Can biomechanical testing after ACL Reconstruction identify athletes at risk for subsequent ACL injury to the contralateral uninjured limb?

Abstract

Background

Athletes are twice as likely to rupture the anterior cruciate ligament (ACL) on their healthy contralateral knee after ACL reconstruction (ACLR). Although physical testing is commonly used after ACLR to assess injury risk to the operated knee, strength, jump, and change of direction performance and biomechanical measures have not been examined in those that go on to suffer contralateral ACL injury to identify factors that may be associated with injury risk.

Purpose

To prospectively examine differences in biomechanical and clinical performance measures in male athletes 9 months post ACL reconstruction (ACLR) between those who rupture their previously uninjured contralateral ACL and those who have not at 2-year follow–up and examine the ability of these differences to predict contralateral ACL injury.

Study Design

Case-control study

Methods

24 A cohort of male athletes returning to level-1 sports after ACLR (n = 1045) underwent

25 isokinetic strength testing and 3D biomechanical analysis of jump and change of direction

26 (CoD) tests 9 months post-surgery. Participants were followed-up at 2 years re-return to play

27 or at second ACL injury. Between-group differences in patient-reported outcomes,

28 performance measures and 3D biomechanics for the contralateral limb and asymmetry were

29 analysed. Logistic regression was applied to determine the ability of identified differences to

30 predict contralateral ACL injury.

31

32 Results

33 Of the cohort, 993 had follow up at 2 years (95%) with 67 suffering contralateral ACL injury

34 and 38 ipsilateral injury. Male athletes who succumbed to contralateral ACL injury had lower

35 quadriceps strength and biomechanical differences on the contralateral limb during double

36 leg drop jump and single leg drop jump tests compared to those who did not experience an

37 injury. Differences related primarily to deficits in sagittal plane mechanics and plyometric

38 ability on the contralateral side. These variables could explain group membership with fair to

39 good ability (AUC: 0.74–0.80). Patient reported outcomes, limb symmetry of clinical

40 performance measure or biomechanical measures in CoD tasks did not differentiate those at

41 risk for contralateral injury.

42

43 Conclusion

44 This study highlights the importance of sagittal plane control during drop jump tasks and the

45 limited utility of limb symmetry in performance and biomechanical measures when assessing

46 future contralateral ACL injury risk in male athletes. Targeting the identified differences in

47 quadriceps strength and plyometric ability during late stage rehabilitation and testing may

48 reduce ACL injury risk in healthy limbs in male athletes playing level-1 sports.

49

50 Clinical Relevance

51 This study highlights the importance of assessing the contralateral limb after ACLR and

52 identifies biomechanical differences, in particular in the sagittal plane in drop jump tasks, that

53 may be associated with injury to this limb. These factors could be targeted during assessment

54 and rehabilitation with additional quadriceps strengthening and plyometric exercises after

55 ACLR to potentially reduce the high risk of injury to the previously healthy knee.

56

57 Key Terms

58 Anterior Cruciate Ligament Reconstruction, Contralateral knee, Return to Play, Re-injury,

59 Biomechanics

60

61 **What is known about the subject?**

62 ACL injury rates to the contralateral healthy knee after ACL reconstruction are twice as high

63 as injury to the reconstructed knee. Clinical testing after ACL reconstruction has been used to

64 assess the rehabilitation status of the operated limb and previous research has demonstrated

65 that insufficient rehabilitation after surgery can influence re-injury rates. However, no

66 prospective studies have examined the ability of physical testing and biomechanical analysis

67 to identify risk factors for ACL injury to the contralateral knee.

