Factors associated with a more rapid recovery after anterior cruciate ligament reconstruction using multivariate analysis

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ABSTRACT

Background: In the past, several studies investigated factors that are prognostic or associated with outcome after anterior cruciate ligament (ACL) reconstruction. A recent review showed that only limited evidence is available for most studied factors, and that insufficient analysis methods were used commonly. Therefore, the aim of this study was to add more weight to the existing evidence, about factors that are associated with a more rapid outcome after ACL reconstruction. The second aim was to use multivariate analysis to study the possible factors independently.

Methods: A cohort study was conducted with a follow-up of six months. Before surgery, patient variables were scored. Surgical variables were scored during arthroscopic ACL reconstructions with a single-bundle technique and hamstring autograft. The Lysholm score and subscales of the Knee Injury Osteoarthritis Outcome Score (KOOS) were assessed six months post surgery. A multiple analysis of variance (ANOVA) model was used to identify prognostic factors for outcome.

Results: In total, 118 patients were included. Patients, aged ≤30 years, with a subjective knee score ≥six, with normal flexion range of motion (ROM) of the knee, with flexion and extension strength deficit of ≤20%, and those with no previous knee surgery in the patients' history at baseline scored significantly higher on outcome after multivariate analysis. No significant effect of surgical factors could be found.

Conclusion: Younger age, higher subjective knee score, normal knee flexion, normal knee flexion and extension strength, and no previous knee surgery in the patients' history at baseline are associated with a more rapid recovery after ACL reconstruction.

Level of evidence: Level III, prognostic study.

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1. Introduction

Anterior cruciate ligament (ACL) rupture is a common knee injury, which usually results in the loss of knee stability. The injury generally involves young patients who participate in sports. To restore knee stability, surgical ACL reconstruction is commonly performed [1,2].

A systematic review on return to sports showed that 82% of the patients returned to some form of sports after ACL reconstruction. Only 63% of the operated patients returned to their pre-injury level of sports, with only 44% of the patients returning to competitive sports [3]. In clinical practice, it is hard to predict who will do well after ACL reconstruction. Recently, a systematic review on prognostic factors for outcome after single-bundle ACL reconstruction with hamstring autograft was published [4]. This review, by our group, showed that mainly limited evidence for an association between prognostic factors and outcome for ACL reconstruction was found [4]. Furthermore, it was shown that mostly only univariate analysis was used instead of multivariate analysis, to study possible prognostic parameters independently [4].

Because of the limited evidence about factors that are prognostic for the outcome after ACL reconstruction, we wanted to investigate preoperative patients and surgical factors that are associated with a more rapid recovery after ACL reconstruction with single-bundle hamstring autograft technique. This was done by investigating the recovery results six months after surgery and using multivariate analysis.

The aim of this article was to add evidence about factors that are associated or are prognostic for a more rapid recovery after ACL reconstruction.
reconstruction, thereby improving the percentage of operated patients returning to their pre-injury level of sport and competitive sport. Based on the available literature, we hypothesized that gender, age, body mass index (BMI), smoking status, and time from injury until surgery would be associated with a more rapid recovery after ACL reconstruction.

2. Methods

We performed a cohort study to identify factors that are associated with a more rapid recovery after ACL reconstruction. We examined patients who underwent ACL reconstruction at our clinic between January 2010 and January 2013. Based on the available literature [4] and after a consensus meeting with the authors, preoperative and surgical variables were chosen for analysis. We investigated the recovery results six months after surgery to see if those factors are associated with a more rapid recovery after ACL reconstruction.

We chose to study the results six months after ACL reconstruction, because most athletes are allowed to return to sport around six months after injury [34]. Moreover, Valk et al. showed that only few studies examined prognostic factors in this time frame [4]. Before the start of the study, the local medical ethical commission (Verenigde Commissies Mensgebonden Onderzoek (VCMO), Nieuwegein, the Netherlands) approved the study (registration number W14.069).

2.1. Patients

2.1.1. Inclusion

Patients who rehabilitated at our adjacent clinic for physiotherapy were included in this study. In addition, patients were included if at six months after ACL reconstruction at least 95% of the preoperative variables, surgical variables, and outcome variables were available. Another inclusion criterion was that an ACL reconstruction with single-bundle technique and hamstring autograft was performed. This technique is most widely used at our clinic. Patients with associated cartilage damage and meniscal injury were also included. All procedures were performed by two experienced orthopedic surgeons (24 and 14 years of experience in ACL surgery).

