

# Hyaluronic acid instillation following arthroscopic anterior cruciate ligament reconstruction: a double-blinded, randomised controlled study

Jackie YM Chau, WL Chan, SB Woo, SC Cheng, TM Wong, TK Wong, CH Yen, K Wong, WC Wong  
Department of Orthopaedics and Traumatology, Kwong Wah Hospital, Hong Kong

---

## ABSTRACT

**Purpose.** To assess the effect of hyaluronic acid instillation after arthroscopic anterior cruciate ligament (ACL) reconstruction for improving pain, range of movement, and function of the knee.

**Methods.** 28 men and 4 women underwent arthroscopic ACL reconstruction for isolated ACL rupture (partial or complete) and instability after recreational sports injury 2 to 120 months earlier. They were randomised to undergo arthroscopic ACL reconstruction followed by intra-articular viscosal instillation (13 men and 3 women) or arthroscopic ACL reconstruction alone (15 men and 1 woman). The knee injury osteoarthritis outcome score (for pain, symptoms, activities of daily living, sport and recreation function, and quality of life), range of movement, knee circumference, and analgesic use were assessed on days -1, 1, and 2, and weeks 2, 6 and 12.

**Results.** Patient demographics were similar at baseline. At postoperative days 1 and 2, all subscales

of the knee injury osteoarthritis outcome score (except for quality of life) were significantly higher in the viscosal group. At weeks 2, 6, and 12, improvement in both groups equalised. Knee swelling (change in knee circumference) was significantly less in the viscosal group at days 1 and 2 ( $p=0.009$  and  $p=0.038$ , respectively, Mann-Whitney  $U$  test). Only one patient in the viscosal group had a limited range of movement. No patient developed any adverse reaction.

**Conclusion.** Intra-articular viscosal instillation improved pain control and swelling 2 days after arthroscopic ACL reconstruction.

**Key words:** anterior cruciate ligament; arthroscopy; hyaluronic acid; synovial fluid; viscosal

---

## INTRODUCTION

After primary anterior cruciate ligament (ACL) reconstruction, 62 to 90% of patients achieve good-to-excellent long-term outcomes.<sup>1,2</sup> Nonetheless, complications of arthrofibrosis and post-arthroscopic

symptoms (pain, swelling, and impaired joint mobility) are common.<sup>1-3</sup> During arthroscopy, synovial fluid-containing hyaluronic acid is drained from the joint. In addition to its viscoelastic properties for lubrication and shock absorption, hyaluronic acid enables biological inhibition of arachidonic acid release, the matrix metalloproteinase pathway, and tissue nociceptors. Exogenous hyaluronic acid increases endogenous hyaluronic acid production.<sup>4-6</sup> Moreover, the macromolecular meshwork impedes the movement of inflammatory cells and mediators within the synovial fluid.<sup>6</sup> The biomechanical and histological effects of hyaluronic acid on ACL ligaments and bone-tendon healing have been reported in animal studies.<sup>7,8</sup> We therefore assessed the effect of hyaluronic acid instillation after arthroscopic ACL reconstruction for improving pain, range of movement, and function of the knee.

## MATERIALS AND METHODS

Between September 2009 and April 2010, 28 men and 4 women underwent arthroscopic ACL reconstruction for isolated ACL rupture (partial or complete) and instability after recreational sports injury 2 to 120 months earlier. Patients with (1) severe meniscal or chondral injury requiring repair, (2) concomitant injury of another ligament, or (3) osteoarthritis (Kellgren-Lawrence grade II, III or IV) of the knee were excluded. Informed consent from each patient was obtained.

Patients were randomised to undergo arthroscopic ACL reconstruction followed by intra-articular viscosal instillation (13 men and 3 women) or arthroscopic ACL reconstruction alone (15 men and 1 woman). Respectively, the mean patient ages were 27 (standard deviation [SD], 6) and 26 (SD, 7) years, the mean patient weights were 70 (SD, 15) and 70 (SD, 7) kg, the mean patient heights were 172 (SD, 8) and 175 (SD, 4) cm, and the mean intervals from injury to operation were 18 and 16 months.

All surgeries were performed or supervised by a senior arthroscopic surgeon. An upper thigh tourniquet was used. Under general anaesthesia, single-bundle reconstruction with a hamstring graft was performed using the transportal technique. Normal saline solution at room temperature was used as irrigation fluid via an arthroscopic pump. Endopearl and BioRCI screws were used for femoral fixation, whereas Biointrafix was used for tibial fixation. 8 patients in the viscosal group and 9 of the controls underwent partial meniscectomy (at least one third of the meniscus was retained). At the

end of the surgery, irrigation fluid was drained, and in the viscosal group, 10 ml of sodium hyaluronate 0.5% (viscosal) was instilled through an arthroscopic portal with a cannula. No additional local anaesthetic agents or intra-articular analgesics were given. Diclofenac SR 100 mg daily was allowed as rescue pain medication, and patients were instructed not to take additional analgesics or over-the-counter medication. Postoperatively, an ACL rehabilitation protocol was followed.

