Impact of Perioperative Pregabalin on Early Rehabilitation Milestones, Pain Control, and Functional Outcomes After Arthroscopic ACL Reconstruction: A Propensity-Matched Retrospective Cohort Study

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Abstract

Background: Effective postoperative pain management is essential for successful rehabilitation following arthroscopic anterior cruciate ligament (ACL) reconstruction. **Objective:** To evaluate the impact of perioperative pregabalin on early rehabilitation milestones, postoperative pain control, and functional outcomes following arthroscopic ACL reconstruction using a propensity score-matched retrospective cohort. **Methods:** This propensity score-matched retrospective cohort study was conducted at Sri Siddhartha Medical College and Hospital, Tumkur from Feb 2024 to Feb 2026 and included 190 patients undergoing primary arthroscopic ACL reconstruction. Patients receiving perioperative pregabalin were matched 1:1 with patients receiving standard perioperative analgesia without pregabalin. **Results:** Baseline demographic and surgical characteristics were comparable between the two matched groups. Patients receiving pregabalin demonstrated significantly lower postoperative pain scores at 24 hours (3.4 ± 1.2 vs. 5.1 ± 1.4; $p<0.001$) and reduced opioid consumption (18.6 ± 7.4 vs. 29.7 ± 9.8 mg; $p<0.001$). Straight-leg raising was achieved earlier (19.4 ± 6.2 vs. 27.8 ± 8.6 hours; $p<0.001$), while independent ambulation within 24 hours (83.2% vs. 61.1%; $p=0.001$) and full weight-bearing within 48 hours (76.8% vs. 53.7%; $p=0.001$) were more frequent. Hospital stay was shorter among patients receiving pregabalin (1.8 ± 0.6 vs. 2.4 ± 0.8 days; $p<0.001$). Functional recovery was significantly better, with greater knee flexion at two weeks (108.5 ± 11.4° vs. 97.8 ± 12.6°; $p<0.001$), higher Lysholm scores (89.6 ± 6.8 vs. 84.1 ± 8.3; $p<0.001$), higher IKDC scores (84.7 ± 7.5 vs. 79.3 ± 8.1; $p<0.001$), earlier return to daily activities (4.8 ± 1.3 vs. 6.1 ± 1.6 weeks; $p<0.001$), and greater patient satisfaction (92.6% vs. 77.9%; $p=0.005$). **Conclusion:** Perioperative pregabalin is associated with superior postoperative analgesia, reduced opioid requirements, faster rehabilitation, and improved short-term functional outcomes following arthroscopic ACL reconstruction.

Keywords: Anterior cruciate ligament reconstruction; pregabalin; arthroscopy; multimodal analgesia; rehabilitation

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Introduction

Anterior cruciate ligament (ACL) reconstruction is one of the most frequently performed orthopedic procedures to restore knee stability, enhance functional performance and to allow return to sports after an ACL rupture [1]. New minimally invasive surgical techniques and faster rehabilitation protocols have not completely eliminated postoperative pain, which continues to be a significant barrier to early mobilization, rehabilitation and functional recovery [2]. Poorly managed postoperative pain can result in delayed weight-bearing, lack of quadriceps muscle activation, longer hospital stays, higher opioid usage, and poorer patient satisfaction and long-term clinical outcomes [3]. Since arthroscopic ACL reconstruction, multimodal analgesia has been the basis for perioperative pain management. Multimodal pain management is a strategy that uses more than one mechanism of drug action to achieve greater pain relief and also reduce opioid-related

side effects, including nausea, vomiting, sedation, constipation, and respiratory depression [5]. Pregabalin is one of the several adjunctive analgesics which has gained a lot of interest because of its ability to modulate the release of neurotransmitters through modulation of calcium channels, which leads to a reduction in central sensitization and postoperative hyperalgesia [6]. Pregabalin is a structural analogue of gamma-aminobutyric acid (GABA) which has been selectively shown to bind to the α2δ subunit of voltage-gated calcium channels in the central nervous system [7]. Pregabalin does not directly bind to GABA receptors, but it does decrease the release of other excitatory neurotransmitters that play a role in pain transmission, leading to lower pain intensity after surgery and lower consumption of opioid analgesics [8]. Pregabalin use perioperatively has been suggested to enhance analgesia following orthopaedic surgery in several clinical trials but their effects have been inconsistent depending on the surgical procedures, dose and timing of use [9]. Focusing on early rehabilitation following ACL reconstruction can be important to restore knee range of motion, decrease joint stiffness, prevent quadriceps muscle loss and encourage return to functional activities [10]. Proper achievement of early rehabilitation milestones such as independent ambulation, full weight-bearing, straight leg raising and adequate knee flexion are strongly correlated with the long-term function [11]. Postoperative pain management can aid in participation with rehabilitation by minimizing pain that occurs during the range of motion, and that this may make rehabilitation more successful due to patient confidence [12].

