Original Article

Operative Versus Conservative Treatment of Anterior Cruciate Ligament Rupture

A Systematic Review of Functional Improvement in Adults

Matthias Krause, Fabian Freudenthaler, Karl-Heinz Frosch, Andrea Achtnich, Wolf Petersen, Ralph Akoto

Summary

<u>Background:</u> Anterior cruciate ligament (ACL) rupture is a serious injury in patients who are typically young and athletically active, with potential long-term complications including functional limitation, posttraumatic osteoarthritis of the knee, and impaired quality of life. ACL reconstruction is now considered the gold standard of treatment for regaining stability and improving knee function. Conservative treatment is an alternative.

<u>Methods:</u> To compare operative and conservative treatment, we reviewed pertinent publications retrieved by a systematic search in Ovid MEDLINE, the Cochrane Database of Systematic Reviews, and other databases. PROSPERO registration of the study protocol: CRD42017060462 on 31 March 2017.

Results: 13 publications concerning a total of 1246 patients were included in the analysis; only two were reports of randomized controlled trials (RCTs). In one of the RCTs, ACL reconstruction was found to yield better functional outcomes than conservative management. The other RCT did not reveal any harm from initial conservative management, although the conservative-to-operative crossover rate in this trial was 51%. The functional outcomes were heterogeneous. In six observational studies, knee function was significantly better after surgery; in seven others, it was not. Five out of nine analyses in which knee-joint stability was restored after surgery showed superior functional outcomes after ACL reconstruction compared to conservative management. Three studies in which no satisfactory postoperative knee-joint stability was found did not show any functional difference between surgery and conservative management.

<u>Conclusion</u>: On the basis of RCTs published to date, it cannot be definitively concluded whether surgery or conservative (expectant) management of ACL rupture yields a better functional outcome. There is a trend in observational studies toward better functional outcomes after ACL reconstruction. As an average across studies, conservative treatment fails in 17.5% (\pm 15.5%) of patients.

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R upture of the anterior cruciate ligament is a common injury (incidence: 68.6 per 100 000 patient years) that mostly affects young, physically active patients and can lead to chronic instability (1). The lateral tibial plateau in particular is prone to anterior subluxation (anteroposterior instability), as the ligament no longer restricts movement and the axis of rotation can shift medially. Isolated injury to the posterior cruciate ligament is rarer (incidence: 1.8 per 100 000 patient years) (2).

Chronic anteroposterior instability, which manifests in 8 to 50% of cases after surgical treatment and 75 to 87% after conservative treatment (3-7), is associated with increased risk of posttraumatic osteoarthritis of the knee (prevalence: 24.5 to 51.2%) (8), restricted knee function with reduced activity level (17% of competitive athletes do not return to competitive level) (9), and reduced quality of life (score of 54 to 77 on the KOOS QOL [Knee injury and Osteoarthritis Outcome Score: Quality of Life] versus 81 to 92 points in the uninjured population) (10). Despite intensive research into anterior cruciate ligament rupture, there is a lack of high-quality studies to determine clear treatment strategies for anterior cruciate ligament-deficient adults. According to the current S1 Guideline of the Association of Scientific Medical Societies in Germany (AWMF, Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften), anterior cruciate ligament reconstruction with autologous tendon graft is indicated for associated injuries to the collateral ligaments, meniscal injuries suitable for reconstruction, or a marked feeling of instability or subjective loading requirement. It is the first-line treatment for symptomatically unstable patients, in order to restore passive stability of the knee joint. According to meta-analyses and cohort studies, anterior cruciate ligament reconstruction can prevent secondary meniscal and cartilage injuries and restore previous activity levels (11-13).

Until recently there was only one randomized controlled trial, though this was widely recognized, comparing outcomes following early surgery and following conservative treatment with optional delayed surgery. The findings of this trial indicate that non-surgical treatment with possible delayed surgery leads to comparable subjective knee function and quality of life (14, 15). On the basis of these findings, coverage

in the lay press suggested that anterior cruciate ligament reconstruction and conservative treatment were of equal value.

Because the evidence for preferring specific treatment options was limited, the aim of this systematic review was to analyze functional differences between surgical and conservative treatment, dependent upon quality of the surgical process (5, 16). Our hypothesis was that stable quality of surgical care (as measured using passive knee stability) results in better functional outcomes than conservative treatment.

Methods

Search strategy

A systematic search of the literature based on the PRISMA guidelines was performed concerning functional outcome following surgical or conservative treatment for ruptures of the anterior cruciate ligament. The search included Ovid MEDLINE, the Cochrane Database of Systematic Reviews, ACP Journal Club, the Database of Abstracts of Reviews of Effects, the Cochrane Central Register of Controlled Trials, the Cochrane Methodology Register, Health Technology Assessment, the NHS Economic Evaluation Database, and PsycINFO. It covered the period from the foundation of these sources to 29 July 2018 (eTable 1) (17). The study protocol was registered prospectively with PROSPERO (CRD42017060462, 31 March 2017). The articles to be included were selected by two independent authors (MK and FF) on the basis of abstracts, fulltext versions, and bibliographies.

