

1 **Arthrogenic muscle inhibition and return to sport after arthrofibrosis complicating**  
2 **anterior cruciate ligament surgery**

3

4 Marc Dauty<sup>1,2,3</sup>, Pierre Menu<sup>1,2,3</sup>, Olivier Mesland<sup>1,2</sup> and Alban Fouasson-Chailloux<sup>1,2,3</sup>

5

6 <sup>1</sup>CHU Nantes, Physical Medicine and Rehabilitation Center, University Hospital of Nantes,  
7 France;

8 <sup>2</sup>CHU Nantes, Service de Médecine du Sport, University Hospital of Nantes, France;

9 <sup>3</sup>INSERM UMR U1229/RMeS, Regenerative Medicine and Skeleton – Nantes University,  
10 France

11

12 Corresponding author: Alban Fouasson-Chailloux

13 MPR Locomotrice et Respiratoire, CHU de Nantes, Hôpital St Jacques, 85 rue Saint Jacques,  
14 44093 Nantes, Cedex 1.

15 E-mail: [alban.fouassonchailloux@chu-nantes.fr](mailto:alban.fouassonchailloux@chu-nantes.fr)

16 Tel: +33 240 846 211

17

18 **Abstracts**

19 Arthrofibrosis is a devastating complication after Anterior Cruciate Ligament reconstruction  
20 (ACLR) characterized by a muscle weakness secondary to an arthrogenic muscle inhibition  
21 process. The loss of knee isokinetic strength due to arthrogenic muscle inhibition may be  
22 more important after arthrofibrosis, compared to an ACLR population with no complication.  
23 The isokinetic strength deficit [Limb Symmetry Index (LSI) at 60 and 180°/s of angular  
24 speed] was measured at 4, 7 and 12 post-operative months. Knee function, return to running  
25 and return to sport were evaluated. A comparison of the Quadriceps and the Hamstring LSI  
26 between patients with arthrofibrosis and those without post-operative complication was  
27 performed according to time and taking into consideration the type of surgical procedure. 539  
28 primary ACLR patients were assessed. The arthrofibrosis group presented at 4, 7 et 12 post-  
29 operative months a Quadriceps LSI significantly lower compared to the control group,  
30 without influence of the graft procedure (LSI: 38, 53, 68% vs 63, 73, 85% at 60°/s  
31 respectively). The Hamstring LSI was significantly lower at 4 and 7 post-operative months,  
32 but comparable at 12 months with an influence of the Hamstring procedure. Knee function  
33 was significantly lower at 4 and 7 post-operative months. Few arthrofibrosis ACLR patients  
34 returned to running at 7 post-operative months (6.8% vs 69.9%;  $p < 0.0001$ ). An important and  
35 durable Quadriceps muscle weakness occurred after arthrofibrosis, whatever the type of graft  
36 procedure. This is explained by an Arthrogenic muscle inhibition which compromised the  
37 return to sport at the same level until 12 post-operative months.

38 **Key Terms:** Knee, ACL reconstruction, Isokinetic, Arthrogenic muscle inhibition.

39

## 40 **Introduction**

41 Each year, many patients have anterior cruciate ligament reconstruction (ACLR), in order to  
42 return to sport<sup>19,27</sup>. The process of post-operative recovery takes time to obtain a painless and  
43 movable knee which associates stability and strength recovery<sup>5,6</sup>. A medical follow-up is  
44 recommended to assess the recovery process in order to return to sport at the same level<sup>2</sup>. A  
45 quadriceps strength deficit of 30% (Limb Symmetric Index (LSI) of 70%) between the  
46 operated and the non-operated side may allow the return to running<sup>28</sup>. A symmetrical strength  
47 of the quadriceps (LSI  $\geq$  90%) would be preferable to return to a competitive sport involving  
48 contacts and pivoting movements<sup>7</sup>.

49 Usually, muscular strength is reliably and reproducibly assessed with an isokinetic  
50 dynamometer<sup>13</sup>. The LSI highlights the arthrogenic muscle inhibition which predominates on  
51 the quadriceps on the operated side, because of post-operative joint swelling and local  
52 inflammation<sup>29</sup>. A gradual improvement over several months is expected during the post-  
53 operative follow-up after ACLR<sup>38</sup>. Yet, the LSI can be particularly reduced and takes long  
54 time to recover in case of post-operative complications such as anterior knee pain, posterior  
55 knee pain or arthrofibrosis<sup>4</sup>. Moreover, the type of graft may influence the hamstring  
56 arthrogenic inhibition in case of hamstring<sup>3</sup>.

57 The arthrofibrosis represents a formidable post-operative complication with a variable  
58 incidence of 4 to 38%<sup>8</sup>. It is explained by a joint invasion of fibrous tissues responsible for a  
59 joint ankyloses. Three topographies are described: intercondylar, suprapatellar or lateral, and  
60 supracondylar<sup>12</sup>. It is secondary to a fibroblastic and endothelial proliferation - a dense type I,  
61 II and IV collagen fibers formation depending on an overexpression of cytokines such as  
62 TGF- $\beta$ , platelet-derived growth factor and fibroblastic growth factor<sup>9,11,18</sup>.

63 Clinically, knee range of motion decreases, which is easily observable, and enables the  
64 surgeon to propose a mobilization under general anesthesia or an early arthrolysis<sup>1,15,22,31,40</sup>.

65 Different types of arthrofibrosis have been described in the reference classification of  
66 Shelbourne et al <sup>8,33</sup>. Type 1 corresponds to an isolated knee extension decrease inferior to 10°  
67 (due to an insufficient rehabilitation?). Type 2 is characterized by an isolated knee extension  
68 decrease superior to 10°, usually secondary to a « Cyclops syndrome » <sup>14,18,39</sup>. Types 3 and 4  
69 have a decrease of the extension and the flexion associated to a decrease or an absence of  
70 patella mobility, described as « Infrapatellar contracture syndrome »<sup>23,24</sup>. « Complex Regional  
71 Pain Syndrome » has also been used to describe these 2 last types <sup>3,18,21</sup>.