68

69 **How might it impact clinical practice in the future?**

70 This study highlights the importance of assessing biomechanics of the contralateral limb after

71 ACL reconstruction. No differences in patient reported outcome, and commonly used

72 measures of symmetry of strength, jump and CoD performance were identified between those

73 who suffered contralateral ACL injury and those that did not. The findings highlight the

74 importance of the sagittal plane, in particular plyometric ability and vertical stiffness which

75 may be targeted in future assessment and rehabilitation to reduce the high rate of contralateral

76 ACL injury.

77

78 **Introduction**

79 The primary concern after anterior cruciate ligament (ACL) reconstruction (ACLR) is

80 minimising risk of re-rupture of the reconstructed ACL.[29, 31] Risk of re-injury to the

81 reconstructed graft [44, 49] as well as the native ACL on the contralateral limb [51] is considerably

82 higher than risk of ACL injury in previously un-injured healthy athletes.[40, 49, 54, 58] Further, a

83 review of second ACL injury rates (within 5 years) reported a pooled incidence of 5.8% for

84 injury to the ipsilateral operated limb and 11.8% for ACL injury of the contralateral limb.[59]

85 Given this high injury rate after ACLR, identifying risk factors for ACL injury to the

86 contralateral healthy knee that can be addressed or targeted during rehabilitation may be

87 important for improving short and long-term outcomes for athletes.

88

89 Multiple factors have been outlined in the previous research as requiring consideration as part

90 of the RTP process to mitigate against future injury including: time from surgery, muscle

91 strength, clinical examination, hop testing, performance-based criteria and patient reported

92 outcomes (PRO).[3] However the validity of these measures collectively or in isolation in

93 identifying those that will suffer adverse outcomes is unknown.[3, 53] PRO and symmetry of

94 clinical performance measures of isokinetic strength, jump performance, and CoD time in

95 combination are commonly used to assess rehabilitation status after ACLR and have been

96 suggested to influence injury risk to both knees after ACLR.[13, 29] However, these studies did

97 not examine contralateral second knee injuries to identify risk factors specific to injury in the

98 previously healthy knee.

99

Landing and change of direction (CoD) are the two most common ACL injury mechanisms.[1]

Biomechanical variables during landing have been suggested to predict ACL second injury

after ACLR yet CoD has not been explored. Paterno et al. identified several biomechanical

factors predicting second ACL injury during double leg drop jump (DLDJ) tests, including

un-involved limb hip rotation moment, asymmetry of knee extension moment at initial

contact, and knee valgus range of motion during landing.[41] However this study combined

male and female athletes, did not report variables specific to injury to either the ACLR or

contralateral knee or examine single leg drop jump (SLDJ) even though single leg landing is

a more common injury mechanism. Biomechanical differences in kinetic and kinematic

variables in all three planes relating to the ankle, knee, hip and thorax to pelvis in both jump

and CoD tests have been demonstrated between ACLR and contralateral limbs in male

athletes 9 months after ACLR.[21, 25] These same asymmetries are greater than those in healthy,

uninjured control athletes, potentially due to incomplete rehabilitation of the ACLR limb.[22]

Whether these biomechanical differences in relation to greater asymmetry (insufficient

rehabilitation of ACLR limb) or deficits specific to the contralateral limb influence injury risk

to the contralateral knee has not been prospectively examined. Biomechanical differences

have been reported despite no differences in hop and CoD performance between limbs. There

were however large performance differences during the SLDJ which is a measure of

plyometric ability.[21] Plyometric ability, as measured by reactive strength, refers to the

capacity to absorb and then produce force, over short ground contact times, primarily using

the stretch shortening cycle and thus maximising whole body stiffness. These deficits reflect

an inability to absorb and produce force during landing and may reflect a relevant injury risk

factor. Biomechanical differences during jump and CoD tests have been found between those

who re-rupture their reconstructed ACL graft compared to those who do not, despite no

124   differences in clinical performance measures.(in review along with this paper) However, non-

125   physical factors such as graft type[23] graft healing time [5], and surgeon experience [50] may

126   influence ipsilateral graft re-rupture but are not applicable to contralateral ACL injury.

127   Therefore, investigation of the influence of biomechanical and performance measures on risk

128   of ACL injury to the contralateral knee is warranted.

129

130   The aim of this study was to identify differences in strength, jump, and CoD performance,

131   PRO and landing biomechanics associated with future ACL injury to the contralateral limb

132   and assess the ability of these differences to predict who will be injured. Our hypothesis was

133   that there would be differences in strength and biomechanics throughout the kinetic chain

134   during jump and CoD testing and these variables will predict contralateral injury.

