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## Osteoarthritis: Does post-injury ACL reconstruction prevent future OA?

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*Published in:*  
Nature Reviews Rheumatology

*DOI:*  
[10.1038/nrrheum.2014.120](https://doi.org/10.1038/nrrheum.2014.120)

2014

[Link to publication](#)

*Citation for published version (APA):*

Wen, C., & Lohmander, S. (2014). Osteoarthritis: Does post-injury ACL reconstruction prevent future OA? *Nature Reviews Rheumatology*, 10(10), 577-578. <https://doi.org/10.1038/nrrheum.2014.120>

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## 1 OSTEOARTHRITIS

2  
3 Does post-injury ACL reconstruction prevent later OA?

4  
5 Chunyi Wen and L. Stefan Lohmander

6  
7 *Young adults with an acute rupture of the anterior cruciate ligament of the knee are*  
8 *faced with the decision of whether or not to undergo early reconstructive surgery.*  
9 *However, a lack of high-quality evidence means questions remain about whether this*  
10 *surgical strategy protects against later development of osteoarthritis.*

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12 Wen, C. & Lohmander, L. S. *Nat. Rev. Rheumatol.* advance online publication XX  
13 Month 2014; doi:10.1038/  
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15 Return to an active lifestyle and risk of future osteoarthritis (OA) are two, sometimes  
16 conflicting, concerns of the young adult with an acute rupture of the anterior cruciate  
17 ligament (ACL) of the knee, which could influence the decision of whether or not to  
18 undergo early surgery to reconstruct the torn ligament. Brophy and colleagues  
19 recently reported the results of a retrospective study into the prevalence of previous  
20 knee surgery, such as anterior cruciate ligament (ACL) reconstruction and  
21 meniscectomy, in an arthroplasty registry of 1,286 patients with a diagnosis of late-  
22 stage OA or post-traumatic arthritis<sup>1</sup>. Strikingly, they found that patients with a  
23 history of ACL reconstruction received their knee replacement at ~50 years of age,  
24 compared with age ~67 years for those without a history of knee surgery. With knee  
25 replacement at a young age markedly increasing the risk of later revision surgery, the  
26 results of Brophy *et al.*'s study highlight the problem of OA resulting from knee  
27 injury, and raise the question of whether we can prevent this serious late sequel.

28  
29 The rate of radiographic OA after ACL rupture and reconstruction varies widely in  
30 different reports, with a crude estimate of 50% at about 15 years after injury<sup>2</sup>. This  
31 high rate of radiographic signs of OA has remained unchanged despite refinements to  
32 surgical reconstruction techniques<sup>2</sup>.

33  
34 The patient-reported outcome of an ACL rupture and reconstruction is influenced by  
35 patient-related factors such as sex, BMI, smoking status, pre-surgery activity level,  
36 whether the patient returns to sports and the patient's expectations (Figure 1).  
37 Trauma-related factors, such as concomitant injuries to the meniscus or joint cartilage,  
38 are highly relevant as well<sup>3</sup>. The only recent randomized controlled trial (RCT) to  
39 compare early ACL reconstruction plus structured rehabilitation with rehabilitation  
40 alone failed to show a difference between patient-reported outcomes of the two  
41 strategies at 2 or 5 years<sup>4,5</sup>, suggesting that many patients do as well for at least 5  
42 years without undergoing early surgical reconstruction. Furthermore, no high-level  
43 evidence exists to support a protective effect of ACL reconstruction against later  
44 development of OA. On the contrary, an RCT comparing early reconstruction and

45 structured rehabilitation found no difference in the rate of radiographic or clinical  
46 signs of OA 5 years after the injury<sup>5</sup>.

47

48 The development of OA following an ACL rupture and reconstructive surgery  
49 remains an unsolved problem. To better understand the role of patient-related and  
50 injury-related factors in the choice of treatment and in the outcome, we need large and  
51 long-term prospective cohort studies that include those treated with and without ACL  
52 reconstruction, to complement additional RCTs comparing the efficacy of different  
53 interventions.

54

55 We also need further basic research to better understand the role of the immediate  
56 joint trauma at the time of the ACL rupture in the development of OA, as well as the  
57 relative contribution of long-term chronic derangement of joint loading. Chondral  
58 injury and bone contusion is present in essentially all patients with acute traumatic  
59 ACL rupture<sup>6</sup>. This immediate mechanical insult activates inflammatory cytokine and  
60 protease cascades in cartilage, synovial and bone cells, and triggers apoptosis and  
61 catabolic responses in the articular cartilage that degrade the cartilage matrix<sup>7</sup>. These  
62 processes release matrix molecule fragments that represent damage associated  
63 molecular patterns (DAMPs), which activate Toll-like receptors, to potentially  
64 prolong the inflammatory response. The possibility needs to be considered that  
65 surgery in this acute phase adds an additional trauma that might enhance the early-  
66 phase pathological processes and extend the joint damage: to replace a torn ACL,  
67 bone tunnels are drilled for the tendon graft, resulting in stress deprivation and  
68 substantial bone loss<sup>8</sup>. This intervention might compromise not only graft fixation but  
69 also the long-term outcome.