The current methods used to assess functional recovery after ACL reconstruction are based on validated outcome measures including the Lysholm Knee Score, International Knee Documentation Committee (IKDC) score, Tegner Activity Scale, and Knee injury and Osteoarthritis Outcome Score (KOOS) [13]. These include the assessment of knee stability, pain, symptoms, daily activities, sports participation, and quality of life. Optimisation of peri-operative pain control can thus be expected to not only improve early recovery from surgery but also medium-term functional outcome [14]. Retrospective observational studies can suffer from treatment-selection bias as patients using adjunctive analgesics might be systematically different from the patients using standard analgesics [15].

Objective

To evaluate the impact of perioperative pregabalin on early rehabilitation milestones, postoperative pain control, and functional outcomes following arthroscopic ACL reconstruction using a propensity score-matched retrospective cohort.

Methodology

This was a propensity score–matched retrospective cohort study conducted at Sri Siddhartha Medical College and Hospital, Tumkur from Feb 2024 to Feb 2026 including 190 patients. Patients aged 18–50 years with isolated ACL rupture confirmed clinically and by magnetic resonance imaging (MRI), who underwent primary arthroscopic ACL reconstruction using either hamstring tendon or bone–patellar tendon–bone autografts, were included. Patients who completed the standardized postoperative rehabilitation protocol and had complete perioperative records with a minimum follow-up duration of six months were considered eligible. Patients undergoing revision ACL reconstruction, multi ligament knee injuries, associated fractures requiring fixation, severe cartilage defects (Outerbridge grade III–IV), inflammatory arthritis, chronic opioid use, neuropathic pain disorders, renal insufficiency, hepatic dysfunction, allergy or contraindication to pregabalin, incomplete medical records, or loss to follow-up were excluded.

Data Collection

After obtaining ethical approval, data were extracted from electronic medical records, anesthesia charts, operative notes, physiotherapy records, and outpatient follow-up files using a standardized data collection form. Patients were divided into two matched groups based on perioperative pregabalin administration. The pregabalin group received perioperative pregabalin as part of a multimodal analgesic protocol, whereas the control group received standard perioperative analgesia without pregabalin. Propensity score matching was performed using age, sex, body mass index, smoking status, graft type, associated meniscal procedures, preoperative functional score, and American Society of Anesthesiologists (ASA) physical status to minimize selection bias. Baseline variables included age, gender, body mass index, mechanism of injury, time from injury to surgery, graft type, concomitant meniscal injury, operative duration, tourniquet time, and preoperative functional scores. Primary outcomes included postoperative pain assessed using the Visual Analog Scale (VAS) at 6, 12, 24, and 48 hours, cumulative opioid consumption during the first 48 postoperative hours, and achievement of early rehabilitation milestones, including time to straight-leg raise, independent ambulation, full weight-bearing, active knee flexion of 90°, and hospital discharge. Secondary outcomes included postoperative nausea

and vomiting, dizziness, excessive sedation, rehabilitation compliance, knee range of motion, Lysholm Knee Score, International Knee Documentation Committee (IKDC) subjective score, Tegner Activity Scale, time to return to sports, and postoperative complications including arthrofibrosis, wound infection, deep vein thrombosis, and graft failure.

Statistical Analysis

Data were analyzed using SPSS version 26.0. Continuous variables were expressed as mean ± standard deviation, whereas categorical variables were presented as frequencies and percentages. Propensity score matching was performed using one-to-one nearest-neighbor matching without replacement with a caliper width of 0.2 standard deviations of the propensity score. Baseline balance between matched groups was assessed using standardized mean differences. Independent *t*-tests were used to compare continuous variables, while Chi-square or Fisher's exact tests were used for categorical variables. Statistical significance was defined as a p-value ≤0.05.

Results

Both groups were well matched at baseline. Mean age, gender distribution, BMI, sports-related injury, meniscal injury, graft type, operative time, preoperative Lysholm score, and IKDC score were comparable between the pregabalin and control groups, with all p-values >0.05.

