^{1 2 3} Because this procedure is rarely performed, however, detailed information on cystectomy, such as candidate selection, surgical procedures, possible complications, and treatment prognosis, is limited. The present study describes our 20 years' experience with 17 patients who underwent subtrigonal partial cystectomy with augmentation ileocystoplasty (PC–CP) or total cystectomy with ileal conduit (TC–IC) for end-stage HIC.

Methods

Ethics statement

The Institutional Review Board of the University of Tokyo approved the study protocol, including the use of an opt-out methodology to obtain informed consent (approval no. 3124). Participants were informed about the study using generally accessible contact information. Written informed consent was provided by participants who chose to take part in this study. All procedures followed appropriate guidelines.

Patients

The clinical database of the University of Tokyo Hospital was retrospectively reviewed to identify patients with end-stage HIC who underwent PC–CP or TC–IC between 2002 and 2020. Diseases were diagnosed and classified according to East Asian and European clinical guidelines for IC/BPS.¹¹⁸

Surgical procedures

Cystectomy was considered for patients with end-stage HIC if their QOL was markedly impaired or if they had experienced significant complications in the upper urinary tract, such as persistent hydronephrosis and/or recurrent (defined as three times or more per year) pyelonephritis. The former was characterized by intractable and persistent bladder pain, extraordinarily frequent urination, or continued urinary leakage that could not be controlled by an indwelling urethral catheter. A thorough personal consultation was performed prior to surgery. Patients were informed of related risks, such as persistence/recurrence of symptoms, the need for CIC, the irreversibility of the procedure and body image of the stoma, and the risk of perioperative complications. All patients provided informed consent for cystectomy and the procedure, PC–CP or TC–IC.

The PC–CP procedure involved excision of the bladder wall while preserving the bladder neck and trigonal area with bladder augmentation using ileal segments. The TC–IC procedure consisted of simple cystectomy and ileal conduit formation, with urethrectomy in male patients, as indicated. TC–NB was not attempted because of the higher risks of complications and postoperative CIC.

Postoperative complications in both groups were monitored by assessing symptoms, by performing blood tests and urinalysis, by urine culture, by measurements of post-void residual urine, and by ultrasound scanning. Postoperative complications were managed by additional interventions, as needed. All operations were performed using an open approach by one of the four specialized urologists (YA, ANi, YI, YH) at our facility.

Assessment and evaluation

Symptoms were assessed using an 11-point numerical rating of pain intensity, with 0 indicating no pain and 10 indicating the worst pain imaginable. QOL scores were measured on a 7-grade QOL scale derived from the International Prostate Symptom Score, with 0 indicating an excellent QOL and 6 indicating a terrible QOL. OSSI/OSPI indices were assessed pre- and postoperatively in patients who underwent PC–CP alone, as questions on voiding frequency and urgency are inapplicable to patients who undergo TC–IC. Patients were closely monitored for anticipated complications, such as voiding difficulty necessitating CIC, hydronephrosis, and pyelonephritis. Hydronephrosis was graded according to the Society for Fetal Urology ultrasound grading system.¹⁹ Patients' overall satisfaction with surgical outcomes was assessed using a yes-or-no question 1 year after surgery or when complications were stabilized.

Statistical analysis

Symptom parameters before and after surgery in each group were compared by Wilcoxon signed rank tests, whereas symptom parameters in the two groups were compared by Wilcoxon rank sum tests. Categorical variables were compared using Fisher's exact tests. All statistical analyses were performed using JMP® software, version 14 (SAS Institute, Cary, NC, USA), with *P*-values <0.05 considered statistically significant.

Results

A retrospective review of the clinical database of our institution identified 17 patients with end-stage HIC who underwent cystectomy between 2002 and 2020. Four patients, three men and one woman, underwent PC–CP, whereas 13 patients, nine women and four men, underwent TC–IC. Treatments before cystectomy included oral analgesic drugs, such as nonsteroidal anti-inflammatory drugs (NSAIDs), pregabalin, and opioids; anti-cholinergic agents; beta-3 adrenoceptor agonists; tricyclic antidepressants such as amitriptyline; anti-allergic agents such as suplatast tosilate, hydroxyzine, and cimetidine; oral steroids; intravesical instillation, including with dimethyl sulfoxide, alkalized heparin and lidocaine, and botulinum toxin; and electrocautery of Hunner lesions with hydrodistension.