135

136

137   **Methods**

138   Athletes were recruited into this prospective case-control study at the Sports Surgery Clinic

139   (Dublin, Ireland) before ACLR from January 1, 2014–December 31, 2016. Before surgery,

140   athletes completed a pre-operative questionnaire outlining their sport, mechanism of injury,

141   and level of desired return after surgery. Males aged 18–35 years who played level-1 sports

142   (multidirectional field sports involving landing, pivoting, and change of direction) and

143   intended to return to the same level of sport were included in the study (n = 1045). All

144   participants underwent primary ACLR using either a bone-patellar tendon-bone or hamstring

145   (gracilis/semitendinosus) graft from the ipsilateral limb. Those who were undergoing second

146   or subsequent ACLR, did not intend to return to level-1 sports, or had meniscal or additional

147   ligament repair at the time of surgery were excluded. The study was registered at

148   clinicaltrials.gov (NCT02771548) and received approval from the clinics ethic committee

149   (25-AFM-010).

150

151   **Testing Protocol**

152   After ACLR, all participants underwent a rehabilitation protocol with weight bearing as

153   tolerated on crutches for 2 weeks, followed by progressive blocks of strength, power, and

154   plyometric exercises, progressing to on-field running and CoD. Athletes were rehabilitated

155   locally by their referring physiotherapist and reviewed by their orthopaedic surgeons at 2

156   weeks, 3 months, and 6–9 months after surgery. As part of their final orthopaedic review,

157   athletes took part in a physical testing protocol at 9 months (range 8-10) post-surgery. Before

158   testing, all participants completed PRO: International Knee Documentation Committee

159   (IKDC; scaled 0-100),[20] Marx Activity Scale (scaled 0-16),[35] and ACL Return to Sport after

160   Injury questionnaire (ACL-RSI; scaled 0-100)[56] with higher scores reflecting higher self-

161   reported knee function, activity levels and self-reported readiness to return to sport

162   respectively. A list of the acronyms used to describe tests and variables is outlined in Table 1.

163

164   Table 1 Acronyms used for tests and variables used

Acronym	Variable
CI	Contralateral Injury Group
NCI	No Contralateral Injury Group
PRO	Patient Reported Outcome
DLDJ	Double Leg Drop Jump
SLDJ	Single Leg Drop Jump
SLCMJ	Single Leg Countermovement Jump
SLHD	Single Leg Hop for Distance
CoD	Change of Direction
IKDC	International Knee Documentation Committee
ACL RSI	Anterior Cruciate Ligament Return to Sports after Injury
COM	Centre of Mass
LSI	Limb Symmetry Index

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166

167

168   Data were collected in a 3D biomechanics laboratory as part of a larger prospective research

169   project and included a DLDJ from 30 cm, single leg drop jump (SLDJ) from 20 cm, and 90°

170   planned and unplanned CoD,[21, 25] as well as measurement of single leg countermovement

171   jump (SLCMJ) height and single leg hop for distance (SLHD).[13, 29, 39] Participants performed

172   a standardised warm-up: 2-min jog, 5 bodyweight squats, and 2 submaximal and 3 maximal

173   double leg countermovement jumps. Each participant performed two sub-maximal practice

174   trials of each movement before three valid test trial attempts (maximal effort and full foot

175   contact on force plate) were captured, with mean of the three trials used for analysis. A 30-

176   second recovery was taken between trials. Lab testing was followed by concentric isokinetic

177   testing of quadriceps and hamstring muscle groups in both limbs at 60°/s from 0-100° knee

178   flexion, reporting peak torque/body mass.[52]

179

180   Movement mechanics data collection took place using an eight-camera motion analysis

181   system (Bonita-B10, Vicon, UK) capturing at 200 Hz, synchronised with two force platforms

182   (BP400600, AMTI, USA) sampling at a frequency of 1000 Hz, recording motion data from

183   24 reflective markers (diameter: 14 mm) and ground reaction forces (Vicon Nexus 1.8.5),