Table 1: Baseline Characteristics of Propensity-Matched Patients Undergoing Arthroscopic ACL Reconstruction (N = 190)

Variable	Pregabalin Group (n=95)	Control Group (n=95)	p-value
Age (years), Mean ± SD	28.9 ± 6.8	29.4 ± 7.1	0.62
Male, n (%)	71 (74.7)	69 (72.6)	0.74
Body Mass Index (kg/m²), Mean ± SD	25.3 ± 3.2	25.6 ± 3.5	0.55
Sports-related Injury, n (%)	63 (66.3)	60 (63.2)	0.66
Associated Meniscal Injury, n (%)	38 (40.0)	35 (36.8)	0.65
Hamstring Autograft, n (%)	74 (77.9)	72 (75.8)	0.73
Operative Time (minutes), Mean ± SD	82.6 ± 16.3	84.1 ± 15.7	0.52
Preoperative Lysholm Score	58.4 ± 9.7	57.8 ± 10.1	0.68
Preoperative IKDC Score	49.6 ± 8.9	48.8 ± 9.3	0.54

Pregabalin was associated with better early pain control and rehabilitation. The pregabalin group had lower 24-hour VAS pain scores (3.4 ± 1.2 vs. 5.1 ± 1.4; p<0.001), reduced opioid consumption (18.6 ± 7.4 vs. 29.7 ± 9.8 mg; p<0.001), earlier straight-leg raise (19.4 ± 6.2 vs. 27.8 ± 8.6 hours; p<0.001), higher ambulation within 24 hours (83.2% vs. 61.1%; p=0.001), and shorter hospital stay (1.8 ± 0.6 vs. 2.4 ± 0.8 days; p<0.001).

Table 2: Comparison of Early Postoperative Pain Control and Rehabilitation Milestones

Variable	Pregabalin Group (n=95)	Control Group (n=95)	p-value
VAS Pain Score (24 hours), Mean ± SD	3.4 ± 1.2	5.1 ± 1.4	<0.001
Total Opioid Consumption (Morphine Equivalent, mg), Mean ± SD	18.6 ± 7.4	29.7 ± 9.8	<0.001
Time to Straight-Leg Raise (hours), Mean ± SD	19.4 ± 6.2	27.8 ± 8.6	<0.001
Independent Ambulation Within 24 Hours, n (%)	79 (83.2)	58 (61.1)	0.001
Full Weight-bearing Within 48 Hours, n (%)	73 (76.8)	51 (53.7)	0.001
Hospital Stay (days), Mean ± SD	1.8 ± 0.6	2.4 ± 0.8	<0.001

Functional recovery was better in the pregabalin group. Knee flexion at 2 weeks was higher (108.5 ± 11.4° vs. 97.8 ± 12.6°; p<0.001), with better 3-month Lysholm scores (89.6 ± 6.8 vs. 84.1 ± 8.3; p<0.001) and IKDC scores (84.7 ± 7.5 vs. 79.3 ± 8.1; p<0.001). Return to daily activities was earlier (4.8 ± 1.3 vs. 6.1 ± 1.6 weeks; p<0.001), and satisfaction was higher (92.6% vs. 77.9%; p=0.005).

Table 3: Functional Outcomes and Postoperative Recovery

Variable	Pregabalin Group (n=95)	Control Group (n=95)	p-value
Knee Flexion at 2 Weeks (°), Mean ± SD	108.5 ± 11.4	97.8 ± 12.6	<0.001
Lysholm Score (3 Months), Mean ± SD	89.6 ± 6.8	84.1 ± 8.3	<0.001
IKDC Subjective Score (3 Months), Mean ± SD	84.7 ± 7.5	79.3 ± 8.1	<0.001
Return to Normal Daily Activities (weeks), Mean ± SD	4.8 ± 1.3	6.1 ± 1.6	<0.001
Arthrofibrosis, n (%)	4 (4.2)	9 (9.5)	0.15
Patient Satisfaction, n (%)	88 (92.6)	74 (77.9)	0.005

Absence of perioperative pregabalin independently predicted delayed ambulation (AOR=3.48, 95% CI: 1.72–7.03; p<0.001) and poor functional outcome (AOR=2.86, 95% CI: 1.36–6.02; p=0.006). Pain score >5, meniscal injury, opioid use >25 mg, and knee flexion <100° at 2 weeks were also significant predictors of delayed rehabilitation or poorer recovery.

Table 4: Multivariable Logistic Regression Analysis of Predictors of Delayed Rehabilitation and Poor Functional Outcome

Outcome	Predictor	Adjusted OR	95% CI	p-value
Delayed Independent Ambulation (>24 Hours)	No Perioperative Pregabalin	3.48	1.72–7.03	<0.001
	VAS Pain Score >5	2.91	1.44–5.88	0.003
	Associated Meniscal Injury	2.13	1.05–4.31	0.036
Poor Functional Outcome (Lysholm Score <85)	No Perioperative Pregabalin	2.86	1.36–6.02	0.006
	Opioid Consumption >25 mg	2.57	1.22–5.41	0.013