Inclusion criteria:

- Adults with closed epiphyseal plates
- Anterior cruciate ligament rupture diagnosed via magnetic resonance imaging (MRI) or arthroscopy
- At least one subgroup receiving conservative as well as surgical treatment, including any injuries to the menisci or collateral ligaments
- Use of one of the established scores to evaluate knee function (Lysholm, IKDC [International Knee Documentation Committee], Tegner, or KOOS)
- Follow-up period of 12 months or more
- Postoperative anteroposterior translation reported (extent of anterior drawer, i.e. anterior translation of lower leg in relation to upper leg with the knee bent at 10 to 20°; measured using arthrometry, for example)

Exclusion criteria:

- Posterior cruciate ligament injuries
- Suturing of the anterior cruciate ligament
- Preclinical laboratory tests
- Studies in patients with advanced osteoarthritis of the knee (Kellgren–Lawrence grade III/IV), inflammatory arthropathies
- Studies analyzing the same study group at various follow-up times
- Other systematic reviews and meta-analyses.

Primary and secondary endpoints

Our primary endpoint was knee function, which was evaluated using validated scores, such as Lysholm, KOOS, IKDC, or Tegner, or kinematic parameters. The secondary endpoint was the extent to which preinjury sport or activity level was restored.

Evaluation of knee stability

Quality of the surgical process was evaluated according to Noyes et al. (18) and the recommendation of the International Knee Documentation Committee (19), which rates postoperative anteroposterior translation as follows: mean side-to-side difference of less than 3 mm is optimum stability, 5 mm or less is suboptimum stability, and 6 mm or more is insufficient stability.

Evaluation of study quality

The methodological quality of the studies included in the review was evaluated using the Cochrane Quality Assessment Tool of the Cochrane Bone, Joint and Muscle Trauma Group (20). This awards a maximum of 2 points to each of 12 different aspects of a clinical study. As there were few randomized controlled trials, the criterion of whether or not a power analysis had been performed was also included in evaluation of study quality.

Findings

Search results

As in an earlier systematic review (5), the 2 studies by Frobell et al. (14, 15) and those by Meuffels et al. (3, 6) were counted as one study each. Eleven studies were excluded due to a lack of data on postoperative knee stability. Other reasons for exclusion were suturing of the anterior cruciate ligament (n = 7) and no allocation to a surgery group (n = 1). A total of 13 studies were included (*Figure*).

Study characteristics

This review included 2 prospectively randomized controlled trials (RCTs) (14, 15, 21), 5 nonrandomized prospective cohort studies (22–26), and 6 retrospective observational studies (3, 4, 6, 7, 27–29). A total of 1246 patients were investigated (anterior cruciate ligament reconstruction: n = 675; conservative treatment: n = 571). The median time from injury to anterior cruciate ligament reconstruction was 5.5 months (1.5 to 44.4). The median time to surgery in the studies that found surgery to be superior was 3.3 months (1.5 to 35.0), versus 6.0 months (2.5 to 44.4) in studies that found surgery and conservative treatment to be of equal value. The mean follow-up period was 117.2 months (12 to 276) (*Table 1*).

Evaluation of knee joint stability

Turning first to the 2 RCTs, Tsoukas et al. (21) found better anteroposterior stability following surgery ($1.5 \pm 0.2 \text{ mm}$) than following conservative treatment ($4.5 \pm 0.5 \text{ mm}$) after 10 years. In contrast, the data obtained by Frobell et al. (15) indicates insufficient anteroposterior

stability following surgery (mean KT-1000 score for side-to-side difference: 6.6 mm) (*eTable 2c*). In total, optimum stability following surgery was achieved in 9 of the 13 studies (*eTables 2a, 2b*).

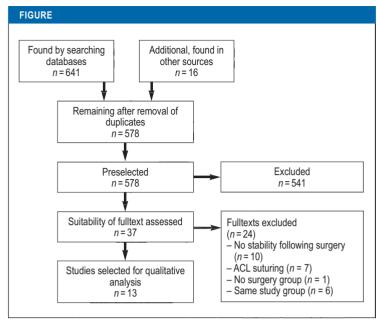
Primary outcome

The 2 RCTs had differing knee function-related findings. Whereas Tsoukas et al. (21) found that reconstruction of the anterior cruciate ligament was functionally superior to conservative treatment (IKDC score $86.8 \pm$ 6.5 points versus 77.5 ± 13.8 points), Frobell et al. (14, 15) found no significant differences in KOOS or Tegner score between surgery and nonsurgical treatment with optional delayed surgery. Of the 13 studies included in the review, 6 showed significantly better knee function (Lysholm, KOOS, IKDC, Tegner, or kinematic parameters) following anterior cruciate ligament reconstruction (4, 7, 21, 22, 27, 29). Seven studies described similar functional outcomes in both treatment groups (3, 14, 15, 23-26, 28). Of the 6 studies that found surgery to be superior, 5 found optimum stability following surgery. Of the 7 studies that yielded no evidence of superiority for either surgical or conservative treatment, only 4 achieved anteroposterior translation of less than 3 mm (eTables 2b, 2c) (3, 14, 23, 24). Although Markström et al. (26) found comparable Lysholm and Tegner scores and better KOOS ADL (activities of daily living) and KOOS Sport scores following conservative treatment, they found evidence of significantly better functional stability in hop tests following anterior cruciate ligament reconstruction (take-off: R2 = 0.15 to 0.26; landing: R2 = 0.2 to 0.28) after 23 years. This was not confirmed in 2 other studies; in these, either follow-up lasted only one year (25) or patients with time to surgery of more than 20 years were included (3).