72 A strength deficit, difficult to improve by rehabilitation, has also been described in case of  
73 arthrofibrosis<sup>33</sup>. However, this strength deficit is almost never measured, while it is certainly  
74 responsible for difficulties to return to daily activities or previous sport <sup>21</sup>. It is the  
75 consequence of the arthrogenic muscle inhibition, which may be associated to a mechanical  
76 part due to the joint stiffness.

77 The main objective of this work was to assess if the arthrogenic muscle inhibition (in  
78 accordance with the Quadriceps and Hamstring LSI) was higher in a group of patients with  
79 arthrofibrosis compared to a control ACLr group at 4 and 12 months after surgery. We also  
80 evaluated arthrofibrosis consequences according to the number of physiotherapy sessions  
81 performed before 4 months, according to the function of the operated knee and according to  
82 the return to running and to sport at the same level.

83

## 84 **Materials and Methods**

### 85 **Population**

86 Since 2005, all our patients operated on an ACLr performed an accelerated post-operative  
87 rehabilitation (Early full weight-bearing with crutches, early passive and active knee  
88 extension)<sup>17,32</sup>. Cycling was proposed at the 2nd post-operative month and the practice of  
89 jogging at the 3<sup>rd</sup> one by the orthopedic surgeon<sup>22</sup>. At 4 months after surgery, the follow-up  
90 was performed by an independent physician of Physical Medicine and Rehabilitation, to  
91 assess the isokinetic strength recovery of the quadriceps and the hamstrings. The objective of  
92 this isokinetic evaluation was to detect the consequences of any post-operative complications  
93 on the knee muscle strength and to advise the return to sport until competition<sup>3</sup>. Yet, some  
94 patients developed arthrofibrosis with difficulties of hamstrings and quadriceps strength  
95 recovery, despite continuing rehabilitation care. Return to sport at the same level was in these  
96 cases compromised. So, from a historical cohort between 2008 and 2018, we retrospectively  
97 included all the patients who underwent a primary ACLr (Bone-Patella-Tendon-Bone (BPTB)  
98 or Hamstring (H) procedure) with or without meniscus lesion or extra articular tenosis, and  
99 performed isokinetic tests at 4, 7 and 12 months after surgery. We excluded patients who had  
100 an associated osteotomy, an ACLr revision, a concomitant other ligament reconstruction, a  
101 posterior cruciate ligament injury or reconstruction, a knee arthrolysis, a malposition of the  
102 drill tunnels on post-operative x-rays or a Cyclops syndrome surgery. We also excluded ACLr  
103 patients who had a post-operative infection, a knee swelling, an anterior or posterior knee pain  
104 without ROM reduction or a contralateral knee pathology. Patients who performed less than 3  
105 isokinetic tests during the follow-up were not included.

106 We identified 2 ACLr groups of patients at 4 months after surgery: an arthrofibrosis ACLr  
107 group which had the type 3 of the Shelbourne et al.'s classification<sup>33</sup> and a control ACLr  
108 group without complications. Diagnosis criteria were, at 4 months, a reduction of the knee

109 extension superior to 10° and a reduction of the knee flexion superior to 25°, and no knee  
110 instability. This association of clinical signs present at 4 months enabled us to exclude  
111 surgical failures that might have induced a loss of knee flexion or extension, but not both at  
112 the same time (incorrect position of the bone tunnels or excess of graft tension)<sup>11,18,20,30</sup>.

113

#### 114 **Isokinetic evaluation**

115 All the first isokinetic measurements were performed at the 4<sup>th</sup> postoperative month after  
116 ACLr, using a CybexNorm® isokinetic dynamometer (Ronkonkoma, NY, USA). All subjects  
117 were seated with a hip angle of 85°. The mechanical axis of the dynamometer was aligned  
118 with the lateral epicondyle of the knee. The trunk and the thigh were stabilized with belts. The  
119 knee range of motion was 100° (100 to 0° = maximal knee extension). Torque was gravity-  
120 corrected at 45° of knee flexion and the dynamometer calibration was monthly performed in  
121 accordance with the manufacturer's instructions. Every session was preceded by  
122 familiarization with the isokinetic movements (3 submaximal movements). The patients were  
123 tested over 3 maximal repetitions at the angular speed of 60°/s followed by 5 maximal  
124 repetitions at 180°/s. A 30-second recovery period was allowed between both series. The non-  
125 operated knee was always first evaluated after instruction and with verbal encouragement and  
126 visual feedback. We considered the maximal strength in Newton-meter (Nm) of the different  
127 repetitions. All evaluation tests were conducted by the same PM&R physician. The main  
128 parameter was the strength deficit, defined by the Limb Symmetry Index (LSI) for the knee  
129 extensors (Quadriceps) and the knee flexors (Hamstrings). The LSI was expressed in  
130 percentage and calculated with the formulae: maximal strength of the non-operated knee /  
131 maximal strength of the operated knee) x 100<sup>28</sup>. The LSI enabled us to compare the external  
132 load produced on the healthy side and the one produced on the operated side. A Quadriceps  
133 and Hamstrings LSI lower on the operated side was the sign of the arthrogenic muscle

134 inhibition in case of arthrofibrosis. The reliability of Quadriceps and Hamstring maximal  
135 strength is considered as excellent (ICC: 0.93-0.98) and this of LSI as low (ICC: 0.43-78)<sup>13</sup>.

136 At 4 months after surgery, the number of physiotherapy sessions was noticed. The function of  
137 the operated knee was assessed with the Lysholm score<sup>35</sup>. The return to running was  
138 considered effective at 7 months if the patients were able to run at least 15 minutes. The type  
139 of sport and the level were described with the Tegner score, before and after<sup>36</sup>. The knee  
140 range of motion (ROM) has been measured at 4 and 7 months after surgery, and expressed in  
141 degrees in the group with arthrofibrosis.