2.1.2. Exclusion

Patients were excluded if they had incomplete survey data (>5% data missing), if the surgical technique used was different from the one described earlier, and if revision ACL reconstruction was performed. The ACL injury was initially confirmed by magnetic resonance imaging (MRI) or arthroscopic surgery.

2.2. Outcome variables

The outcome variables six months after ACL reconstruction were Lysholm score and the Knee Injury Osteoarthritis Outcome Score (KOOS) subscales: symptoms, sports and recreation (sport/rec), and quality of life (QOL). Physiotherapists assessed the scores during rehabilitation. The Lysholm score was scored between 0 and 100, where 0 indicates a very poor score and 100 an excellent score [5,6]. The Lysholm score was categorized as “excellent (>90),” “good (84–90),” “reasonable (65–83),” and “bad (<65)” [7]. With the help of a native speaker in English, who is a sport physician, the Lysholm score was translated into Dutch. The Dutch-validated version of KOOS was used [8–10]. A previous study showed that the questions for KOOS subscales, pain and function in daily living (ADL), can be regarded as nonrelevant and/or specific for patients with ACL injuries, because of the high percentage of maximal score at baseline [11]. Therefore, we only analyzed the results for KOOS subscales: symptoms, sport/rec, and QOL (all 0–100 scales, worst to best).

2.3. Patient variables

Demographic variables, subjective variables, and knee function variables were analyzed as possible prognostic factors, and they were obtained 4 weeks before surgery by the physiotherapist in a standardized manner. All variables were documented in our own developed system (combined quality care) for integrated care between physiotherapists and orthopedic surgeons.

2.3.1. Demographic variables

The following demographic variables were scored at baseline: gender, age, smoking status, BMI, highest level of education, time from injury until surgery in weeks, side of the injury, and knee surgery in medical history (see Table 1).

2.3.2. Subjective variables

Four questions (limitations with social activities, highest possible level of activities, pain during the past four weeks, and rated knee function on a 1 to 10 scale) from the Dutch version of the International Knee Documentation Committee Subjective Knee Form (IKDC) were chosen to assess the subjective variables [12] (see Table 1).

2.3.3. Knee function variables

The following knee function variables were assessed: passive knee ROM deficit for flexion and extension, pivot shift test, knee laxity, and knee strength. Passive ROM deficits and pivot shift test were performed and documented according to the 2000 IKDC knee examination form [13]. Preoperative knee laxity was defined as the difference in knee laxity between the injured and non-injured knee in millimeters, using the KT-2000 arthrometer (MEDmetric, San Diego, CA, USA). Preoperative muscle flexion and extension strength were measured by using Biodex System 4 Pro (Biodex Medical Systems Inc., Shirley, NY, USA). The difference between the injured and non-injured knee was defined as a percentage value, by using the formula (1 – (injured/non-injured)) × 100. This was measured for both flexion and extension, with five repetitive movements at 60°/sec, five repetitive movements at 120°/sec, and 20 repetitive movements at 180°/sec. Before testing, all patients were warmed up on a stationary cycle for 10 minutes (see Table 1).

2.4. Surgical variables

During arthroscopic surgery, the presence of chondral and meniscal injury was examined. If indicated, meniscus tears were treated. Afterwards, all findings were documented in the operative report. The surgical variables included for analyses as possible prognostic factor are listed in Table 1.

2.4.1. Surgical technique

Surgery was performed arthroscopically, using a nonanatomic single-bundle technique with a four-strand hamstring graft. The tendon of the semitendinosus muscle and the gracilis muscle were harvested in a standard way with a small incision over the pes anserinus [14]. Femoral fixation took place with a transfixation technique (TransFix, Arthrex R, Naples, FL, USA); tibial fixation was performed with a 9/35-mm bioComposite interference screw.

2.4.2. Rehabilitation

Postoperatively, all patients included in this study followed the same standardized rehabilitation protocol (modification of Ref. [15]). This protocol was supervised by our physiotherapists. Rehabilitation was started within one week of surgery. The first weeks of rehabilitation focused on muscle and joint flexibility. Patients were allowed partial weight bearing with crutches during the first four weeks. After this period, muscle strength training, balance training, and coordination
training were started. This period was followed by sports-specific training programs.

2.5. Statistics

The statistical analyses were performed using IBM Statistical Package for Social Science (SPSS) Statistics V21.0 (SPSS, Chicago, IL, USA). First, the independent variables were classified as dichotomous or categorical. Variables were tested for a parametric distribution. Independent t-test was used for univariate analyses between two groups. One-way analysis of variance (ANOVA) was used for univariate analyses of more than two groups. Variables with a p-value of ≤0.1 were included for further analyses. A p-value of ≤0.1 was chosen to have broad inclusion criteria at this first step.