184   which were low-pass filtered using a fourth-order Butterworth filter (cut-off frequency of

185   15Hz).[27] Markers were placed on the lower legs and trunk according to the adapted Plug-in-

186   Gait and kinematic data calculated.[34] Performance measures were calculated for jump (height

187   and length) and CoD (time) tasks. Jump height was calculated using the take-off vertical

188   velocity derived from the vertical ground reaction force signal using the impulse-momentum

189   theorem. Jump length was calculated as the horizontal distance from heel marker at start of

190   the jump to landing using MATLAB (MathWorks Inc, Natick, MA, USA). Reactive strength

191 index was calculated for the DLDJ and SLDJ as jump height divided by ground contact

192 time.[14] Time to complete the 90° CoD was recorded using speed gates (Smartspeed, Fusion

193 Sport, Chicago, Illinois, USA) with a trigger gate 2 m from the start line and exit gate 2 m to

194 the left and right of force plates to indicate end of the manoeuvre.[25]

195

196 Standard inverse dynamics analysis was used to calculate kinetic variables (reported as

197 internal moments) at the ankle, knee, and hip. All kinetic variables were normalised to body

198 mass. A custom MATLAB program was used for processing and calculating trunk-to-pelvis

199 angles, and distance from center of mass (COM) to ankle and knee joint in all three planes.[24]

200 Whole body stiffness when the body was accepting load was calculated as:

201 $$\text{stiffness } (k) = \text{delta vGRF} / \text{sqrt(delta CoMz} \wedge 2)$$

202 where delta for both variables is from impact (the point of initial ground contact) to and end

203 of eccentric phase defined as the first instance at which COM vertical power > 0. Kinetic and

204 kinematic analysis was carried out for the stance phase of each jump and CoD test (defined

205 by ground reaction force [GRF] > 20 N). Curves were normalised to 101 frames and

206 landmark-registered to when centre of mass power reached zero in the Z (vertical) axis,

207 aligning onset of the eccentric phase to 50% of the stance phase, to ensure appropriate

208 comparison of neuromuscular characteristics between limbs and participants during

209 continuous waveform analysis.[36, 45] Limb symmetry index (LSI) for strength and jump

210 performance measures was calculated as: [ACLR side/contralateral side] x 100. The

211 magnitude of asymmetry of biomechanical variables was calculated by subtracting the

212 contralateral limb from the ACLR limb throughout the stance phase.

213

214 **Follow-Up**

215 Participants were followed-up via e-mail to identify second ACL injuries (i.e., ACL injury

216 confirmed on MRI to either the ACLR knee or contralateral knee) at 1 year and 2 years post-

217 surgery using a return-to-play (RTP) questionnaire or were identified if they returned to their

218 original surgeon with diagnosis of another ACL injury. If participants did not reply to the e-

219 mail questionnaire, they received a follow-up phone call to complete the questionnaires. All

220 participants who had surgery and were identified to have ACL injury to their contralateral

221 knee, but no injury to ACLR knee, were included in the contralateral injury (CI) group (n =

222 67) which set the sample size for the study. A cohort of participants who had returned to

223 multidirectional field sports after ACLR and had not experienced a second ACL injury to

224 either knee at 2 years follow-up were assigned to the NCI (no contralateral injury) group. The

225 NCI group was matched to the CI group mean for time from surgery to RTP, time from

226 surgery to 3D biomechanical testing, age, and distribution of graft type (n = 60) to ensure that

227 appropriate comparison and minimise potential influence of non-physical factors on

228 contralateral ACL injury (Figure 1).

229

230

231 Figure 1. Flow diagram of matching process for CI and NCI groups.

232

233 **Statistical Analysis**

234 Differences between CI and NCI groups in LSI, PRO, isokinetic peak torque of quadriceps

235 and hamstrings, planned and unplanned 90° CoD time, and SLDJ, SLCMJ, and SLHD jump

236 performance on the contralateral side were examined using student's independent t-test.