Secondary outcome

All the studies, including the 2 RCTs, reported a significant decrease in activity level (Tegner score) following injury to the anterior cruciate ligament (0.55 to 5.25 points) (3, 6, 14, 15, 22, 21, 22, 26–28).

Whereas Frobell et al. (14, 15) found no significant improvement in activity level following anterior cruciate ligament reconstruction and Tsoukas et al. (21) provided no specific data, in 4 of the 8 nonrandomized studies anterior cruciate ligament reconstruction led to a significantly higher level of activity (Tegner score: 0 to 1.5 points) than conservative treatment (-2 to -3 points) (4, 7, 21, 22). Seitz et al. (4) and Fink et al. (29) showed higher rates of return to preinjury sporting level after surgery, with optimum stability following surgery. In contrast, Grindem et al. (25) found no significant differences in terms of return to sport, even with optimum stability following surgery. The higher return rates for conservative treatment than surgery found by Myklebust et al. (23) should be interpreted in the context of suboptimum quality of surgical process.



Flow diagram of systematic search of literature ACL: anterior cruciate ligament

Crossover rates

On average, $17.5 \pm 15.5\%$ of patients who initially received conservative treatment switched study group during the studies and underwent surgery. While Tsoukas et al. described a rate of 0% after 10 years, Frobell et al. reported the highest crossover rate, 51% after 5 years (*Table 1*).

Evaluation of study quality

The quality of the studies was generally low (Table 2). Only 2 prospective randomized trials were identified (14, 15, 21). Even these RCTs have a high potential for bias, as the outcome assessor was not blinded. Tsoukas et al. (21) did not perform an a priori power analysis. The studies by Frobell et al. (outcome: KOOS [14, 15]) and Markström et al. (outcome: knee flexion [26]) were the only ones in which power analyses were performed to determine the probability of type II errors. There were only 2 studies that included blinding before group allocation (14, 15, 21). Only Frobell et al. (14, 15) described intention-to-treat analysis (point B), only 2 studies included blinding of outcome assessors (point C) (3, 28), and there was no attempt to blind subsequent treatment providers in any of the studies (point F). There were only 2 studies in which the patient groups had identical rehabilitation programs (21, 27) (point G).

Discussion

This systematic review identified only 2 prospectively randomized controlled trials, and these yielded conflicting findings for stability scores. Five of the 9 studies with optimum stability following surgery and one further study that showed suboptimum quality of

TABLE 1

Characteristics and functional outcomes of studies included in review (surgery/conservative treatment)