142

### 143 **Ethics**

144 Applicable institutional and governmental regulations concerning ethics were followed during  
145 the course of this research. The data report form was declared to the French data protection  
146 authority (CNIL) and to the Research Department of the University Hospital. Since data were  
147 collected retrospectively and that patients' management was not modified, according to  
148 French law, this study did not need to be approved by a research ethics committee (articles  
149 L.1121-1 paragraph 1 and R1121-2, Public Health code).

150

### 151 **Statistical analysis**

152 Statistical analysis was performed using the SPSS 23.0® software package (IBM corp.  
153 Ireland). The quantitative variables were expressed by average and standard deviation. The  
154 categorical variables were expressed by median, maximum and minimum values, or  
155 frequency. The comparison between arthrofibrosis and control ACLr groups was assessed by  
156 the Student's *t* test and the  $\chi^2$  test. Non parametric Spearman correlations between the muscle  
157 LSI and the Lysholm and the Tegner scores were searched at the 7<sup>th</sup> postoperative month for  
158 both groups. The arthrogenic muscle inhibition was established by two-way repeated-

159 measures ANOVA [3 times (4 vs 7 vs 12 months) x 2 knees (ACLR vs non-operative)] of the  
160 Quadriceps and Hamstring isokinetic strength for the 2 angular speeds (60 and 180°/s).  
161 arthrofibrosis and graft procedures types were studied as factors between patients. Firstly, the  
162 normal distribution of different 3 times of strength measurements was verified by the  
163 Kolmogorov-Smirnov test. Secondly, a correction of Greenhouse-Geisser was used if the  
164 Mauchly test of sphericity of variance/covariance matrix was not respected. A Bonferoni post-  
165 hoc test was used to establish difference between isokinetic parameters depending of different  
166 times of isokinetic assessment and of operative or non-operative knees. Results were  
167 considered significant at  $p < 0.05$ .

168

## 169 **Results**

170 908 patients with ACLR had criteria of inclusion, and 85 cases of stage 3 arthrofibrosis were  
171 clinically diagnosed, that is to say an incidence of 9.4% (Figure).

172 203 patients have been excluded and 160 dropped out the study, including 26 cases of  
173 arthrofibrosis among which 4 cases underwent a knee arthrolysis at 4 months after surgery.

174 The proportion of patients lost to follow-up (30.5 vs 22.0%;  $p = 0.5$ ), the anthropometric and  
175 surgical parameters were not different between the group of patients with arthrofibrosis and

176 those without. 539 patients have been studied with 59 cases of arthrofibrosis and 480 control  
177 ACLR patients. We assessed 384 men and 155 women; their mean age was  $25 \pm 7$  years old.

178 Before ACL traumatism, the most practiced sports were soccer (46.8%), basketball (19.3%)  
179 and handball (12.6%), that is to say pivoting sports with contact in nearly 78.7% of the cases.

180 The median Tegner score was 7.0 [4 - 10] before ACLR. The ACLR had been performed by 13  
181 different surgeons, 198  $\pm$  282 days from the ACL traumatism, with 176 BPTB procedures

182 and 363 H procedures, associated to 114 meniscus surgeries and 45 extra-articular tenodesis.



183 Isokinetic evaluations have been performed at 131 +/- 13 days, 210 +/- 16 days and 348 +/- 21  
184 days.

185 The arthrofibrosis ACLr group and the control group were not different concerning  
186 anthropometric parameters (Table I). Four months after surgery, the arthrofibrosis ACLr  
187 group had performed significantly more sessions of physiotherapy than the control ACLr  
188 group ( $p < 0.0001$ ). All the patients with arthrofibrosis had continued sessions of physiotherapy  
189 after 4 months in order to improve their knee ROM. Between the 4<sup>th</sup> and the 7<sup>th</sup> months after  
190 surgery the knee ROM increased by  $20.0^\circ \pm 6.0$ ,  $2.0^\circ \pm 0.9$  for the knee extension and  
191  $17.0^\circ \pm 5.0^\circ$  for the flexion. The Lysholm score was lower in the arthrofibrosis ACLr group  
192 at 4 and 7 post-operative months, but it was similar at 12 months after surgery (Table I). At  
193 the 7<sup>th</sup> month after surgery, only 6.8% of the patients with arthrofibrosis had returned to  
194 running whereas 69.9% of the patients in the control group had returned ( $p < 0.0001$ ; Table 1).  
195 The level of sport was significantly lower in the arthrofibrosis ACLr group at 4, 7 and 12  
196 months after surgery (Table I). The Quadriceps and the Hamstring LSI were also lower at 4  
197 and 7 months after surgery in the arthrofibrosis group (Table 2). At 12 post-operative months,  
198 the Quadriceps LSI remained lower whereas the Hamstring LSI was comparable to the control  
199 group. At 7 post-operative months, the Quadriceps LSI at 60 and 180°/s were significantly  
200 correlated with the sport level in the arthrofibrosis ACLr group ( $r = 0.329$  and  $r = 0.321$ ,  
201 respectively;  $p < 0.01$ ) and in the control ACLr group ( $r = 0.301$  and  $r = 0.31$ , respectively;  $p$   
202  $< 0.01$ ). Yet, the Lysholm score was not correlated with the muscles LSI.

203 The arthrogenic muscle inhibition of the quadriceps was significant on the operated side  
204 independently of the type of the graft procedure, whereas concerning the hamstrings, the  
205 degree of arthrogenic muscle inhibition was dependent on the surgical procedure (Table 3).

206

207 **Discussion**

208 Arthrofibrosis of the knee is a disabling and severe complication after ACLr<sup>31,33</sup>. We have  
209 reported an incidence of nearly 10%, that can be explained because we studied all the cases of  
210 arthrofibrosis, including those not operated. Considering only the operated cases of  
211 arthrofibrosis under-estimates the incidence of this complication<sup>31</sup>. Indeed, all the cases of  
212 arthrofibrosis may not be diagnosed or operated or may be lost of follow-up<sup>8</sup>.