237 Effect sizes for differences between groups for each variable were calculated using Cohen's d

238 (0.2–0.49 = small; 0.5–0.79 = medium; ≥0.8 = strong).[6] Odds ratio were calculated for

239 subjects being in the NCI group when they had >90% LSI for quadriceps strength, hamstring

240 strength SLCMJ and SLDJ jump height for all five tests collectively. SPM (1d, unpaired t-

241 test; parametric) was used to examine differences in biomechanical variables (vGRF, angles

242 and moments at hip, knee and ankle, thorax to pelvis angles and COM to ankle and knee in

243 all three planes) between CI and NCI groups for the contralateral limb and asymmetry

244 between limbs (ACLR limb minus contralateral limb) between groups for each

245 biomechanical variable for DLDJ, SLDJ, and planned and unplanned 90° CoD during stance.

246 Mean effect size across phases with significant differences ($p < 0.05$) was reported, excluding

247 phases with Cohen's d < 0.5. Time points and mean effect sizes with a significant difference

248 between the two groups and mean values for each group across that phase are reported.

249 Graphs for biomechanical variables with differences are displayed in Appendix A.

250

251 To assess the ability of the results to predict ACL re-injury, logistic regressions were

252 performed using a maximum of 5 predictor variables that were chosen based on the largest

253 effect sizes of the identified differences for the magnitude and symmetry analysis. Only these

254 features were chosen to achieve an input to observations ratio of 1:10 to 15, to generate a

255 model avoiding overfitting the model to the data.[2, 42] It should be noted that if a feature was

256 multicollinear (correlation between them >.70) with a higher ranked feature it was excluded

257 and an additional lower ranked feature was included. Predictor variables utilized were the

258 average value of the phases within a biomechanical waveform that differed between groups.

259 Before fitting the logistic regression predictor variables were transformed into z-scores and

260 cohorts were balanced so that the sample size of CI and NCI was equal. To transform a

261 predictor variable vector **x** (e.g. contact time; n x m; n = 88 subjects; m = 1 feature) into z

262 scores the following equation was used:

263 $$z = (\mathbf{x} - \bar{\mathrm{x}}) / S,$$

264

265 with x̄ being the average and *S* is standard deviation of the sample within **x**. During the

266 fitting, data were balanced (using Synthetic Minority Over-sampling Technique)[4] so the

267 minority class contained the same number of observations as the majority class. To interpret

268 predictive ability of the logistic regression, receiver operating curve (RoC) and prediction

269 accuracy are reported. Area under the curve (AUC) was used to classify findings (nil = 0.50;

270 poor > 0.60; fair > 0.70; good > 0.80), while the accuracy measure was compared to expected

271 accuracy (accuracy if the most frequent class was guessed). A summary of the data points

272 and statistical analysis is outlined in Table 2.

273

274 Table 2 Summary of data points and statistical analysis

Dataset	Analysis
PRO data	Mann-Whitney U Test
Strength, Jump and CoD Performance Contralateral side and LSI	Independent Student's t-test Odds Ratio CI if ≥ 90% LSI Logistic Regression
Biomechanics Contralateral side and ASYM	1D SPM independent Student's t-test Logistic Regression

275 PRO – patient reported outcome; CoD - change of direction; LSI - limb symmetry index,

276 ASYM - asymmetry; SPM - statistical parametric mapping

277

278 **Results**

279 Of the 1045 male primary ACLRs, 67 contralateral ACL injuries were recorded, 38 ipsilateral

280 ACL injuries and 52 were lost to follow up (95% follow up). Of those participants who

281 suffered contralateral ACL injury (CI group), 3D biomechanical analysis was recorded on 55

282 contralateral participants (12 did not attend follow-up 3D biomechanical analysis) and was

283 matched to 60 athletes who completed 3D biomechanical analysis but did not experience

284   ACL injury to either knee 2 years after surgery (NCI group). Mean time to contralateral

285   injury was 23.3 (±9.8) months (Table 3). There was no significant difference in IKDC, ACL-