			,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,		
First author, year (ref- erence), design	 n (surgery/conservative treatment) Age (surgery/con- servative treatment) Follow-up, months 	Anteroposterior stability (side-to-side difference [mm]) (surgery/conservative treatment)	Lysholm score (surgery/conser- vative treatment)	Mean IKDC score: 1. Normal 2. Almost normal 3. Abnormal 4. Very abnormal (surgery/conser- vative treatment)	KOOS score (surgery/ conservative treatment): 1. Symptoms 2. Pain 3. ADL 4. Sport 5. QOL
Seitz 1994 (4) RCS	 63/24 Surgery: 27 (15 to 42) Conservative: 28 (18 to 56) 102 (60 to 144) 	<3 mm category: 86% / 8%	100 to 91 (49/12) 90 to 84 (14/-) 83 to 65 (-/6) 64 to 0 (-/6)	-	-
Wittenberg 1998 (7) RCS	1. 30/30 2. 34.3 (22 to 50) 3. 39 (24 to 36)	2/4*1	86/72*1	-	-
Fink 2001 (29) RCS	1. 72/41 2. 33.0 (±9.0) 3. Surgery: 132.1 (±8.1) Conservative: 140.0 (±9.6)	2.0 (±1.5) / 4.0 (±2.0)* ¹	96/83* ¹	1. 0% / 0% * ¹ 2. 44% / 4% 3. 52% / 52% 4. 4% / 44%	-
Fithian 2005 (22) PCS	 63 (early surgery) / 33 (delayed surgery) / 113 (conservative) 39.0 (16–69) 79 	$\begin{array}{llllllllllllllllllllllllllllllllllll$	92 (±10)/ 88 (±14)* ^{1.2}	1. 33% / 10% * ^{1.2} 2. 50% / 23% 3. 16% / 66% 4. 1% / 2%	-
Kessler 2008 (27) RCS	1. 60/49 2. 30.7 (12.5 to 54.0) 3. 132	3.9 (0 to 12) / 5.7 (0 to 16)*1	-	1. 53% / 14% * ¹ 2. 18% / 41% 3. 20% / 31% 4. 8% / 14%	-
Tsoukas 2016 (21) RCT	 17/15 Surgery: 31 (20 to 36) Conservative: 33 (25 to 39) 123 	1.5 (±0.2) / 4.5 (±0.5)* ¹	-	1. 86.8 (± 6.5)/ 77.5 (± 13)* ¹	-
Streich 2011 (28) RCS	1. 40/40 2. 25.8 (17 to 39) 3. 180 (±17)	2.0 / 2.1	68.0 (± 19.8)/ 75.5 (± 15.9)	1. 69.9 (± 17.0)/ 75.9 (± 13.1)	-
Grindem 2012 (25) PCS	1. 69/69 2. 27.6 (13 to 60) 3. 12.8 (± 1.2)	2.7 (±1.8)/5.6 (±2.8)* ¹	-	1. 85.0 (± 11.6)/ 88.5 (± 9.2)	-
Markström 2018 (26) PCS	 327/34 Surgery: 46 (± 4.6) Conservative: 48 (± 5.9) 276 	2.0 (±2.7) / 4.9 (±2.9)	81 (±64)/ 73 (±61)	-	1. 84/75 2. 82/89 3. 89/98* ¹ 4. 50/75* ¹ 5. 49/69* ¹
Meuffels 2009 (3). van Yperen 2018 (6) RCS	1. 25/25 2. 37.7 (± 6.5) 3. 272	>3 mm category (2009): 6 (24%) / 17 (68%)* ¹ >3 mm category (2018): 10 (40%) / 19 (83%)* ¹	2009: 88.0 (80.5 to 91.0)/ 85.0 (77.0 to 90.0) 2018: 86.0 (75.5 to 91.0)/ 89.0 (75.5 to 95.5)	2009: 1. 77.1 (65.1 to 87.3)/ 77.1 (67.5 to 84.9) 2018: 1. 81.6 (59.8 to 89.1)/ 78.2 (61.5 to 92.0)	2018: 1. 86/93 2. 92/97 3. 96/99 4. 85/85 5. 63/69
Myklebust 2003 (23) PCS	1. 57/22 2. Not stated 3. 94	>3 mm category: 40% / 41%	85 (± 13)/ 85 (± 13)* ²	1. 9% /4% 2. 31% /13% 3. 23% /7% 4. 13% /0%	-
Moksnes 2009 (24) PCS	1. 52/50 2. 27.2 (± 8.6) 3. 12	4.1 (±0.7) / 7.6 (±0.5)* ¹	-	1. 87.0 (± 1.7)/ 86.1 (± 1.6)	-
Frobell 2013 (14) RCT	1. 62* ³ /59 2. 26.5 (±5.0) 3. 62	6.6 / 8.3*1	-	-	1. 83 (78 to 87)/87 (79 to 95)* ³ 2. 91 (88 to 94)/91 (86 to 96) 3. 95 (93 to 97)/97 (93 to 100) 4. 76 (70 to 81)/79 (68 to 90) 5. 71 (65 to 76)/69 (58 to 80)

*1p<0.05; *2 copers; *3 including delayed anterior cruciate ligament reconstruction ADL: activities of daily living; IKDC: International Knee Documentation Committee; KOOS: Knee Injury and Osteoarthritis Outcome Score; QOL: quality of life; PCS: prospective cohort study; RCT: randomized controlled trial; RCS: retrospective cohort study

Summary of methodologica	l quality	: Assess	sment To	ool of th	e Cochr	ane Bon	e, Joint	and Mu	scle Tra	uma Gro	oup (20)	
Author, year (reference)	Α	В	С	D	Е	F	G	н	I.	J	К	L
Seitz 1994 (4)	0	0	0	0	0	0	1	2	2	2	2	2
Wittenberg 1998 (7)	0	0	0	2	0	0	0	0	1	2	2	2
Fink 2001 (29)	0	0	0	1	0	0	0	1	2	2	2	2
Myklebust 2003 (23)	0	0	0	0	0	0	0	0	2	2	2	2
Fithian 2005 (22)	0	0	0	1	0	0	1	2	2	2	2	2
Kessler 2008 (27)	0	0	0	2	0	0	2	2	2	2	2	2
Moksnes 2009 (24)	0	0	0	2	0	0	0	2	1	2	2	1
Meuffels & van Yperen 2009, 2018 (3, 6)	0	0	1	2	0	0	0	0	2	2	2	2
Streich 2011 (28)	0	0	2	2	0	0	0	2	2	2	2	2
Grindem 2012 (25)	0	0	0	2	0	0	1	2	2	2	2	2
Frobell 2013, 2010 (14, 15)	1	2	0	2	0	0	1	2	1	2	2	2
Tsoukas 2016 (21)	1	0	0	2	0	0	2	2	2	2	2	2
Markström 2017 (26)	0	0	0	0	0	0	1	2	2	2	2	2
Mean	0.15	0.15	0.23	1.38	0.00	0.00	0.69	1.46	1.77	2	2	1.92

TABLE 2

A Was the assigned treatment adequately concealed prior to allocation?

B Were the outcomes of participants who withdrew described and included in the analysis (intention to treat)?

C Were the outcome assessors blinded to treatment status?

D Were the treatment and control group comparable at entry?

E Were the subjects blind to assignment status after allocation?

F Were the treatment providers blind to assignment status? G Were care programs, other than the trial options, identical?

H Were the inclusion and exclusion criteria clearly defined?

Were the interventions clearly defined?

J Were the outcome measures used clearly defined?

K Were diagnostic tests used in outcome assessment clinically useful?