213 The arthrofibrosis is responsible for a strength deficit difficult to improve despite  
214 rehabilitation<sup>1,33</sup>. This deficit of strength is rarely studied while it may be responsible for the  
215 impossibility to return to sport at the same level, just like the loss of knee ROM. The main  
216 originality of our study was to assess the evolution of the Quadriceps and Hamstring LSI and  
217 their consequences on the return to sport in case of arthrofibrosis. We have shown that in case  
218 of arthrofibrosis, the Quadriceps LSI was low, but also the Hamstring LSI in smaller  
219 proportions. The Quadriceps LSI remained low 12 months after surgery despite continuing  
220 rehabilitation; running was rarely practiced before 7 months after surgery and the return to  
221 sport was low.

222 Our results are difficult to compare because few studies have evaluated the isokinetic LSI of  
223 the knee in case of arthrofibrosis after ACLr. Over 25 years ago, Shelbourne et al. had shown  
224 that the patients that had been operated before 21 days post-injury had a low quadriceps LSI  
225 of 51%, at 4 months post-surgery, due to more frequent cases of<sup>34</sup>. In 1996, Shelbourne et al.  
226 showed a low Quadriceps LSI of 72% in case of cyclops syndrome, of 67 and 73% in case of  
227 type 3 and 4 of arthrofibrosis at 12 months after ACLr<sup>33</sup>. The Quadriceps LSI of the  
228 arthrofibrosis ACLr group were of 68 and 74% at the angular speeds of 60 and 180°/s.  
229 Previous authors had shown the evolution of the isokinetic strength according to the  
230 complications of the hamstring procedures<sup>3</sup>. The arthrofibrosis was the most serious  
231 complication in terms of Quadriceps LSI. According to 7 cases of arthrofibrosis, named at  
232 that time « diffuse pain limited joint motion », we showed a low Quadriceps LSI at 4 months

233 after surgery (42% at 60°/s), which remained low at 12 post-operative months (61% at 60°/s).  
234 A low Hamstring LSI was also present at 4 months after surgery (51% at 60°/s) but then, it  
235 was comparable to the control group at 12 months (89% at 60°/s). The return to sport was also  
236 difficult, none of the 7 cases had returned to sport at the same level, 12 months after surgery<sup>3</sup>.  
237 In case of ACLr, the low LSI is the consequence of the arthrogenic muscle inhibition<sup>29</sup>. The  
238 reason is not clear, but it could be secondary to the swelling and the pain after surgery<sup>29</sup>.  
239 These symptoms would stimulate the knee articular sensory receptors which would modulate  
240 the spinal and supra-spinal centers<sup>16</sup>. The spinal reflex pathways contribute to the arthrogenic  
241 muscle inhibition, especially the nonreciprocal inhibitory pathway (Ib), the flexion reflex and  
242 the gamma-loop. The supraspinal may also play an important role in the muscle inhibition<sup>16,25</sup>.  
243 That would generate a muscular atrophy and an ineffective muscle strengthening as if a  
244 muscle proportion could not be activated<sup>10,37</sup>. Yet, 4 months after surgery, these clinical signs  
245 have disappeared, at the time of the isokinetic test. The arthrogenic muscle inhibition is also  
246 present on the non-operated side<sup>16,26,29,38</sup>. We have confirmed this phenomenon on the non-  
247 operated knee of the ACLr control patients and we have noticed no increase of this  
248 phenomenon in case of arthrofibrosis.

249 On the operated side, the arthrogenic muscle inhibition may have been associated to a  
250 mechanical component. Indeed, concerning the arthrogenic hamstring inhibition, the  
251 transmission of the muscular force to achieve knee flexion could be reduced due to the  
252 removal of the semi-tendinosus tendon during the Hamstring procedure<sup>4</sup>. A mechanical  
253 component could also be associated to the arthrogenic quadriceps inhibition because of the  
254 joint stiffness due to the intra-articular fibrosis development. Yet, this explanation has not  
255 been proven.

256 Our study has also some limits. The ROM of the arthrofibrosis ACLr group have not been  
257 compared to those of the ACLr group. Indeed, in the absence of complications, the ROM are

258 quite symmetrical between the operated and the non-operated knees from the 4<sup>th</sup> months after  
259 surgery. The increase of 20° of the ROM in the arthrofibrosis ACLr group, may have  
260 explained why the functional knee scores (Lysholm score) was comparable between the 2  
261 groups at the 12<sup>th</sup> post-operative month. However, the quadriceps LSI remained lower in the  
262 arthrofibrosis ACLr group, despite a favorable evolution. The post-operative follow-up was  
263 certainly too short to know the final evolution of the arthrogenic muscle inhibition in case of  
264 arthrofibrosis. Strength recovery generally takes more than 12 months. A 24-month follow-up  
265 may be useful to know potential sequels of the arthrofibrosis, in terms of strength loss, return  
266 to sport and osteoarthritis evolution<sup>21</sup>.

267

## 268 **Conclusion**

269 Arthrofibrosis is a serious complication after ACLr because of the intensity of the post-  
270 operative arthrogenic muscle inhibition. It is responsible for a long-term strength deficit of the  
271 quadriceps, still present 12 months after surgery. The mechanical component may be added  
272 due to the knee joint stiffness. According to Lysholm score, the knee function improves at 12  
273 months. But the return to running is unusual before 7 post-operative months, despite the  
274 continuation of the rehabilitation care. Likewise, the return to a pivoting and contact sport is  
275 still compromised 1 year after surgery. These findings open perspectives for the management  
276 of arthrofibrosis. Particular attention should be paid to the fight against the arthrogenic  
277 quadriceps inhibition. The treatment may combine technics of neural rehabilitation, such as  
278 contralateral lower-limb strengthening, transcutaneous electrical nerve stimulation or  
279 electrical neuromuscular stimulation. The interest of the surgical revision should be  
280 considered according to this type of rehabilitation and the delay from the surgery.