286   RSI, or Marx Activity Scale scores between groups (Table 4).

287   Table 3. Anthropometric data

	CI (mean ± SD)	NCI (mean ± SD)	p-value
Subject Numbers	55	60	
Graft Type (BPTB/HT)	46/9	48/12	0.61
Age (years)	21.3 (±4.2)	21.9 (±4)	0.43
Mass (Kg)	80.7 (±10)	81.5 (±11.6)	0.69
Height (cm)	179.4 (±6.3)	180.4 (±5.6)	0.36
Surgery to RTP (months)	10.3 (±4.3)	9.7 (±2.3)	0.35
Surgery to Testing (months)	9.0 (±3.1)	9.4 (±1.2)	0.32
Surgery to Re-Injury (months)	23.3 (±9.8)		
RTP to Re-Injury (months)	13.0 (±9.5)		

288   CI – contralateral injury; NCI – no contralateral injury; SD – standard deviation; BPTB – bone patellar tendon bone; HT – hamstring

289 tendon; RTP – return to play

290

291   Table 4. Patient-reported outcome (PRO) measures for the contralateral injury (CI) and no

292   contralateral injury (NCI) groups

293

PRO	CI	NCI		
	Mean (±SD)		p-value	Effect Size
IKDC	79.1 (12.0)	82.4 (10.6)	0.17	0.21
ACL RSI	75.8 (17.8)	78.1 (15.3)	0.49	0.10
Marx	10.8 (3.5)	11.2 (3.2)	0.29	0.12

294

295 PRO – patient-reported outcome measure; CI – contralateral injury; NCI – no contralateral injury; SD – standard deviation; IKDC –

296 International Knee Documentation Committee; ACL-RSI – anterior cruciate ligament return to sport after injury; Marx – Marx Activity

297 Scale

298

299 ***Strength, Jump, and CoD Performance Measures***

300 There was a significant difference with a small effect size in quadriceps peak torque on the

301 contralateral side (effect size d = 0.39), with significantly lower strength in the CI group

302 (Table 5). No difference was observed between groups on the contralateral side for hamstring

303 strength, SLCMJ and SLDJ height, or SLHD distance, or for the corresponding LSI. The

304 odds of being in the NCI group were 0.54 (95% CI: 0.02–16.39) if the athlete achieved >90%

305 LSI across all five tests. Similarly, no differences were detected between contralateral limbs

306 in planned CoD performance time (1.45 ± 0.12 s vs. 1.42 ± 0.08 s; $p = 0.162$) or LSI (98.9 ±

307 4.8% vs. 98.9 ± 4.7%; $p = 0.982$), or for the unplanned CoD (1.56 ± 0.02 s vs. 1.52 ± 0.09 s;

308 $p = 0.206$) or LSI (98.5 ± 4.5% vs. 98.3 ± 5.3%; $p = 0.840$).

309

310

Table 5. Strength and jump performance measures (mean (±SD)) and limb symmetry index

(LSI)

Test	Contralateral Injury		Contralateral Matched		p-value	Effect Size
		95% CI		95% CI		
Quadriceps (N/Kg)	216.3 (38.8)	206 to 227	231.3 (36.3)	222 to 240	0.032*	0.39
LSI (%)	80.9 (14.6)	76 to 85	84.2 (14.6)	80 to 88	0.235	0.22
>90% LSI success rates	31%		36%		0.593	
Hamstring (N/Kg)	127.3 (24.9)	120 to 134	135.7 (23.4)	130 to 142	0.063	0.34
LSI (%)	96.9 (14.5)	92.9 to 100	96.5 (10.6)	93 to 99	0.894	0.02
>90% LSI success rates	73%		73%		0.982	
SLCMJ (cm)	12.1 (2.3)	11.5 to 12.8	11.9 (2.4)	11.2 to 12.5	0.561	0.11
LSI (%)	85.8 (13.2)	82 to 90	84.4 (14.6)	81 to 88	0.627	0.09
>90% LSI success rates	40%		38%		0.792	
SLDJ (cm)	12.1 (3.2)	11.2 to 13.0	12.4 (2.7)	11.7 to 13.1	0.564	0.11
LSI (%)	78.1 (16.7)	73 to 83	74.1 (14.8)	70 to 78	0.186	0.25
>90% LSI success rates	12%		18%		0.393	
SLHD (cm)	152.3 (27.0)	144 to 160	154.9 (19.9)	150 to 160	0.562	0.11
LSI (%)	95.1 (15.5)	90 to 99	94.2 (12.4)	91 to 97	0.749	0.06
>90% LSI success rates	61%		66%		0.645	
>90% LSI success rates for all 4 tests	2%		2%		0.921	