L Was the surveillance active, and of clinically appropriate duration?

surgical process found functional superiority in terms of clinical scores (Tegner, Lysholm, KOOS, or IKDC) for surgery versus conservative treatment. In contrast, 3 of the 4 studies that did not find optimum knee joint stability after surgery found no difference between conservative treatment and surgery in terms of functional improvement. This confirmed our initial hypothesis.

A mean of 83% of competitive athletes return to their preinjury sporting level following surgery; this figure varies according to the type of sport in question (9, 30). Similarly, 80% of amateur athletes return to sport following anterior cruciate ligament reconstruction (31). However, without surgery only 19% of patients return to their preinjury sporting level (32). Good outcomes for conservative treatment are primarily correlated with a reduction in activity level and individual motivation (29, 33, 34). Register data on a large group of patients provides evidence that anterior cruciate ligament reconstruction can lead to better quality of life, higher levels of sporting activity, and lower subjective instability than conservative treatment (35). Although the differences were small, they were statistically significant (35). Data on anterior cruciate ligament reconstructions that were subjectively perceived as unstable during studies was

not explicitly excluded (35). In addition to exposure to repeat injury and individual risk-factor constellations, surgical technique is an important guarantor of success in anterior cruciate ligament reconstruction (36). Good stability—and other outcomes—can be achieved only with correct drill-tunnel placement, correct graft selection, and secure graft anchoring, and by addressing associated peripheral instabilities (29, 36). Stable anterior cruciate ligament reconstruction leads to improved proprioception and superior knee-joint kinematics in comparison to conservative treatment. The objectively measurable functional gain is, however, not necessarily reflected in subjective parameters (26, 37).

Tsoukas et al. (21), whose trial was the only randomized prospective trial with confirmed optimum knee-joint stability following surgery, found better functional outcomes following surgery than following conservative treatment, and the difference was statistically significant. These findings are limited because of the small case number and the absence of a power analysis to validate their level of certainty. In contrast, in the other RCT Frobell et al. (14, 15) found no evidence of superior function following anterior cruciate ligament reconstruction. However, this

Key messages

- Rupture of the anterior cruciate ligament can lead to persistent functional limitations, posttraumatic osteoarthritis of the knee, and reduced quality of life.
- Conservative/expectant treatment is an option (not inferior to early surgery in one RCT). In the authors' view it is more suitable for patients who have neither a high activity level nor associated lesions.
- In the authors' view, the premise that conservative treatment is of equal value to surgery is not confirmed. Conservative treatment fails in a mean of 17.5% of cases.
- Functional improvement following anterior cruciate ligament reconstruction seems to be greater than that following conservative treatment. It is dependent upon the quality of surgery.

study's data on postoperative stability indicates that the quality of the surgical process was poor. KT-1000 stability scores of 6.6 mm 2 years after surgery correspond clinically to persistent anterior cruciate ligament insufficiency; the aim of surgery, a postoperatively stable knee joint with typical stability scores between -0.1 and 2.3 mm, was not achieved (18, 19, 38).

Furthermore, it is misleading to interpret the findings of Frobell et al. as being those of a study of superiority (15). Although they found no difference between the 2 treatment groups, it is not correct to conclude the reverse, i.e. that the 2 treatment options are of equal value (absence of evidence is not evidence of absence; [39]). Rather, a noninferiority analysis is required. In addition, the as-treated analysis-which is different from the intention-to-treat analysis-has a high risk of bias. Patients who chose surgery during the study may have been more severely injured than those who received conservative treatment. The individual comparison of groups was no longer protected by randomization. Even if assuming that around 49% of patients could have avoided anterior cruciate ligament reconstruction, the study provides no indication of which patients would cope without surgery. This is critical in that according to data from observational studies delayed surgery leads to a statistically significantly increased risk of subsequent associated injuries such as meniscal ruptures and of increased prevalence of osteoarthritis of the knee (22). The RCTs, however, do not find this increased risk. Conservative treatment is a clear treatment option. However, there are currently no clear criteria to identify which patients will cope without surgery. One suitable way would be to explain to patients that in half of cases surgery will still be needed. Conservative treatment or delayed surgery may even be inferior to early surgery because of the potentially higher risk of secondary injuries, particularly in young, physically active patients; nevertheless, the RCTs found only weak evidence of this. Frobell et al. could not confirm that the 2 treatment options were of equal value, but neither do the primary endpoints indicate that early surgery is superior.

Of the 4 studies that found optimum stability following surgery but no advantages in terms of functional improvement, one nevertheless found significantly better functional stability in hop tests in the group that had undergone surgery (26). The 3 other studies had quality-related shortcomings. One other study found high rates of persistent rotational instability (50%) despite optimum anteroposterior stability, which limits the conclusion that the two treatment options are of equal value (28). While the follow-up period in the third study is only 12 months (25), the fourth includes patients with time to surgery of up to 21.5 years (3).

The RCTs included in this review found no evidence of a protective effect of anterior cruciate ligament reconstruction in terms of secondary associated lesions (meniscus or cartilage) or secondary arthritis. However, this was not the subject addressed by our review. Other scientific literature published on this subject to date is conflicting.