DiscussionThis retrospective study using a propensity score matched cohort design compared the use of perioperative pregabalin to the absence of this medication on postoperative pain, early rehabilitation, and functional recovery after arthroscopic ACL reconstruction. The results showed that peri-operative pregabalin use was effective in improving postoperative analgesia, decreasing opioid consumption, advancing rehabilitation milestones, improving functional outcomes and increasing patient satisfaction. The findings indicate that pregabalin is a component of multimodal analgesia that is effective in ACL reconstruction surgery. In order to compare demographic and clinical parameters in both the treatment groups, propensity score matching was used, and both groups had similar baseline parameters such as age, gender, body mass index, mechanism of injury, graft type, operative duration, and functional scores before surgery. Lack of significant pre-treatment differences increases the validity of comparisons due to less selection bias. Analogous previous studies have also shown that propensity scores are able to effectively control for differences in patient characteristics when comparing the effectiveness of perioperative analgesic interventions [16]. Patients that received pregabalin experienced significantly better postoperative pain control. The pregabalin group had significantly reduced opioid use (18.6 ± 7.4 vs. 29.7 ± 9.8 mg) and 24-hour VAS pain scores (3.4 ± 1.2 vs. 5.1 ± 1.4). Pregabalin has been consistently shown to lower pain intensity and opioid use after arthroscopic knee surgery by acting as an inhibitor of central sensitization and a down-regulator of nociceptive transmission in previous studies. Better pain control led to quicker attainment of early rehabilitation goals. Patients treated with pregabalin were able to perform straight leg raises significantly earlier (19.4 ± 6.2 vs. 27.8 ± 8.6 hours), and were able to walk independently more often within 24 hours (83.2% vs. 61.1%) and earlier in reaching full weight bearing (76.8% vs. 53.7%). From these improvements, there were significant reductions in the length of hospital stays (1.8 ± 0.6 days vs. 2.4 ± 0.8 days). Previous studies have also shown that this perioperative analgesia results in early mobilization, increased physiotherapy compliance and promotes earlier postoperative discharge after ACL reconstruction [17]. The improvement in functional recovery was also noticeably improved in patients taking pregabalin. Knee flexion at two weeks was greater (108.5 ± 11.4° vs. 97.8 ± 12.6°), while Lysholm (89.6 ± 6.8 vs. 84.1 ± 8.3) and IKDC scores (84.7 ± 7.5 vs. 79.3 ± 8.1) at three months were significantly higher. Patients who received pregabalin were also able to resume normal daily activities sooner (4.8 ± 1.3 weeks vs. 6.1 ± 1.6 weeks). Previous studies have also found the same positive results in early functional recovery, which eans patients are more able to participate in rehabilitation exercises and regain knee function with better pain control [18].

No significant differences were seen in arthrofibrosis (4.2% vs. 9.5%). But, the satisfaction level among the patients who were given pregabalin was much more high (92.6% vs. 77.9%). Studies have also shown that better postoperative pain management leads to higher levels of patient satisfaction and adherence to rehabilitation and recovery programs, and a better recovery experience [19]. Further, multivariate analysis revealed that lack of perioperative pregabalin was an independent risk factor for delayed independent ambulation, with an almost 3.5-fold increase in risk (AOR=3.48). Postoperative pain scores and associated meniscal injuries were also associated with delayed rehabilitation. Uncontrolled postoperative pain has been previously identified as being one of the major hindrances to early mobilization after arthroscopic knee surgery [20].

Limitations

This study has several limitations. First, its retrospective observational design may have introduced selection bias despite the use of propensity score matching to balance baseline characteristics between groups. Second, the study was conducted at a single center, which may limit the generalizability of the findings to other institutions with different surgical techniques, rehabilitation protocols, and patient populations. Variations in perioperative anesthetic management, physiotherapy compliance, and individual pain perception could also have influenced postoperative recovery. The dosage and timing of pregabalin administration were standardized within the institution but may differ from protocols used elsewhere. Additionally, long-term outcomes such as return to competitive sports, graft survival, radiographic progression, and quality of life beyond six months were not evaluated. Future multicenter prospective randomized controlled trials with extended follow-up are warranted to confirm the long-term benefits and safety of perioperative pregabalin following arthroscopic ACL reconstruction.

Conclusion

Perioperative pregabalin significantly improved postoperative pain control, reduced opioid consumption, accelerated achievement of early rehabilitation milestones, and enhanced functional recovery following arthroscopic ACL reconstruction. Patients receiving pregabalin demonstrated earlier straight-leg raising, independent ambulation, full weight-bearing, shorter hospital stay, improved knee range of motion, higher Lysholm and IKDC scores, and greater patient satisfaction. Absence of perioperative pregabalin independently predicted delayed rehabilitation and poorer functional outcomes.

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