313 *$p < 0.05$. CI – contralateral injury; NCI – no contralateral injury; LSI – limb symmetry index; SLCMJ – single leg countermovement jump;

314 SLDJ – single leg drop jump; SLHD – single leg hop for distance; Cint – confidence interval; SD – standard deviation

315

Biomechanical Analysis

Differences on contralateral side

No significant differences were detected in joint mechanics during planned and unplanned

CoD. For DLDJ, there were strong effect size differences between groups on the contralateral

side for ground contact time (d = 0.83), COM vertical stiffness (d = 0.80), and COM vertical

distance to the knee and ankle (both d = 0.80), with significantly longer contact times, less

COM stiffness, and lower COM distances in the CI group (Table 6; Figure 2). There were

medium effect size differences between groups for vertical GRF (30%–73% and 83%–99%;

d = 0.74 and d = 0.78, respectively; Figure 3), with significantly lower vertical GRF through

most of the stance but higher towards the end. This was reflected in lower reactive strength

index in the CI group (d = 0.62).

Figure 2. Illustration of biomechanical differences on contralateral side during DLDJ in CI group (bold image)

compared to NCI group (blurred image).

Figure 3. Vertical GRF on contralateral side for the CI group and matched NCI cohort during first ground

contact of DLDJ. Top panel illustrates mean and SD clouds for CI group (black) and NCI group (blue). Middle

panel illustrates SPM{t}, the t-statistic as a function of time describing difference between groups. Bottom panel

illustrates effect size as a function of time, describing magnitude of the effect. Shaded portions of the bottom

panel indicate average Cohen's d > 0.5, with orange indicating medium effect size throughout those phases.

Several significant joint kinematic differences, primarily in the sagittal plane, were detected

between CI and NCI groups, including more hip flexion (14%–95%; d = 0.76), knee flexion

(14%–94%; d = 0.71), ankle dorsiflexion (69%–92%; d = 0.63), anterior pelvic tilt (43%–

342   88%; d = 0.61), and thorax to pelvis flexion (24%–100%; d = 0.6) in the CI group. In

343   addition, there were several joint kinetic differences between CI and NCI groups in the

344   sagittal plane, including lower and then greater hip extension moment (0%–6% and 62%–

345   82%; d = 0.62 and d = 0.71, respectively), lower ankle plantar flexion moment through mid-

346   stance and greater at end stance (24%–74% and 84%–93%; d = 0.76 and d = 0.68,

347   respectively), and increased knee extension moment in early and late stance but lower in mid

348   stance (3% - 7%, 17%–21%, 44%-59% and 82%–93%; d = 0.62, d = 0.60, d - 0.59 and d =

349   0.72, respectively) on the contralateral side in the CI group.

350   Outside of the sagittal plane, there was less knee valgus moment during the middle of stance

351   followed by greater valgus moment at end of stance (42% - 62%, 84% - 94%; d = 0.60 d =

352   0.64). The variables selected for inclusion in the regression model included contact time,

353   COM to ankle, hip extension moment (62-82%) and hip rotation moment (both phases

354   identified as significantly different) and could predict membership of the CI group with an

355   accuracy of 71.2% (baseline 53.2%), with a sensitivity of 0.83 and specificity of 0.58 (AUC

356   = 0.80).