After univariate analyses, the variables with a p-value of ≤0.1 were entered in a multiple ANOVA model. In the multiple ANOVA model, the least significant variable was extracted from the model. With the remaining variables, a new model was constructed. This process was repeated until only significant variables remained in the multiple ANOVA model. A p-value of ≤0.05 was regarded as significant.

3. Results

A total of 118 patients were included in this study between January 2010 and January 2013, and their baseline characteristics can be found in Table 1. Concerning the history of the ACL injuries, 94.1% of the patients sustained the injury during sports participation. In 66.9% of them, the onset was traumatic without physical contact. Most of the ACL injuries occurred during soccer (38.1%), followed by skiing and field hockey (both 13.6%).

3.1. Univariate analysis and multiple ANOVA model

The results of the univariate analysis are shown in Table 3. The variables about limitations in daily activities and the highest level of activity were excluded for analysis, because the patients were not evenly distributed among the various categories. (See Table 2.)
Table 2
Outcome variables of patients six months after surgery (n = 118).

<table>
<thead>
<tr>
<th>Outcome variable</th>
<th>Means (SD)</th>
<th>Number of patients (missing)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lysholm score</td>
<td>89.75 (11.12)</td>
<td>118 (0)</td>
</tr>
<tr>
<td>KOOS symptoms</td>
<td>86.98 (11.50)</td>
<td>118 (0)</td>
</tr>
<tr>
<td>KOOS sport/rec</td>
<td>78.49 (19.42)</td>
<td>118 (0)</td>
</tr>
<tr>
<td>KOOS QOL</td>
<td>59.27 (20.88)</td>
<td>118 (0)</td>
</tr>
</tbody>
</table>

Abbreviations: SD, standard deviation.

3.2. Patient variables

After analyses of the multiple ANOVA model, age (F(1,87) = 5.085, p = 0.027), subjective knee score after injury (F(1,87) = 9.397, p = 0.003), and flexion strength deficit at 120°/s (F(1,87) = 6.573, p = 0.012) were found to be significant factors for the Lysholm score. Together, these three variables explained 22.3% of the variance of the Lysholm score (see Table 4).

The different KOOS subscales (symptoms, sport/rec, and QOL) were investigated using the multiple ANOVA model as well. Knee ROM flexion deficit was found to be a significant factor (F(4, 113) = 4.500) for KOOS symptoms, explaining 13.7% of the variance. Regarding KOOS sport/rec, analyses showed that preoperative subjective knee score (F(1,81) = 5.033, p = 0.028), previous knee surgery (F(1,81) = 6.457, p = 0.013), knee ROM flexion deficit (F(4, 81) = 3.552, p = 0.010), and knee extension strength at 60°/s (F(1,81) = 4.714, p = 0.033) were found to be significant factors. Together, these four variables explained 31.2% of the variance of KOOS sport/rec. For KOOS QOL, none of the investigated patient variables showed to be a significant factor (see Table 4).

3.3. Surgical variables

None of the variables that were scored during surgery were found as a significant factor, for both the Lysholm and KOOS scores.

4. Discussion

This cohort study showed that preoperative age, subjective knee score, knee ROM, knee flexion strength, knee extension strength, and knee surgery are factors that are associated with a more rapid recovery after ACL reconstruction.

Patients aged ≤30 years (mean = 90.44; excellent) scored significantly (p = 0.027) higher on the Lysholm score compared with patients aged >30 years (mean = 84.79; good). This is in line with the review of de Valk et al. [4]. They also concluded that patients younger than 30 years reached higher activity levels than older patients after ACL reconstruction. These data suggest that younger patients recover faster after ACL reconstruction.

In previous studies [3,16–18], psychological characteristics are mentioned as an explanation why some patients fail to return to sports after ACL reconstruction. We found that patients with a preoperative subjective knee function score of ≥6 at baseline scored significantly (p = 0.003) higher on the Lysholm score (91.93 = excellent vs. 83.30 = reasonable) and significantly (p = 0.028) higher on KOOS sport/rec (difference of 14.08).

Swirtum and Rentröm [19] found that patients with a high level of embitterment after injury scored significantly lower on KOOS pain and KOOS symptoms six years after surgery. Thomée et al. [20] showed that perceived self-efficacy at completing knee-related tasks in the future was predictive for an acceptable Lysholm score, KOOS sport/rec, and KOOS QOL. We also showed that the patients’ own perception of knee function is a factor that is associated with a more rapid recovery after ACL reconstruction. Because of this result, it is relevant to preoperatively discuss with patients about their expectations. Patients with a preoperative low subjective knee function score and unrealistic expectations may be disappointed by the results of ACL reconstruction.