70

71 The loading patterns of the knee with a ruptured ACL, whether reconstructed or not,  
72 are not normal, with increased mechanical load on the cartilage and altered location of  
73 the load on the joint surfaces<sup>9</sup>. A damaged meniscus will further enhance this  
74 abnormal loading. Joint cartilage with an impaired matrix, such as occurs soon after  
75 injury, is most sensitive to high loading rates<sup>10</sup>. Recognizing this consequence of  
76 injury is important for planning the rehabilitation and activity counseling for patients  
77 with these injuries.

78

79 These early consequences of ACL rupture suggest that, in order to rectify the  
80 continued high rate of OA following ACL rupture, we need to direct our attention to  
81 the acute phase after injury. We need to explore if early interventions to decrease  
82 cartilage cell death, harness inflammatory cascades, prevent activation of Toll-like  
83 receptors or slow the breakdown of cartilage matrix could prevent or decrease some  
84 of the downstream, late consequences of these common injuries. To save the acutely  
85 injured joint, we might, in the future, need the same attitudes and urgent actions as  
86 now exercised when trying to save myocardium or brain cells in patients with acute  
87 infarction or stroke, respectively.

88

89 The clinical management of the young active person with OA from a previous knee  
90 injury remains a challenge. A structured, personalized exercise program should be the  
91 basic and primary approach, together with advice and support to maintain a normal  
92 body weight. Patients should be encouraged to stay physically active, but to avoid  
93 high-impact, pivoting activities. Intermittent use of analgesics or a brace might be  
94 helpful for some. Knee replacement can be effective for those with severe symptoms  
95 of OA, and should be considered before they have lost too much function and become  
96 deconditioned. Long-term risk of need for implant revision surgery remains a concern  
97 for those who undergo knee replacement at a young age.

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108 **Competing interests:**

109 The authors declare no competing interests.

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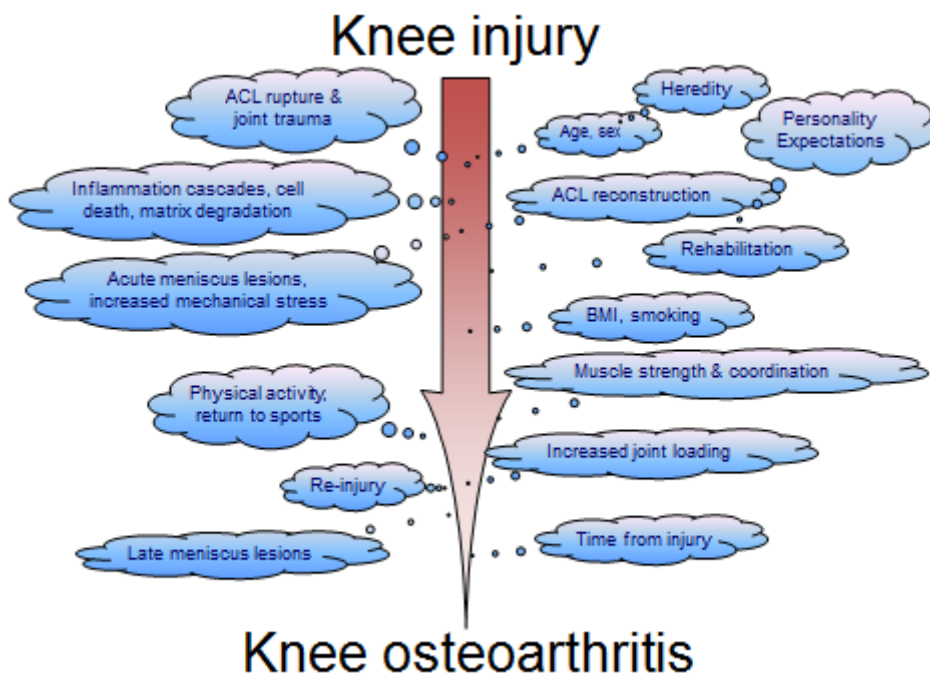
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154 **Figure 1.** Development of OA after acute rupture of the ACL of the knee. OA  
155 following ACL rupture is the consequence of the interaction between many risk  
156 factors, some associated with the person, such as heritability, and others with the  
157 environment, such as the severity of the trauma. Evidence that current interventions  
158 are able to alter the course from ACL rupture to OA is lacking. (Modified from  
159 Lohmander et al. AJSM 2007).

160 Abbreviations: ACL, anterior cruciate ligament; OA, osteoarthritis.

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