The major limitation of this systematic review was the low level of evidence of the studies included in it. It was only possible to include 2 RCTs, and even these were of poor quality (16). There were also substantial differences between times from injury to surgery. Despite the lack of prospectively randomized trials, early surgery-within 10 to 12 weeks-seems to be superior in terms of rotational stability, functional outcome, secondary injury to the menisci or cartilage, and general cost-efficiency (14, 15, 22, 40). Only 3 of the studies included in this review examined patients who underwent early surgery (less than 12 weeks postinjury). Studies that found no difference between surgical and conservative treatment generally examined anterior cruciate ligament ruptures that received delayed surgery, including as late as 21.5 years postinjury (3). As a result, a group of patients for whom conservative treatment had failed, including cases of secondary associated injury, were compared with patients who had undergone successful conservative treatment.

Summary

As proposed in our initial hypothesis, a majority of studies in which postoperative knee-joint stability was optimum found better knee function following anterior cruciate ligament reconstruction than following conservative treatment, although the latter is an alternative treatment option.

The design of future studies should make a clear distinction between anterior cruciate ligament reconstruction for acute or subacute anterior cruciate ligament injuries on the one hand and surgery for patients for whom conservative treatment has failed on the other. Because potential differences between groups can only be detected with very high patient numbers if the distinction made between subjective functional parameters is insufficiently clear, a standardized method should be used to examine surgical technique and outcome of surgery, with sufficient power determined in advance.

Conflict of interest statement

Prof. Frosch has received lecture fees and reimbursement of participation fees from Arthrex GmbH.

Prof. Petersen has received royalties, consultancy fees, lecture fees, and reimbursement of travel costs for participation in continuing education events from Storz and Otto Bock. He has received consultancy fees and reimbursement of travel costs from Ossür.

Dr. Akoto has received reimbursement of participation fees for a conference or continuing education event from Conmed and Smith & Nephew and reimbursement of travel or accommodation costs from Conmed, Arthrex, Smith & Nephew, and Mathys.

The other authors declare that no conflict of interest exists.

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► Supplementary material

eTables: www.aerzteblatt-international.de/18m0855

CLINICAL SNAPSHOT

An Extreme Case of Systemic Metallosis After Implantation of a Hip Prosthesis

A 62-year-old man presented with chronic fatigue and increasing pain in the right hip 7 years after a broken ceramic head had been replaced by a combination of a metal head and a polyethylene inlay during revision surgery. The revision surgery had been followed by transient loss of vision, deafness, and heart muscle inflammation. Hip radiography showed deformation of the inserted metal head and extensive radiodense areas in the thigh. Laboratory analysis revealed that the concentrations of chromium and cobalt were, respectively, 600 and 1000 times higher than normal. Surgery revealed that the femur was completely coated with abscess-like structures of metallic material and a dark-colored fluid. The thigh muscles and the polyethylene inlay contained large numbers of ceramic particles. There ensued a further revision to insert an implant with a ceramic-ceramic interface. After this operation the levels of metal ions de-



creased and the symptoms regressed. Metallosis is a rare but potentially serious late complication of implantation surgery. It is generally associated with metal-metal bearing interfaces, but isolated cases have been described with other interfaces. After ceramic head fracture, switching to a metal-polyethylene interface is contraindicated. The German Implant Registry (*Endoprothesenregister Deutschland*, EPRD) collects all relevant data after every insertion of an artificial joint in order to optimize quality and patient safety.

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Conflict of interest statement: The authors declare that no conflict of interest exists.

Translated from the original German by David Roseveare.

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Supplementary material to:

Operative Versus Conservative Treatment of Anterior Cruciate Ligament Rupture

A Systematic Review of Functional Improvement in Adults

by Matthias Krause, Fabian Freudenthaler, Karl-Heinz Frosch, Andrea Achtnich, Wolf Petersen, and Ralph Akoto