281

282

283 **References**

- 284 1. Calloway SP, Soppe CJ, Mandelbaum BR. Clinical Outcomes After Arthroscopic  
285 Release of Patellofemoral Arthrofibrosis in Patients With Prior Anterior Cruciate  
286 Ligament Reconstruction. *Arthroscopy*. 2018;34(5):1603-1607.  
287 doi:10.1016/j.arthro.2017.12.011
- 288 2. Cavanaugh JT, Powers M. ACL Rehabilitation Progression: Where Are We Now? *Curr*  
289 *Rev Musculoskelet Med*. 2017;10(3):289-296. doi:10.1007/s12178-017-9426-3
- 290 3. Dauty M, Tortelier L, Huguet D, Potiron-Josse M, Dubois C. Consequences of pain on  
291 isokinetic performance after anterior cruciate ligament reconstruction using a  
292 semitendinosus and gracilis autograft. *Rev Chir Orthop Reparatrice Appar Mot*.  
293 2006;92(5):455-463.
- 294 4. Dauty M, Tortellier L, Rochcongar P. Isokinetic and anterior cruciate ligament  
295 reconstruction with hamstrings or patella tendon graft: analysis of literature. *Int J Sports*  
296 *Med*. 2005;26(7):599-606. doi:10.1055/s-2004-821342
- 297 5. Davies GJ, McCarty E, Provencher M, Manske RC. ACL Return to Sport Guidelines and  
298 Criteria. *Curr Rev Musculoskelet Med*. 2017;10(3):307-314. doi:10.1007/s12178-017-  
299 9420-9
- 300 6. Dingenen B, Gokeler A. Optimization of the Return-to-Sport Paradigm After Anterior  
301 Cruciate Ligament Reconstruction: A Critical Step Back to Move Forward. *Sports Med*.  
302 2017;47(8):1487-1500. doi:10.1007/s40279-017-0674-6
- 303 7. Edwards PK, Ebert JR, Joss B, et al. Patient Characteristics and Predictors of Return to  
304 Sport at 12 Months After Anterior Cruciate Ligament Reconstruction: The Importance of  
305 Patient Age and Postoperative Rehabilitation. *Orthop J Sports Med*.  
306 2018;6(9):2325967118797575. doi:10.1177/2325967118797575
- 307 8. Ekhtiari S, Horner NS, de Sa D, et al. Arthrofibrosis after ACL reconstruction is best  
308 treated in a step-wise approach with early recognition and intervention: a systematic  
309 review. *Knee Surg Sports Traumatol Arthrosc*. 2017;25(12):3929-3937.  
310 doi:10.1007/s00167-017-4482-1
- 311 9. Fischer K, van der Bom JG, Mauser-Bunschoten EP, et al. The effects of postponing  
312 prophylactic treatment on long-term outcome in patients with severe hemophilia. *Blood*.  
313 2002;99(7):2337-2341.
- 314 10. Fukunaga T, Johnson CD, Nicholas SJ, McHugh MP. Muscle hypotrophy, not inhibition,  
315 is responsible for quadriceps weakness during rehabilitation after anterior cruciate  
316 ligament reconstruction. *Knee Surg Sports Traumatol Arthrosc*. 2019;27(2):573-579.  
317 doi:10.1007/s00167-018-5166-1
- 318 11. Gillespie MJ, Friedland john, Dehaven K. Arthrofibrosis: Etiology,classification,  
319 histopathology, and treatment. *Operative Techniques in Sports Medicine*. 1998;6(2):102-  
320 110.
- 321 12. Hughston JC. Complications of anterior cruciate ligament surgery. *Orthop Clin North*  
322 *Am*. 1985;16(2):237-240.

- 323 13. Impellizzeri FM, Bizzini M, Rampinini E, Cereda F, Maffiuletti NA. Reliability of  
324 isokinetic strength imbalance ratios measured using the Cybex NORM dynamometer.  
325 *Clin Physiol Funct Imaging*. 2008;28(2):113-119. doi:10.1111/j.1475-  
326 097X.2007.00786.x
- 327 14. Jackson DW, Schaefer RK. Cyclops syndrome: loss of extension following intra-  
328 articular anterior cruciate ligament reconstruction. *Arthroscopy*. 1990;6(3):171-178.  
329 doi:10.1016/0749-8063(90)90072-1
- 330 15. Klein W, Shah N, Gassen A. Arthroscopic management of postoperative arthrofibrosis  
331 of the knee joint: indication, technique, and results. *Arthroscopy*. 1994;10(6):591-597.  
332 doi:10.1016/s0749-8063(05)80053-2
- 333 16. Kuenze CM, Hertel J, Weltman A, Diduch D, Saliba SA, Hart JM. Persistent  
334 neuromuscular and corticomotor quadriceps asymmetry after anterior cruciate ligament  
335 reconstruction. *J Athl Train*. 2015;50(3):303-312. doi:10.4085/1062-6050-49.5.06
- 336 17. MacDonald PB, Hedden D, Pacin O, Huebert D. Effects of an accelerated rehabilitation  
337 program after anterior cruciate ligament reconstruction with combined semitendinosus-  
338 gracilis autograft and a ligament augmentation device. *Am J Sports Med*.  
339 1995;23(5):588-592. doi:10.1177/036354659502300512
- 340 18. Magit D, Wolff A, Sutton K, Medvecky MJ. Arthrofibrosis of the knee. *J Am Acad*  
341 *Orthop Surg*. 2007;15(11):682-694. doi:10.5435/00124635-200711000-00007
- 342 19. Mall NA, Chalmers PN, Moric M, et al. Incidence and trends of anterior cruciate  
343 ligament reconstruction in the United States. *Am J Sports Med*. 2014;42(10):2363-2370.  
344 doi:10.1177/0363546514542796
- 345 20. Markolf KL, Hame S, Hunter DM, et al. Effects of femoral tunnel placement on knee  
346 laxity and forces in an anterior cruciate ligament graft. *J Orthop Res*. 2002;20(5):1016-  
347 1024. doi:10.1016/S0736-0266(02)00035-9
- 348 21. Mayr HO, Weig TG, Plitz W. Arthrofibrosis following ACL reconstruction--reasons and  
349 outcome. *Arch Orthop Trauma Surg*. 2004;124(8):518-522. doi:10.1007/s00402-004-  
350 0718-x
- 351 22. Myer GD, Paterno MV, Ford KR, Quatman CE, Hewett TE. Rehabilitation after anterior  
352 cruciate ligament reconstruction: criteria-based progression through the return-to-sport  
353 phase. *J Orthop Sports Phys Ther*. 2006;36(6):385-402. doi:10.2519/jospt.2006.2222
- 354 23. Paulos LE, Rosenberg TD, Drawbert J, Manning J, Abbott P. Infrapatellar contracture  
355 syndrome. An unrecognized cause of knee stiffness with patella entrapment and patella  
356 infera. *Am J Sports Med*. 1987;15(4):331-341. doi:10.1177/036354658701500407
- 357 24. Paulos LE, Wnorowski DC, Greenwald AE. Infrapatellar contracture syndrome.  
358 Diagnosis, treatment, and long-term followup. *Am J Sports Med*. 1994;22(4):440-449.  
359 doi:10.1177/036354659402200402
- 360 25. Perraton L, Clark R, Crossley K, et al. Impaired voluntary quadriceps force control  
361 following anterior cruciate ligament reconstruction: relationship with knee function.