A third finding was that patients with a preoperative normal knee flexion scored higher on both KOOS symptoms and KOOS sport/rec. We found a significant difference between patients with no flexion deficit compared with patients with a knee flexion deficit of ≥25° at baseline. The mean differences of 14.12 and 27.32 were found, respectively, for KOOS symptoms (p = 0.001) and KOOS sport/rec (p = 0.002). Heijne et al. [21] also found that patients with a normal knee flexion scored significantly higher on KOOS QOL 12 months after surgery.

This suggests that preoperative knee ROM is a factor that is associated with a more rapid recovery after ACL reconstruction. Restoring knee ROM during preoperative rehabilitation should therefore be a priority for physiotherapists and orthopedic surgeons.

A knee strength flexion deficit of ≥20% was associated with significantly (p = 0.012) better outcome (mean = 92.28; excellent) on the Lysholm score compared with those with a deficit of >20% (mean = 82.95; reasonable). In addition, we found that patients with an extension deficit of ≥20% scored significantly (p = 0.033) higher on the KOOS sport/rec (mean difference, 8.12). Eitzen et al. [22] already showed that a preoperative quadriceps muscle strength deficit of >20% resulted in a significantly lower Cincinnati knee score and quadriceps strength two years after surgery. Heijne et al. [21] concluded that low preoperative quadriceps strength compared with the uninvolved leg was predictive for worse KOOS QOL 12 months after surgery. However, to our knowledge, no previous study found that patients with lower preoperative knee flexion strength scored significantly lower on the Lysholm score. Our data show that both flexion and extension strength of the knee are factors that are associated with a more rapid recovery after ACL reconstruction. Therefore, restoring knee flexion and extension strength should be considered in preoperative rehabilitation protocols. A recent study [23], regarding preoperative rehabilitation, already showed that the preoperative strengthening of the lower limb results in improved single-legged hop test and Cincinnati score 12 weeks after ACL reconstruction.

Our final significant finding was that previous knee surgery is a factor that is associated with a more rapid recovery after ACL reconstruction. Patients without previous knee surgery scored significantly (p = 0.013) higher on KOOS sport/rec (mean difference, 8.54). Barenius et al. [24] concluded that previous surgery of meniscus was a predictor for

Table 3
Outcome univariate analysis for Tegner activity scale, Lysholm score, VAS pain, and KOOS (symptoms, sport/rec, QOL).

<table>
<thead>
<tr>
<th>Gender</th>
<th>Lysholm score</th>
<th>KOOS symptoms</th>
<th>KOOS sport/rec</th>
<th>KOOS QOL</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>p</td>
<td>η²</td>
<td>p</td>
<td>η²</td>
</tr>
<tr>
<td>Gender</td>
<td>0.003</td>
<td>0.07</td>
<td>0.090</td>
<td>0.02</td>
</tr>
<tr>
<td>Age</td>
<td>0.001</td>
<td>0.10</td>
<td>0.002</td>
<td>0.14</td>
</tr>
<tr>
<td>Knee surgery before</td>
<td>0.027</td>
<td>0.04</td>
<td>0.089</td>
<td>0.03</td>
</tr>
<tr>
<td>Knee score (subjective rating)</td>
<td>0.027</td>
<td>0.04</td>
<td>0.089</td>
<td>0.03</td>
</tr>
</tbody>
</table>

Only variables with a univariate p-value of <0.1 are shown. η² represent the Eta-squared effect size.
treatment failure after ACL reconstruction. Together with the other prognostic factors described earlier, the patient’s knee surgical history should be taken into consideration when choosing between operative ACL reconstruction and nonoperative ACL rehabilitation.

The systematic review on prognostic factors by de Valk et al. [4] also showed that male gender, BMI, and time until surgery were prognostic for outcome after ACL reconstruction. With univariate analyses, male gender was associated with a more rapid recovery, but it did not reach significance in our multiple ANOVA model. The difference for BMI can be explained by our lower mean BMI, compared with the studies [20,25–27] that found a lower BMI as a factor with a significant better outcome.

Our findings about the time until surgery are in line with some previous studies [24,28–30]. However, some studies [31–33] report better outcome with a shorter time until surgery. The time until surgery may have an influence on knee muscle strength. Shorter time until surgery results in less time to lose knee muscle strength and knee ROM after injury. However, shorter time until surgery results in less time to restore knee muscle strength and knee ROM. In addition, we showed that large deficits between involved and uninvolved leg are associated with a more rapid recovery after ACL reconstruction.