The pre- and perioperative demographic characteristics of these patients are shown in Table 1. Mean overall follow-up time was 4.7 ± 3.6 years overall. At the time of surgery, patients undergoing PC–CP were significantly younger (mean age, 53.5 ± 12.9 years) than those with TC–IC (67.0 ± 10.9 years). Duration of illness, O'Leary and Sant's Symptom (OSS) and Problem (OSPI) scores, pain intensity, quality of life (QOL) scores, daytime frequency, nocturia, maximum voided volume (MVV) on the frequency volume chart, maximum bladder capacity (MBC) at the last hydrodistension (under a pressure of 80 cm H₂O), and the total number of previous sessions of Hunner lesion electrocautery were comparable in these two groups. Operation time, blood loss, and transfusion rate were higher, however, in the TC–IC than in the PC–CP group.

Table 1
Demographic and clinical characteristics of patients who underwent cystectomy for Hunner-type interstitial cystitis

	PC-CP	TC-IC	<i>p</i> -value
No. of patients (female/male)	4 (1/3)	13 (9/4)	
Age at surgery (y)	53.5 ± 12.9 [35–65]	67.0 ± 10.9 [39–79]	< 0.05*
Duration of illness (y)	10.0 ± 8.2 [2–21]	8.3 ± 4.9 [3–18]	0.78
Postoperative follow-up period (y)	5.3 ± 5.9 [1–12]	4.5 ± 3.2 [1–11]	0.95
OSSI	17.3 ± 2.5 [15–20]	15.1 ± 3.8 [8–19]	0.34
OSPI	14.1 ± 2.0 [10–16]	13.1 ± 3.8 [4–16]	0.99
Pain scale [‡]	8.5 ± 1.0 [8–10]	7.4 ± 2.1 [2–9]	0.45
QOL score	5.5 ± 0.6 [5–6]	5.7 ± 0.9 [3–6]	0.25
Daytime frequency	22.3 ± 6.8 [17–30]	18.0 ± 3.9 [13–25]	0.24
Nocturia	6.3 ± 6.7 [2–14]	4.4 ± 1.5 [2–8]	0.57
Maximum voided volume (mL)	87.5 ± 22.2 [60–110]	69.2 ± 23.9 [30–110]	0.18
Maximum bladder capacity at the last hydrodistension (mL)	162.5 ± 85.0 [80–250]	237.5 ± 161.1 [100–300]	< 0.33
No. of previous electrocautery sessions for Hunner lesions	3.3 ± 1.0 [2–4]	3.8 ± 2.0 [1–8]	0.62
Grade of hydronephrosis (no. of pts) [¶]			0.58
Grade 0	3	6	
Grade 1	0	1	
Grade 2	1	2	

Results are reported as mean ± SD [range], unless otherwise indicated.

Abbreviations: PC-CP, supratrigonal partial cystectomy with ileocystoplasty; TC-IC, total cystectomy with ileal conduit; OSSI, O'Leary and Sant's Symptom Index; OSPI, O'Leary and Sant's Problem Index; QOL, quality of life.

**p* < 0.05, statistically significant.

[‡]Assessed using an 11-point pain intensity numerical rating scale from 0, indicating no pain, to 10, indicating the worst pain imaginable.

[¶]Classified using the Society for Fetal Urology ultrasound grading system of hydronephrosis (ref. 19).

	PC-CP	TC-IC	<i>p</i> -value
Grade 3	0	2	
Grade 4	0	2	
Increases in serum creatinine level (no. of pts)	0	5	0.26
Operation time (min)	261.0 ± 48.1 [220–314]	401.8 ± 70.1 [328–531]	< 0.01*
Blood loss (mL)	886.7 ± 496.9.1 [580–1460]	1795.0 ± 1024.0 [555–3615]	0.23
Transfusion (no. of pts)	0	7	< 0.05*
Results are reported as mean ± SD [range], unless otherwise indicated.			
Abbreviations: PC-CP, supratrigonal partial cystectomy with ileocystoplasty; TC-IC, total cystectomy with ileal conduit; OSSI, O’Leary and Sant’s Symptom Index; OSPI, O’Leary and Sant’s Problem Index; QOL, quality of life.			
* <i>p</i> < 0.05, statistically significant.			
‡Assessed using an 11-point pain intensity numerical rating scale from 0, indicating no pain, to 10, indicating the worst pain imaginable.			
¶Classified using the Society for Fetal Urology ultrasound grading system of hydronephrosis (ref. 19).			