- 362 *Knee Surg Sports Traumatol Arthrosc.* 2017;25(5):1424-1431. doi:10.1007/s00167-015-  
363 3937-5
- 364 26. Pietrosimone BG, Lepley AS, Ericksen HM, Clements A, Sohn DH, Gribble PA. Neural  
365 Excitability Alterations After Anterior Cruciate Ligament Reconstruction. *J Athl Train.*  
366 2015;50(6):665-674. doi:10.4085/1062-6050-50.1.11
- 367 27. Rahr-Wagner L, Lind M. The Danish Knee Ligament Reconstruction Registry. *Clin*  
368 *Epidemiol.* 2016;8:531-535. doi:10.2147/CLEP.S100670
- 369 28. Rambaud AJM, Ardern CL, Thoreux P, Regnaud J-P, Edouard P. Criteria for return to  
370 running after anterior cruciate ligament reconstruction: a scoping review. *Br J Sports*  
371 *Med.* Published online May 2, 2018. doi:10.1136/bjsports-2017-098602
- 372 29. Rice DA, McNair PJ. Quadriceps Arthrogenic Muscle Inhibition: Neural Mechanisms  
373 and Treatment Perspectives. *Seminars in Arthritis and Rheumatism.* 2010;40(3):250-266.  
374 doi:10.1016/j.semarthrit.2009.10.001
- 375 30. Romano VM, Graf BK, Keene JS, Lange RH. Anterior cruciate ligament reconstruction.  
376 The effect of tibial tunnel placement on range of motion. *Am J Sports Med.*  
377 1993;21(3):415-418. doi:10.1177/036354659302100315
- 378 31. Sanders TL, Kremers HM, Bryan AJ, Kremers WK, Stuart MJ, Krych AJ. Procedural  
379 intervention for arthrofibrosis after ACL reconstruction: trends over two decades. *Knee*  
380 *Surg Sports Traumatol Arthrosc.* 2017;25(2):532-537. doi:10.1007/s00167-015-3799-x
- 381 32. Shelbourne KD, Nitz P. Accelerated rehabilitation after anterior cruciate ligament  
382 reconstruction. *J Orthop Sports Phys Ther.* 1992;15(6):256-264.  
383 doi:10.2519/jospt.1992.15.6.256
- 384 33. Shelbourne KD, Patel DV, Martini DJ. Classification and management of arthrofibrosis  
385 of the knee after anterior cruciate ligament reconstruction. *Am J Sports Med.*  
386 1996;24(6):857-862. doi:10.1177/036354659602400625
- 387 34. Shelbourne KD, Wilckens JH, Mollabashy A, DeCarlo M. Arthrofibrosis in acute  
388 anterior cruciate ligament reconstruction. The effect of timing of reconstruction and  
389 rehabilitation. *Am J Sports Med.* 1991;19(4):332-336.  
390 doi:10.1177/036354659101900402
- 391 35. Tegner Y, Lysholm J. Rating systems in the evaluation of knee ligament injuries. *Clin*  
392 *Orthop Relat Res.* 1985;(198):43-49.
- 393 36. Tegner Y, Lysholm J, Odensten M, Gillquist J. Evaluation of cruciate ligament injuries.  
394 A review. *Acta Orthop Scand.* 1988;59(3):336-341.
- 395 37. Thomas AC, Wojtys EM, Brandon C, Palmieri-Smith RM. Muscle atrophy contributes  
396 to quadriceps weakness after anterior cruciate ligament reconstruction. *J Sci Med Sport.*  
397 2016;19(1):7-11. doi:10.1016/j.jsams.2014.12.009
- 398 38. Urbach D, Nebelung W, Becker R, Awiszus F. Effects of reconstruction of the anterior  
399 cruciate ligament on voluntary activation of quadriceps femoris a prospective twitch

400 interpolation study. *J Bone Joint Surg Br.* 2001;83(8):1104-1110. doi:10.1302/0301-  
401 620x.83b8.11618

402 39. Wang J, Ao Y. Analysis of different kinds of cyclops lesions with or without extension  
403 loss. *Arthroscopy.* 2009;25(6):626-631. doi:10.1016/j.arthro.2008.12.006