Patients were assessed pre- and postoperatively (on days -1, 1, 2, and weeks 2, 6, 12) by a higher trainee for (1) the knee injury osteoarthritis outcome score, which is a self-administered questionnaire for pain, symptoms, activities of daily living, sport and recreation function, and quality of life (scores range from 0 to 100 for each subscale; higher scores indicate better outcome); (2) knee swelling; (3) range of movement (limited or not limited); (4) knee circumference (measured at the patellar level at the broadest point); and (5) analgesic use (number of diclofenac tablets consumed).

Data were analysed using the non-parametric Mann-Whitney *U* test. A *p* value of <0.05 was considered statistically significant.

## RESULTS

Baseline demographics (age, sex, height, weight, sports participation) were not significantly different between viscosal and control groups, as was the baseline knee injury osteoarthritis outcome score. At postoperative days 1 and 2, all subscales of the knee injury osteoarthritis outcome score (except for quality of life) were significantly higher in the viscosal group. At weeks 2, 6, and 12, improvement in both groups equalised (Table). Analgesic use (number of diclofenac tablets consumed) was slightly lower in the viscosal group at all time points; no patient consumed analgesics after week 6. Knee swelling (change in knee circumference) was significantly less in the viscosal group on days 1 and 2 (*p*=0.009 and *p*=0.038, respectively, Mann-Whitney *U* test). Only one patient in the viscosal group had a limited range of movement. No patient developed any adverse reaction.

## DISCUSSION

Pain management (oral analgesics, femoral nerve block, intra-articular injections) enables early mobilisation and rehabilitation following ACL

**Table**  
**Comparison of the viscoseal and control groups**

Parameter	Mean±SD score		p Value (Mann-Whitney U test)
	Viscoseal group	Control group	
Knee injury osteoarthritis outcome score			
Symptoms			
Day 0	73.0±18.9	80.5±14.9	0.126
Day 1	71.7±17.9	53.6±26.6	0.065
Day 2	69.2±21.5	47.0±23.3	0.018
Pain			
Day 0	77.8±16.5	88.3±7.5	0.026
Day 1	74.1±21.6	49.8±27.0	0.024
Day 2	70.0±22.3	43.6±25.8	0.012
Week 2	61.5±21.1	59.1±14.6	0.780
Week 6	72.9±15.0	72.2±15.2	0.640
Week 12	82.6±15.9	81.2±10.1	0.890
Activities of daily living			
Day 0	89.5±9.4	95.5±5.1	0.023
Day 1	84.0±20.6	52.0±33.1	0.024
Day 2	78.6±21.6	45.1±29.9	0.007
Sports			
Day 0	53.4±21.1	58.3±15.7	0.563
Day 1	55.0±23.7	27.7±28.0	0.013
Day 2	49.7±26.4	15.8±23.9	0.003
Quality of life			
Day 0	44.1±19.4	48.0±24.0	0.498
Day 1	44.2±21.6	39.0±26.0	0.431
Day 2	41.8±21.0	33.7±25.6	0.184
Diclofenac use (no. of tablets)			
Day 1	0.44±0.51	0.75±0.45	0.136
Day 2	0.50±0.52	0.75±0.45	0.234
Week 2	0.94±1.23	2.45±3.4	0.968
Week 6	0.71±2.67	1.67±5.7	1.000
Week 12	0	0	-
Change in knee circumference (cm)			
Day 1	1.56±1.3	3.00±1.10	0.009
Day 2	1.63±1.5	2.63±0.95	0.038
Week 2	1.00±1.6	1.85±1.1	0.063
Week 6	0.64±1.82	1.46±1.9	0.108
Week 12	0.25±1.4	0.5±1.8	0.112
Full range of movement (No. of patients)			
Day 1	0	1	-
Day 2	1	0	-
Week 2	4	3	-
Week 6	12	14	-
Week 12	15	16	-

reconstruction.<sup>9-15</sup> Continuous femoral nerve block reduces pain within 48 hours,<sup>9</sup> but pain or knee function did not differ significantly from controls between day 7 and week 12.<sup>10,11</sup> Compared to the placebo group, those having femoral nerve block had better analgesia 4 hours after the operation.<sup>12</sup>

Intra-articular fentanyl/bupivacaine is as effective as femoral nerve block in the first 24 hours.<sup>13</sup> Nonetheless, in patients receiving intra-articular ropivacaine plus sufentanil, the pain score was inferior to that in patients receiving epidural or femoral nerve block.<sup>14</sup> Intra-articular injection of tenoxicam (a non-steroidal anti-inflammatory drug) also reduces analgesic consumption in the first 3 to 6 hours.<sup>15</sup>