Table 2 displays postoperative outcomes in these patients. Three (75%) of the four patients who underwent PC-CP experienced recurrent pain within 15 months after surgery, compared with none (0%) of the 13 patients who underwent TC-IC. Removal or preservation of the distal urethra was not associated with postoperative symptoms in men undergoing TC-IC (data not shown). Pain intensity and QOL scores were significantly improved in patients who underwent TC-IC, whereas pain intensity, QOL scores, and OSSI/OSPI scores were not significantly improved in patients who underwent PC-CP (Fig. 1). Three (75%) of the four patients in the PC-CP group started clean intermittent catheterization (CIC) within 18 months after surgery, two (Patient nos. 2 and 3) due to voiding dysfunction and one (Patient no. 1) due to recurrent severe pain during urine storage. Two patients who underwent TC-IC experienced stricture of the ureteroileal anastomosis with hydronephrosis and/or pyelonephritis: one (Patient no. 7) was managed by installation of a permanent ureteral stent, and the other (Patient no. 10) by nephrostomy. Preoperative Grade 2 hydronephrosis (without an increase in serum creatinine levels) resolved after surgery in one patient who underwent PC-CP. Seven patients in the TC-IC group had preoperative hydronephrosis, including one with Grade 1 and two each with Grades 2, 3, and 4), with five showing increased serum creatinine concentrations. Of these five patients, four showed normalization of creatinine levels after surgery, whereas one (Patient no. 10) developed postoperative ureteroileal

anastomosis stricture and required nephrostomy replacement. Satisfaction with overall surgical outcomes was significantly higher in the TC-IC than in the PC-CP group (76.9% vs. 25.0%, $p < 0.05$).

Table 2
Postoperative events

Patient no. (age, sex)	Procedure	Recurrent pain (mo) [†]	QOL score	Satisfaction	Complications/Note
1 (65, M)	PC-CP	Yes (15)	5	No	CIC (18 mo) [†]
2 (58, M)	PC-CP	Yes (3)	4	No	CIC (3 mo)
3 (35, F)	PC-CP	No	3	Yes	CIC (6 mo)
4 (56, M)	PC-CP	Yes (2)	6	No	None
5 (76, F)	TC-IC	No	0	Yes	None
6 (73, M)	TC-IC	No	1	Yes	None
7 (73, M)	TC-IC	No	5	No	Ureteroileal anastomosis (2 wk), ureteral stent replacement (6 mo), pyelonephritis (6 mo)
8 (64, M)	TC-IC	No	0	Yes	None
9 (73, M)	TC-IC	No	0	Yes	None
10 (69, F)	TC-IC	No	6	No	Pyelonephritis (15 mo), ureteroileal anastomosis (21 mo), nephrostomy replacement (36 mo)
11 (54, F)	TC-IC	No	0	Yes	None
12 (75, F)	TC-IC	No	0	Yes	None
13 (65, F)	TC-IC	No	0	Yes	None
14 (39, F)	TC-IC	No	0	Yes	Adhesive ileus (14 d)

Abbreviations: PC-CP, supratrigonal partial cystectomy with ileocystoplasty; TC-IC, total cystectomy with ileal conduit; CIC, clean intermittent catheterization; QOL, quality of life.

[†]Time from surgery.

Patient no. (age, sex)	Procedure	Recurrent pain (mo) [†]	QOL score	Satisfaction	Complications/Note
15 (61, F)	TC-IC	No	0	Yes	None
16 (79, F)	TC-IC	No	0	Yes	None
17 (71, F)	TC-IC	No	1	Yes	None
Abbreviations: PC-CP, supratrigonal partial cystectomy with ileocystoplasty; TC-IC, total cystectomy with ileal conduit; CIC, clean intermittent catheterization; QOL, quality of life.					
[†] Time from surgery.					

Discussion

The present study reports outcomes in 17 consecutive patients who underwent cystectomy for end-stage HIC at a tertiary referral center for IC/BPS in Japan. Although TC-IC was a more invasive procedure and more likely to cause postoperative complications than PC-CP, TC-IC was able to achieve almost complete pain relief and a higher rate of patient satisfaction.

Endoscopic electrocautery of Hunner lesions with bladder hydrodistension is regarded as the most promising treatment for HIC.^{4 5} However, intractable bladder pain and associated lower urinary tract symptoms may persist even after repeated sessions of electrocautery.⁶ Some patients progressively develop contracted bladder, which frequently induces VUR and/or hydronephrosis. Cystectomy may be an option for these patients with end-stage HIC.^{1 2 3} To date, however, optimal patient selection and standardized surgical procedures have not been established.