Dtsch Arztebl Int 2018; 115: 855-62. DOI: 10.3238/arztebl.2018.0855

eTABLE 1

Control of	stern by the system is of Ovid Medline	
	ategy by the example of Ovid Medline	
Step	Search terms	Number of studies
1	((anterior adj2 cruciate* adj2 ligament*) or acl).mp.	22 238
2	Surgical Procedures, Operative/	53 971
3	Orthopedics/	19 821
4	Traumatology/	3246
5	Anterior Cruciate Ligament Reconstruction/	3499
6	Orthopedic Fixation Devices/	5020
7	Suture Techniques/	42 233
8	Orthopedic Procedures/	23 861
9	Arthroscopy/	22 300
10	(surg* or operat* or reconstruct* or repair* or graft* or arthroscop*).mp.	3 872 087
11	2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10	3 887 896
12	Physical Therapy Modalities/	37 140
13	orthotic devices/	6614
14	braces/	5523
15	(non-surg* or nonsurg* or non-operat* or nonoperat* or conserv* or rehab* or physiotherapy or physical therapy or brace* or exercis* or cast*1).mp.	1 351 837
16	12 or 13 or 14 or 15	1 354 925
17	1 and 11 and 16	3797
18	Randomized controlled trial.pt.	917 153
19	controlled clinical trial.pt.	182 849
20	randomized.ab.	819 780
21	randomly.ab.	499 737
22	placebo.ab.	409 265
23	clinical trials as topic/	217 662
24	trial.ti.	416 417
25	cohort studies/	233 803
26	(random* or RCT or placebo or allocat* or crossover* or ,cross over' or trial or (doubl* adj1 blind*) or (singl* adj1 blind*)).ti,ab.	2 300 780
27	18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26	2 883 698
28	(Animal or Animals* or "not Humans*" or Human cell* or Nonhuman* or non-human*).mp.	7 219 240
29	27 not 28	2 064 766
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e a	Age Fo	Follow-up	Anteroposterior	Clinical stability,		Lysholm	Tegner	IKDC	KOOS	Single-leg	RTS/RTPL
(s	5		stability (side-to-side difference [mm]) (surgery/conservative treatment)	pivot shift, Lachman (surgery/conser- vative treatment) (clinical [%])	over rate (%)	(surgery/ conservative treatment)	(surgery/ conser- vative treatment)	(surgery/ conservative treatment)	(surgery/ conser- vative treat- ment)	hop test (surgery/ conser- vative treatment)	(surgery/ conser- vative treatment) (%)
Surgery: 27 (15–42) Conser- vative: 28 (18 to 56)	(6	102 (60 to 144)	<3 mm category: 86% / 8%	8/83 (pivot)	1	100 to 91 points: 49/12 90 to 84 points: 14/ – 165 points: – /6 64 to 0 points: –/6	Tegner equal: 67% / 25%	1	1	1	67/25
34.3 (22 to 50)	šč	39 (24 to 36)	2/4*1	19/75 (pivot) 24/81 (Lachman)	I	86/72* ¹	7 to 10* ¹ . 12/6 4 to 6: 15/19 1 to 3: 3/5	1	I	1	1
33.0 (± 9.0)	v ≈ o ≥ t	Surgery: 132.1 (±8.1) Conser- vative: 140.0 (±9.6)	2.0 (± 1.5) / 4.0 (± 2.0)*1	1	4.8 (2/41)	96/83*1	1	Normal* ¹ : 0% / 0% Almost normal: 44% / 4% Abnormal: 52% / 52% Very abnormal: 4% / 44%	I	1	56/30* ¹
39.0 (16 to 69)	1.1.5	62	High risk: 1.6 (± 1.5)/ 3.3 (± 1.5) Moderate risk: 1.7 (± 2.0)/ 3.1 (± 2.0) Low risk: 2.0 (± 2.0)/2.3 (± 1.8)* ¹	Surgery: significantly better pivot	22.6 (33/146)	$92 (\pm 10)/88 (\pm 14)^{*1.2}$	6.0/3.0* ^{1.2}	Normal* ^{1, 2} : 33%/ 10% Almost normal: 50%/ 23% Abnormal: 16%/ 66% Very abnormal: 1%/ 2%	I	1	1
30.7 (12.5 to 54.0)	¥	132	5.7 (0 to 12) / 5.7 (0 to 16)*1	1	18 (12/68)* ³	1	5.3 (2 to 10) / 4.9 (2 to 10)	Normal* ¹ : 53%/14% Almost normal: 18%/41% Abnormal: 20%/31% Very abnormal: 8%/14%	I	1	1
Surgery: 31 (20 to 36) Conser- vative: 33 (25 to 39)	÷*	123	$1.5 (\pm 0.2) / 4.5 (\pm 0.5)^{*1}$	1	0	1	7 (5 to 7)/ 5 (3 to 7)	86.8 (± 6.5)/ 77.5 (± 13)* ¹	1	1	1

IRUC: International Knee Documentation Comr preinjury level; *1p<0.05; *2 coper. *3 excluded before analysis