404 40. Worsham J, Lowe WR, Copa D, et al. Subsequent Surgery for Loss of Motion After  
405 Anterior Cruciate Ligament Reconstruction Does Not Influence Function at 2 Years: A  
406 Matched Case-Control Analysis. *Am J Sports Med.* 2019;47(11):2550-2556.  
407 doi:10.1177/0363546519863347

408

409

410

411

412

413

414

415

416



417 **TABLE 1** Comparison between Arthrofibrosis and control ACLr patient groups

	Arthrofibrosis ACLr group	Control ACLr group	p-value
Age (Year), mean+/-SD <sup>A</sup>	25 +/- 7	25 +/- 6	0.86
Gender n(%) <sup>B</sup>			
Male	39 (66.1%)	345 (71.9%)	0.36
Female	20 (33.9%)	135 (28.1%)	
Weight (Kg) (mean+/-SD) <sup>A</sup>	71 +/- 12	72 +/- 12	0.70
Height (cm) (mean+/-SD) <sup>A</sup>	171 +/- 8	173 +/- 9	0.56
Graft procedure n(%) <sup>B</sup>			
H procedure	33 (55.9%)	330 (68.8%)	0.06
BPTB procedure	26 (44.1%)	150 (31.3%)	
Meniscus procedure n(%) <sup>B</sup>			
Yes	12 (20.3%)	102 (21.3%)	0.99
No	47 (79.7%)	378 (78.8%)	
Extra-articular tenodesis n(%) <sup>B</sup>			
Yes	4 (6.7%)	41 (8.5%)	0.63
No	55 (93.3%)	436 (91.5%)	
Physiotherapy (n sessions+/-SD) <sup>A</sup>	54 +/- 33	41 +/- 18	<0.0001
Lysholm score (mean+/-SD) <sup>C</sup>			
4 months	86 +/- 9 <sup>b</sup>	96 +/- 7	<0.0001
7 months	92 +/- 8 <sup>b</sup>	97 +/- 6	<0.001
12 months	94 +/- 7 <sup>b</sup>	97 +/- 5	0.04
Tegner score (M [min-max]) <sup>C</sup>			
Before ACLr	7 [4-10] <sup>a</sup>	7 [4-10] <sup>a</sup>	0.16
4 months	4 [3-4] <sup>a,b</sup>	4 [3-7] <sup>a,b</sup>	<0.01
7 months	4 [3-6] <sup>a,b,c</sup>	5 [3-10] <sup>a,b,c</sup>	<0.0001
12 months	4 [3-9] <sup>a,b,c</sup>	5 [4-10] <sup>a,b,c</sup>	<0.001
RTS at 7 months n(%) <sup>B</sup>			
No RTS	39 (66.1%)	35 (7.3%)	
Bicycling	16 (27.1%)	109 (22.8%)	<0.0001*
Footing	4 (6.8%)	335 (69.9%)	

418

419 Abbreviations: ACLr: Anterior Cruciate Ligament reconstruction; RTS: Return to Sport; SD:  
 420 Standard deviation; M [min-max]: Median [minimal and maximal values].

421 <sup>A</sup>Student *t* test; <sup>B</sup> $\chi^2$  test, <sup>C</sup>Repeated-measured ANOVA.

422 <sup>a</sup>significant difference between before ACLr and 4 months and 7 months and 12 months.

423 <sup>b</sup>significant difference between 4 months and 7 months and 12 months.

424 <sup>c</sup>significant difference between and 7 months and 12 months.

425

426 **TABLE 2** Limb Symmetry Index comparison at 4 months, 7 months and 12 months after  
 427 ACL reconstruction (repeated-measured ANOVA).  
 428

	Arthrofibrosis ACLr group	Control ACLr group	p-value
<b>LSI Q60 (%)</b>			
4 months	38 +/- 12 <sup>a</sup>	63 +/- 14 <sup>a</sup>	<0.0001
7 months	53 +/- 14 <sup>a</sup>	73 +/- 14 <sup>a</sup>	<0.0001
12 months	68 +/- 13 <sup>a</sup>	85 +/- 11 <sup>a</sup>	<0.0001
<b>LSI Q180 (%)</b>			
4 months	48 +/- 14 <sup>a</sup>	73 +/- 16 <sup>a</sup>	<0.0001
7 months	60 +/- 17 <sup>a</sup>	79 +/- 12 <sup>a</sup>	<0.0001
12 months	74 +/- 11 <sup>a</sup>	89 +/- 11 <sup>a</sup>	<0.0001
<b>LSI H60 (%)</b>			
4 months	66 +/- 16 <sup>a</sup>	88 +/- 14 <sup>b</sup>	<0.0001
7 months	86 +/- 16 <sup>a</sup>	93 +/- 12 <sup>b</sup>	0.01
12 months	92 +/- 16 <sup>a</sup>	93 +/- 13	0.70
<b>LSI H180 (%)</b>			
4 months	77 +/- 25 <sup>a</sup>	93 +/- 17 <sup>b</sup>	<0.0001
7 months	84 +/- 23 <sup>a</sup>	96 +/- 17 <sup>b</sup>	<0.001
12 months	92 +/- 13 <sup>a</sup>	96 +/- 14	0.14

429  
 430 Abbreviations: LSI: Limb Symmetry Index; Q: Quadriceps; H: Hamstring; 60: 60° angular  
 431 speed; 180: 180° angular speed.