Our center regards patients with markedly impaired QOL resulting from intractable bladder pain or extremely severe bladder storage symptoms, or upper urinary tract events such as VUR, persistent hydronephrosis, and recurrent pyelonephritis, as candidates for cystectomy. Because TC is likely to provide greater symptom relief than PC,^{7 8 9 10} we basically propose TC for the surgical approach of choice. For example, complete pain resolution was achieved by nine (90%) of 10 women after TC⁹, with a patient satisfaction rate > 77% despite the high complication rate (60%). By contrast, persistent bladder pain was experienced by eight (33%) of 24 patients⁷ and by six (75%) of eight patients⁸ after PC. Furthermore, persistent/recurrent pain was reported in five (17%) of 29 patients who underwent PC-CP, compared with none (0%) of six patients who underwent TC-IC.¹⁰ Meanwhile, several studies have found that PC-CP has modest success rates in patients with refractory IC/BPS.^{11 12 13} For example, PC-CP had a success rate of 80% in 40 patients with HIC, with five patients requiring CIC during a median

follow-up of 12.0 months.¹¹ A study of 17 patients who underwent TC and six who underwent PC with orthotopic bladder substitution using an ileocecal pouch (Mainz pouch ☒) found that none of the PC patients developed pain recurrence, compared with one TC patient who experienced persistent pain after surgery.¹² A recent meta-analysis reviewing 20 articles demonstrated that symptom improvement rates were 90.5% for TC overall (94.9% for TC with neo-bladder formation, TC–NB and 82% for TC and any diversion), 73.4% for PC–CP, and 63.4% for diversion alone.¹⁴ The overall complication rate was 26.5%, with TC–NB having the highest and TC–IC having the lowest complication rate.

In our facility, cystectomy was not performed in IC/BPS patients without Hunner lesions due to the low expectancy of success. A study reporting the outcomes of various reconstructive surgeries in patients with IC/BPS found that success rates were much higher in patients with HIC (> 80%) than in patients without Hunner lesions (23%).¹⁵ Moreover, PC–CP resulted in symptom resolution in all 10 HIC patients but in none of the three patients without Hunner lesions.¹⁶ Recent evidence revealed that HIC is a robust inflammatory disease of the bladder whereas other forms of IC/BPS that lack Hunner lesions are non-inflammatory disorders, potentially involving psychological and/or neuropathological conditions outside the bladder.¹⁷ Thus, cystectomy outcomes should favor HIC which affects the bladder.

The present study has several limitations, including its retrospective study design and small sample size. In particular, this study was essentially limited to patients who underwent TC–IC, as only four underwent PC–CP and none underwent neo-bladder formation. Further studies are needed to determine the surgical outcomes of cystectomy for refractory IC/BPS and to identify factors prognostic of success, thereby optimizing patient selection and surgical procedures.

In conclusion, TC–IC provided highly reliable pain relief and patient satisfaction in patients with end-stage HIC. Further studies are warranted to identify appropriate candidates and optimal surgical procedures for patients with refractory IC/BPS.

Abbreviations

BPS = bladder pain syndrome

CIC = clean intermittent catheterization

ESSIC = International Society for the Study of BPS

HIC = Hunner type interstitial cystitis

IC = interstitial cystitis

MVV = maximum voided volume

MBC = maximum bladder capacity

NSAID = nonsteroidal anti-inflammatory drug

OSSI/OSPI = O'Leary and Sant's Symptom and Problem Indices

QOL = quality of life

PC-CP = supratrigonal partial cystectomy with ileocystoplasty

TC-IC = total cystectomy with ileal conduit

TC-NB = total cystectomy with neo-bladder

VUR = vesicoureteral reflux

Declarations

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Disclosure statement

All authors declare no conflicts of interest, financial or otherwise, regarding this study.

Consent to participate

Participants were informed about the study using generally accessible contact information, and written informed consent was obtained from participants who chose to participate.

Consent for publication

All authors consent to the publication of the manuscript, should the article be accepted by the Editor-in-Chief upon completion of the refereeing process. All participants consent to the publication of the study in a journal, website, or other form of publication.