A strength of this study is that we investigated a representative population and looked into many different variables at baseline. We analyzed demographic variables, subjective variables, knee variables, and surgical variables. As far as we know, no previous studies analyzed so many variables at baseline. In addition, the possible prognostic parameters were analyzed using a multiple ANOVA model to examine these for their independent association. In the majority of existing studies on prognostic factors, only univariate analysis was used.

In this study, we looked at the follow-up six months after surgery. In similar studies, a minimal follow-up of 12 months is used. We decided to analyze the outcome six months after ACL reconstruction, because six months is the minimal time of rehabilitation before returning to sports. With this study, we intended to offer additional insight into factors that are associated with a more rapid recovery after ACL reconstruction. The relatively short follow-up can be seen as a limitation of this study. However, the six-month follow-up mark is an important point in the process of ACL rehabilitation, because from then on, the patients are able to return to sports. Therefore, more knowledge about these factors could lead to better results and quicker recovery after ACL reconstruction.

A limitation of this study is that not all patients who underwent ACL reconstruction in our clinic were rehabilitated with our own physiotherapists. Therefore, not all our patients who underwent ACL reconstruction in our clinic were available for inclusion. These missing patient data are because we perform ACL reconstruction for people nationwide who cannot attend locally for rehabilitation.

Another limitation is that the patients were not evenly distributed among the subjective variables. The variables “limitations in daily activities” and “highest possible level of activity” were therefore excluded for further analyses. Previous studies mentioned that subjective traits could be an explanation for the lack of return to sports after ACL reconstruction. Therefore, this study could have been contributing to the uncertainty about the prognostic value of psychological characteristics and outcome after ACL reconstruction. Future research should therefore focus on patient psychological characteristics before ACL reconstruction. Another point of interest for future research should be the relationship between the time until surgery, knee muscle strength, knee ROM, and outcome after ACL reconstruction.

5. Conclusion

Preoperative patient factors such as younger age, higher subjective knee score, normal knee flexion and extension strength, and no previous knee surgery in the patients’ history are associated with a more rapid recovery six months after single-bundle ACL reconstruction with hamstring autograft. These factors score significantly better on the Lysholm score, KOOS symptoms, and KOOS sport/rec. None of the surgical factors were found to be associated with a more rapid recovery after ACL reconstruction with hamstring autograft. These findings add weight to the findings in the review by Valk et al. [4].

Conflict of interest statement

We declare that we do not have any conflicts of interest.

**Table 4**

Outcome of multiple ANOVA analysis for Tegner activity scale, Lysholm score, KOOS symptoms, KOOS sport/rec.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Variables in model</th>
<th>Mean (CI)</th>
<th>p-Value</th>
<th>R-squared for model</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lysholm score</td>
<td>Age ≤30: n = 30, n = 65: n = 26</td>
<td>90.44 (85.98–94.91)</td>
<td>0.027</td>
<td>0.223 (p = &lt;0.001)</td>
</tr>
<tr>
<td></td>
<td>Knee score (subjective rating) ≥6: n = 6, n = 73</td>
<td>91.93 (85.99–97.87)</td>
<td>0.003</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Flexion strength deficit 120°/s ≤20: n = 20, n = 81: n = 10</td>
<td>92.28 (89.18–95.38)</td>
<td>0.012</td>
<td></td>
</tr>
<tr>
<td>KOOS symptoms</td>
<td>ROM flexion deficit none: ≥25° n = 68: n = 7</td>
<td>89.10 (86.49–91.71)</td>
<td>0.001</td>
<td>0.117 (p = 0.002)</td>
</tr>
<tr>
<td>KOOS sport/rec</td>
<td>Knee score (subjective rating) ≥6: n = 6, n = 78</td>
<td>79.87 (70.51–89.23)</td>
<td>0.028</td>
<td>0.312 (p = &lt;0.001)</td>
</tr>
<tr>
<td></td>
<td>Knee surgery before no: yes n = 71: n = 26</td>
<td>77.10 (70.52–83.68)</td>
<td>0.013</td>
<td></td>
</tr>
<tr>
<td></td>
<td>ROM flexion deficit none: ≥25° n = 56: n = 7</td>
<td>79.71 (73.32–86.10)</td>
<td>0.002</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Extension strength deficit 60°/s ≤20: n = 20, n = 57: n = 37</td>
<td>80.00 (73.38–86.63)</td>
<td>0.033</td>
<td></td>
</tr>
</tbody>
</table>

Only variables with a p-value of <0.05 are shown. Abbreviations: CI, 95% confidence intervals.
References