432 <sup>a</sup> significant difference between 4 months and 7 months and 12 months

433 <sup>b</sup> significant difference between 4 months and 7 months

434

435

436

437

438

439

440

441

442

443

444 **TABLE 3** Arthrogenic muscle inhibition of ACLr and non-operative knees during the  
 445 evolution in arthrofibrosis and control ACLr groups (two-way repeated-measured ANOVA)  
 446

Graft procedure	Arthrofibrosis ACLr group		Control ACLr group	
	H procedure (n=33)	BPTB procedure (n=26)	H procedure (n=330)	BPTB procedure (n=150)
<b>ACLR Q60 (Nm)</b>				
4 months	72 +/- 32 <sup>a§*</sup>	79 +/- 26 <sup>a§*</sup>	128 +/- 42 <sup>a§*</sup>	120 +/- 34 <sup>a§*</sup>
7 months	106 +/- 52 <sup>a§*</sup>	104 +/- 25 <sup>a§*</sup>	146 +/- 41 <sup>a§*</sup>	141 +/- 37 <sup>a§*</sup>
12 months	130 +/- 52 <sup>a§*</sup>	146 +/- 34 <sup>a§*</sup>	160 +/- 44 <sup>a§*</sup>	162 +/- 38 <sup>a§*</sup>
<b>ACLR Q180 (Nm)</b>				
4 months	58 +/- 28 <sup>a§*</sup>	63 +/- 18 <sup>a§*</sup>	91 +/- 27 <sup>a§*</sup>	88 +/- 21 <sup>a§*</sup>
7 months	81 +/- 37 <sup>a§*</sup>	81 +/- 16 <sup>a§*</sup>	104 +/- 22 <sup>a§*</sup>	100 +/- 23 <sup>a§*</sup>
12 months	98 +/- 34 <sup>a§*</sup>	107 +/- 22 <sup>a§*</sup>	109 +/- 30 <sup>a§*</sup>	113 +/- 25 <sup>a§*</sup>
<b>ACLR H60 (Nm)</b>				
4 months	66 +/- 26 <sup>a§β*</sup>	75 +/- 21 <sup>a§β*</sup>	83 +/- 23 <sup>a§β*</sup>	100 +/- 24 <sup>a§β*</sup>
7 months	87 +/- 31 <sup>a§β*</sup>	106 +/- 20 <sup>a§β*</sup>	97 +/- 26 <sup>a§β*</sup>	115 +/- 26 <sup>a§β*</sup>
12 months	95 +/- 28 <sup>a§β*</sup>	123 +/- 39 <sup>a§β</sup>	102 +/- 27 <sup>a§β*</sup>	120 +/- 25 <sup>a§β</sup>
<b>ACLR H180 (Nm)</b>				
4 months	56 +/- 18 <sup>a§β*</sup>	59 +/- 14 <sup>a§β*</sup>	63 +/- 18 <sup>a§β*</sup>	76 +/- 17 <sup>a§β*</sup>
7 months	64 +/- 21 <sup>a§β*</sup>	84 +/- 14 <sup>a§β</sup>	73 +/- 11 <sup>a§β*</sup>	86 +/- 24 <sup>a§β</sup>
12 months	72 +/- 19 <sup>a§β</sup>	91 +/- 18 <sup>a§β</sup>	76 +/- 20 <sup>a§β</sup>	89 +/- 19 <sup>a§β</sup>
<b>Nop Q60 (Nm)</b>				
4 months	191 +/- 42 <sup>a§</sup>	196 +/- 40 <sup>a§</sup>	188 +/- 47 <sup>a§</sup>	199 +/- 40 <sup>§</sup>
7 months	193 +/- 59 <sup>a§</sup>	199 +/- 45 <sup>a§</sup>	194 +/- 47 <sup>a§</sup>	199 +/- 41 <sup>§</sup>
12 months	196 +/- 54 <sup>a§</sup>	210 +/- 47 <sup>a§</sup>	196 +/- 46 <sup>a§</sup>	211 +/- 41 <sup>§</sup>
<b>Nop Q180 (Nm)</b>				
4 months	124 +/- 31 <sup>a§</sup>	125 +/- 24 <sup>a§</sup>	120 +/- 33 <sup>a§</sup>	127 +/- 31 <sup>a§</sup>
7 months	127 +/- 35 <sup>a§</sup>	127 +/- 24 <sup>a§</sup>	128 +/- 30 <sup>a§</sup>	132 +/- 28 <sup>a§</sup>
12 months	136 +/- 37 <sup>a§</sup>	134 +/- 25 <sup>a§</sup>	136 +/- 31 <sup>a§</sup>	135 +/- 28 <sup>a§</sup>
<b>Nop H60 (Nm)</b>				
4 months	97 +/- 25 <sup>a§β</sup>	115 +/- 25 <sup>a§β</sup>	102 +/- 26 <sup>a§β</sup>	109 +/- 22 <sup>a§β</sup>
7 months	103 +/- 27 <sup>a§β</sup>	122 +/- 27 <sup>a§β</sup>	112 +/- 20 <sup>a§β</sup>	118 +/- 24 <sup>a§β</sup>
12 months	108 +/- 29 <sup>a§β</sup>	130 +/- 32 <sup>a§β</sup>	118 +/- 29 <sup>a§β</sup>	131 +/- 25 <sup>a§β</sup>
<b>Nop H180 (Nm)</b>				
4 months	70 +/- 16 <sup>a§β</sup>	84 +/- 16 <sup>a§β</sup>	75 +/- 20 <sup>a§β</sup>	82 +/- 17 <sup>a§β</sup>
7 months	76 +/- 19 <sup>a§β</sup>	100 +/- 18 <sup>a§β</sup>	84 +/- 22 <sup>a§β</sup>	96 +/- 18 <sup>a§β</sup>
12 months	81 +/- 18 <sup>a§β</sup>	98 +/- 24 <sup>a§β</sup>	86 +/- 22 <sup>a§β</sup>	100 +/- 22 <sup>a§β</sup>

448 Abbreviations: Q: Quadriceps; H: Hamstring; 60: 60° angular speed; 180: 180° angular speed;  
449 ACLr: Anterior Cruciate Ligament reconstruction; BPTB: Bone-Patellar-Tendon-Bone  
450 procedure; Nop: non-operated knee.

451 <sup>a</sup>Significant difference between time of isokinetic measurements

452 <sup>§</sup>Significant difference between the operated and the non-operated knee

453 <sup>β</sup>Significant difference between H and BPTB procedure

454 \*Significant difference between arthrofibrosis and control ACLr group

455

456

457

458 **Figure:** Flowchart