Availability of data and material

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author contributions

YA and ANi collected the data. YA, ANi, YI, and YH performed the operations. YA and ANi analyzed the data. YA and YH wrote the manuscript. YI, AN, YS, YY, HK, and YH revised the manuscript critically. YA and YH provided final approval of the version to be submitted.

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Figures

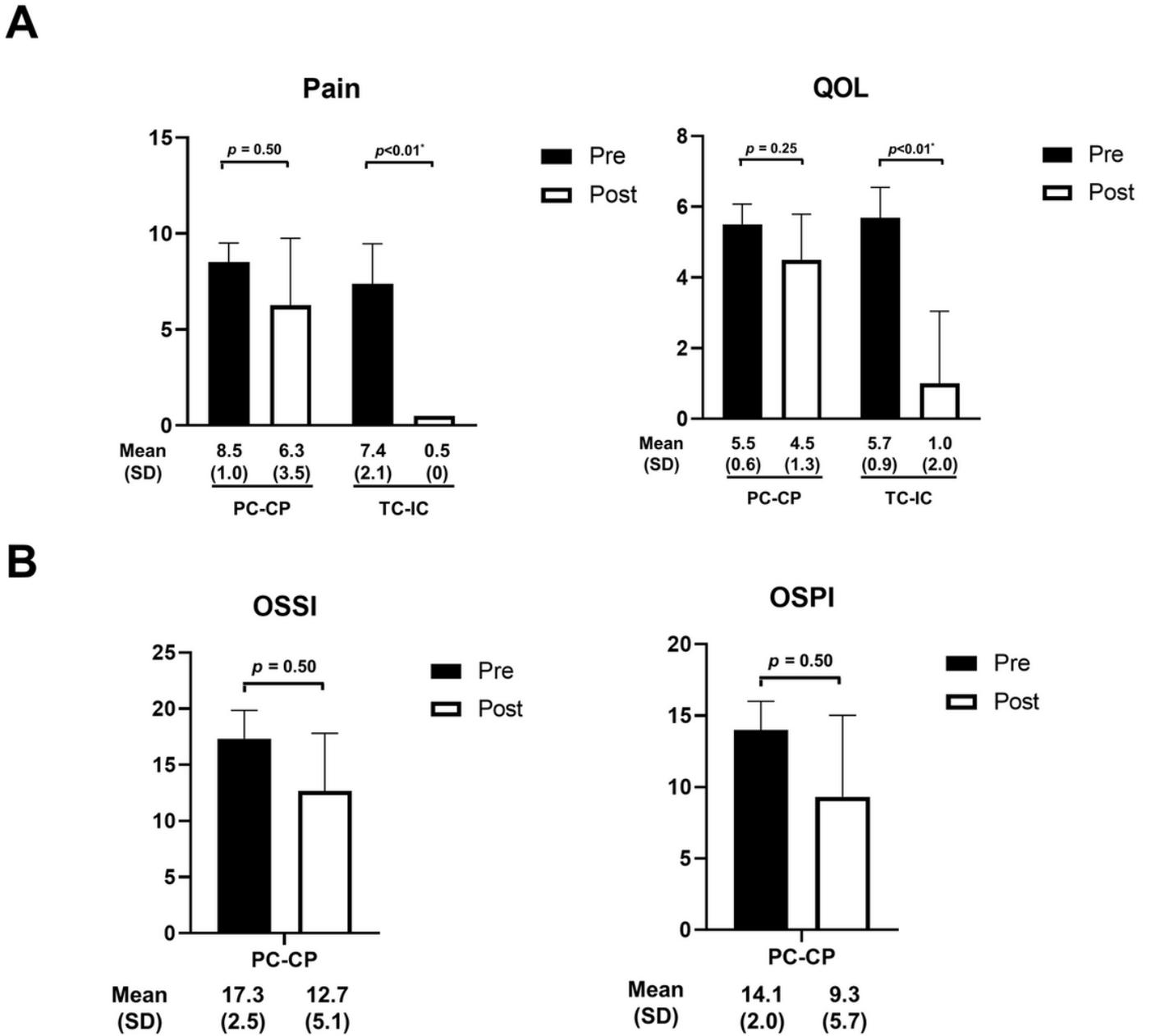


Figure 1

Effects of TC-IC and PC-CP on patient outcomes. A: Changes in pain intensity and QOL scores. * $p < 0.05$ by Wilcoxon signed rank test. B: Changes in OSSI/OSPI scores in patients who underwent PC-CP.