eTABLE 2a

eTABLE 2b

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First author, year (reference) (design)	n (surgery/ conser- vative treat- ment)	Time to surgery (months)	Age (years)	Follow-up (months)	Anteroposterior stability (side-to- side difference [mm]) (surgery/ conservative treatment)	Clinical stability, pivot shift, Lachman (sur- gery/conser- vative treatment) (clinical [%])	Cross- over rate (%)	Lysholm (surgery/ conservative treatment)	Tegner (surgery/ conser- vative treatment)	IKDC (surgery/conser- vative treatment)	KOOS (surgery/ conservative treatment)	Single-leg hop test (surgery/conser- vative treatment)	RTS/RTPL (surgery/ conser- vative treatment) (%)
Streich 2011 (28) (RCS)	40/40	7.3 (± 3.2)	25.8 (17 to 39)	180 (± 17)	2.0/2.1	50 / 57.5 (pivot)	10.2 (10/59)	68.0 (± 19.8) / 75.5 (± 15.9)	4.7 (± 1.8)/ 5.1 (± 1.9)	69.9 (± 17.0) / 75.9 (± 13.1)	I	1	1
Grindem 2012 (25) (PCS)	69 / 69	5.5 (± 2.3) (after 3 months' rehab)	27.6 (13 to 60)	12.8 (± 1.2)	2.7 (±1.8)/5.6 (±2.8*)	I	I	1	1	85.0 (± 11.6)/ 88.5 (± 9.2)	1	90.5 (± 14.0) / 96.3 (±6.4)* (hop distance, LSI)	68.1/68.1
Markström 2018 (26) (PCS)	32/34	44.4 (after 3 months' rehab)	Surgery: 46 (±4.6) Conser- vative: 48±5.9	276	2.0 (± 2.7)/4.9 (± 2.9)	1	1	81 (± 64) / 73 (± 61)	4 (±4) / 4 (±5)	1	Symptoms: 84/75 Pain: 82/89 ADD: S9/98* S9075* 49/69*	0.20 (± 0.04)/0.17 (± 0.03)* (height of hop, m)	1
Meuffels 2009 (3)/ van Yperen (RCS) (RCS)	25/25	6 (2 to 258)	37.7 (±6.5)	272	>3 mm category (2009): 6 (24%)/ 17 (68%)* > 3 mm category (2018): 10 (40%)/19 (83%)*	2009: 20784 (≥1 + pivot) 2018: 32787 (≥1 + pivot)	1	2009: 88.0 (80.5 to 91.0)/ 85.0 (77.0 to 90.0) 2018: 86.0 (75.5 to 91.0) / 89.0 (75.5 to 95.5)	2009: 6 (4 to 7) / 5 (4 to 7) 2018: 5 (3 to 6) / 4 (4 to 6)	2009: 77.1 (65.1 to 87.3) / 77.1 (67.5 to 84.9) (67.5 to 84.9) 81.6 (59.8 to 89.1) / 78.2 (61.5 to 92.0)	2018: Symptoms: 86/93 92/97 92/97 96/99 85/85 85/85 63/69 63/69	2009: 93.7 (80.0 to 100.7)/ 96.1 (84.2 to 100.9) 2018: 85.9 (68.1 to 101.9) / 95.1 (70.8 to 104.7) (hop. % vs. uninjured leg)	1

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Characteristics and functional outcomes of studies included in review that found no significant difference in knee function between conservative treatment and surgery, with suboptimum knee-joint stability

RTS/RTPL (surgery/ conser- vative trreatment) (%)	82			
Single-leg hop test RTS/R (surgery/conser- (surger vative treatment) conser vative treatm (%)	7 (± 3)/2 (± 3) (difference in hop between injured & uninjured legs, cm)	91.8 (± 1.4)/ 95.9 (± 1.4)* ² (hop, % vs. uninjured leg)	1	2009: 93.7 (80.0 to 100.7)/ 96.1 (84.2 to 100.9) 2018: 85.9 (68.1 to 101.9) / 95.1 (70.8 to 104.7) (hop. % vs. uninjured leg)
KOOS (surgery/ ((surgery/ (conservative v treatment)		1	Symptoms: 83 (78 to 87)/ 87 (79 to 95) Pain: 91 (86 to 96) ADL: 95 (93 to 97)/ 97 (93 to 100) 58 ort 66 (70 to 81)/ 79 66 to 90) 00L: 71 (65 to 76)/ 69 (58 to 80)	2018: Symptoms: 86/93 86/99 92/97 4DL: 4DL: 85/85 85/85 00L: 63/69
IKDC (surgery/conser- vative treatment)	Normal: 9% / 4% Almost normal: 31% / 13% Abnormal: 23% / 7% Very abnormal: 13% / 0%	87.0 (± 1.7)/ 86.1 (± 1.6)	1	2009: 77.1 (65.1 to 87.3) / 77.1 (67.5 to 84.9) 2018: 81.6 (59.8 to 89.1) / 78.2 (61.5 to 92.0)
Tegner (surgery/ conser- vative treatment)	1	1	4 (2 to 7) / 4 (2 to 6.5)	2009: 6 (4 to 7) / 5 (4 to 7) 2018: 5 (3 to 6) / 4 (4 to 6)
Lysholm (surgery/ conservative treatment)	85 (± 13) / 85 (± 13)* ¹	I	1	2009: 88.0 (80.5 to 91.0)/ 85.0 (77.0 to 90.0) 2018: 86.0 (75.5 to 91.0)/ 89.0 (75.5 to 95.5)
Cross- over rate (%)	1	16.1 (10/62)	(30/59)	1
Clinical stability, pivot shift, Lach- man (surgery/ conservative treatment) (clinical [%])		I	76/40 (pivot) 76/32 (Lachman)	2009: 20/84 (≥1 + pivot) 2018: 32/87 (≥1 + pivot)
Anteroposterior stability (side-to- side difference [mm]) (surgery/ conservative treatment)	<3 mm category:40%/41%	4.1 (± 0.7) / 7.6 (± 0.5)*2	6.6/8.3* ²	>3 mm category (2009): 6 (24%)/ 17 (68%)*2 17 (68%)*2 10 (40%)/ 19 (83%)*2 19 (83%)*2
Follow- up (months)	94	12	62	272
Age (years)	Not stated	27.2 (± 8.6)	26.5 (±5.0)	37.7 (±6.5)
Time to surgery (months)	Not stated	6 (after 3 months ['] rehab)	<2.5	6 (2 to 258)
n (surgery/ conser- vative treat- ment)	57/22	52/50	62* ³ /59	25/25
First author, year (reference) (design)	Myklebust 2003 (23) (PCS)	Moksnes 2009 (24) (PCS)	Frobell 2013 (14) (RCT)	Meuffels 2009 (3)/ Yperen 2018 (6) (RCS)