Intra-articular viscoseal instillation improved

pain control and swelling 2 days after arthroscopic ACL reconstruction. This may be due to the anti-inflammatory property of hyaluronic acid, particularly in patients with symptomatic osteoarthritis.<sup>4</sup> During the first 4 weeks, patients with viscoseal following arthroscopic meniscectomy achieve better pain control and reduced analgesic use than controls do.<sup>16,17</sup> Nonetheless, the sample sizes in the 2 studies were small (40 and 56 patients). Our sample size was also small. Further large-scale, randomised controlled studies are required to support its clinical application (using cost-benefit analysis) and to compare therapeutic effects with spinal anaesthesia, femoral nerve block, intra-articular opioids, and anti-inflammatory drugs.

**REFERENCES**

1. Moller E, Weidenhielm L, Werner S. Outcome and knee-related quality of life after anterior cruciate ligament reconstruction: a long-term follow-up. *Knee Surg Sports Traumatol Arthrosc* 2009;17:786–94.
2. Moksnes H, Risberg MA. Performance-based functional evaluation of non-operative and operative treatment after anterior cruciate ligament injury. *Scand J Med Sci Sports* 2009;19:345–55.
3. Strum GM, Friedman MJ, Fox JM, Ferkel RD, Dorey FH, Del Pizzo W, et al. Acute anterior cruciate ligament reconstruction. Analysis of complications. *Clin Orthop Relat Res* 1990;253:184–9.
4. Waddell DD, Bert JM. The use of hyaluronan after arthroscopic surgery of the knee. *Arthroscopy* 2010;26:105–11.
5. Hempfling H. Intra-articular hyaluronic acid after knee arthroscopy: a two-year study. *Knee Surg Sports Traumatol Arthrosc* 2007;15:537–46.
6. Westrich G, Schaefer S, Walcott-Sapp S, Lyman S. Randomized prospective evaluation of adjuvant hyaluronic acid therapy administered after knee arthroscopy. *Am J Orthop (Belle Mead NJ)* 2009;38:612–6.
7. Yucel I, Karaca E, Ozturan K, Yildirim U, Duman S, Degirmenci E. Biomechanical and histological effects of intra-articular hyaluronic acid on anterior cruciate ligament in rats. *Clin Biomech (Bristol, Avon)* 2009;24:571–6.
8. Yagishita K, Sekiya I, Sakaguchi Y, Shinomiya K, Muneta T. The effect of hyaluronan on tendon healing in rabbits. *Arthroscopy* 2005;21:1330–6.
9. Williams BA, Kentor ML, Vogt MT, Irrgang JJ, Bottegal MT, West RV, et al. Reduction of verbal pain scores after anterior cruciate ligament reconstruction with 2-day continuous femoral nerve block: a randomized clinical trial. *Anesthesiology* 2006;104:315–27.
10. Williams BA, Dang Q, Bost JE, Irrgang JJ, Orebaugh SL, Bottegal MT, et al. General health and knee function outcomes from 7 days to 12 weeks after spinal anesthesia and multimodal analgesia for anterior cruciate ligament reconstruction. *Anesth Analg* 2009;108:1296–302.
11. Reuben SS, Sklar J. Preemptive multimodal analgesia for anterior cruciate ligament surgery. *Reg Anaesth Pain Med* 2002;27:225–6.
12. Wulf H, Lowe J, Gnutzmann KH, Steinfeldt T. Femoral nerve block with ropivacaine or bupivacaine in day case anterior cruciate ligament reconstruction. *Acta Anaesthesiol Scand* 2010;54:414–20.
13. Mayr H, Entholzer E, Hube R, Hein W, Weig TG. Pre- versus postoperative intraarticular application of local anesthetics and opioids versus femoral nerve block in anterior cruciate ligament repair. *Arch Orthop Trauma Surg* 2007;127:241–4.
14. Dauri M, Polzoni M, Fabbi E, Sidiropoulou T, Servetti S, Coniglione F, et al. Comparison of epidural, continuous femoral block and intraarticular analgesia after anterior cruciate ligament reconstruction. *Acta Anaesthesiol Scand* 2003;47:20–5.
15. Guler G, Karaoglu S, Velibasoglu, et al. Comparison of analgesic effects of intra-articular tenoxicam and morphine in anterior cruciate ligament reconstruction. *Knee Surg Sports Traumatol Arthrosc* 2002;10:229–32.
16. Mathies B. Effects of Visco seal, a synovial fluid substitute, on recovery after arthroscopic partial meniscectomy and joint lavage. *Knee Surg Sports Traumatol Arthrosc* 2006;14:32–9.
17. Thein R, Haviv B, Kidron A, Bronak S. Intra-articular injection of hyaluronic acid following arthroscopic partial meniscectomy of the knee. *Orthopedics* 2010;33:724.