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

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1 **OSTEOARTHRITIS**

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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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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 arthritis¹. 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 injury². This
31 high rate of radiographic signs of OA has remained unchanged despite refinements to
32 surgical reconstruction techniques².

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 well³. 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^{4,5}, 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 injury⁵.

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 rupture⁶. 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 matrix⁷. 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 loss⁸. 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 surfaces⁹. 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 rates¹⁰. 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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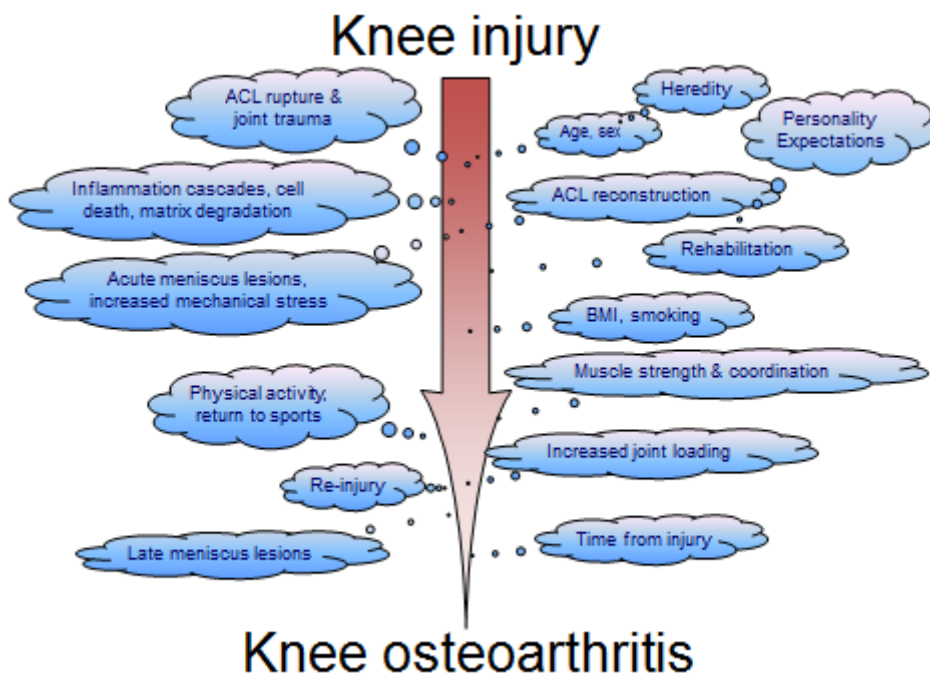
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154 **Figure 1.** Development of OA after acute rupture of the ACL of the knee. OA
155 following ACL rupture is the consequence of the interaction between many risk
156 factors, some associated with the person, such as heritability, and others with 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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