357

358   Table 6. Differences between groups in biomechanical variables on the contralateral side during DLDJ

				Difference Between Contralateral Injury and Contralateral Matched Cohort on ACLR side - DLDJ				
Variable	Start	End	CI non-ACLR mean (± SD)	95% Cint	NCI non-ACLR mean (± SD)	95% Cint	p - value	Effect Size
Contact Time (sec)			0.34 (0.10)	0.32 to 0.37	0.27 (0.06)	0.25 to 0.29	< 0.001	0.83
COM Stiffness (N/Kg/mm)			91.2 (48.8)	77.5 to 104.9	133.5 (50.7)	120.3 to 146.7	< 0.001	0.80
COM to Ankle Vertical (mm/BH)	10	93	0.41 (0.02)	0.40 to 0.42	0.43 (0.02)	0.42 to 0.44	< 0.001	0.80
COM to Knee Vertical (mm/BH)	11	92	0.22 (0.02)	0.21 to 0.22	0.23 (0.14)	0.23 to 0.24	< 0.001	0.80
Vertical GRF (N/Kg)	30	73	18.0 (4.6)	16.7 to 19.3	21.4 (3.7)	20.4 to 22.4	< 0.001	0.74
	83	99	4.1 (1.4)	3.7 to 4.5	3.0 (0.9)	2.8 to 3.3	< 0.001	0.78
Hip Flexion Angle (º)	14	95	54.7 (12.4)	51.3 to 58.3	45.3 (9.9)	42.7 to 47.9	< 0.001	0.76
Ankle Plantarflexion Moment (Nm/Kg)	22	74	2.2 (0.7)	2.0 to 2.4	2.7 (0.6)	2.6 to 2.8	< 0.001	0.76
	84	93	0.7 (0.3)	0.6 to 0.8	0.5 (0.2)	0.4 to 0.6	0.004	0.68
Knee Flexion Angle (º)	14	94	63.8 (12.5)	60.3 to 67.4	55.6 (8.8)	53.3 to 57.9	< 0.001	0.71
Knee Extension Moment (Nm/Kg)	3	7	0.01 (0.42)	-0.12 to 0.11	-0.24 (0.26)	-0.17 to -0.31	0.027	0.62
	17	21	1.3 (0.6)	1.1 to 1.4	0.9 (0.5)	0.8 to 1.1	0.030	0.60

			CI		NCI		p	
	44	59	2.4 (0.8)	2.2 to 2.6	2.8 (0.6)	2.6 to 3.0	< 0.001	0.59
	82	93	0.02 (0.5)	-0.1 to 0.2	-0.4 (0.4)	-0.3 to -0.5	0.001	0.72
Hip Extension Moment (Nm/Kg)	0	6	0.5 (0.6)	0.3 to 0.6	0.8 (0.5)	0.7 to 0.9	0.005	0.62
	62	82	0.7 (0.6)	0.5 to 0.8	0.2 (0.5)	0.1 to 0.4	< 0.001	0.71
Hip External Rotation Moment (Nm/Kg)	4	8	0.03 (0.07)	0.01 to 0.04	-0.02 (0.05)	-0.03 to -0.01	0.021	0.69
	94	98	0.01 (0.05)	0 to 0.03	-0.02 (0.05)	-0.03 to 0.05	0.024	0.64
Knee Valgus Moment (Nm/Kg)	42	62	1.5 (0.6)	1.3 to 1.6	1.9 (0.7)	1.7 to 2.1	< 0.001	0.60
	84	94	0.3 (0.2)	0.2 to 0.4	0.1 (0.2)	0.1 to 0.2	0.010	0.64
Reactive Strength (cm/sec)			0.8 (0.2)	0.7 to 0.8	0.9 (0.2)	0.8 to 1.0	< 0.001	0.62
Anterior Pelvic Tilt (º)	43	88	23.7 (6.1)	22.0 to 25.4	19.8 (5.8)	18.4 to 21.4	0.009	0.61
		10						
Thorax to Pelvis Extension (º)	24	0	5.5 (7.6)	3.4 to 7.7	10.1 (5.9)	8.5 to 11.6	0.007	0.60

359

360 CI – contralateral injury; NCI – no contralateral injury; ACLR – anterior cruciate ligament reconstruction; start/end - % of gait cycle; DLDJ – double leg drop jump; BH - body height; sec - seconds; Cint – confidence

361 interval; Contra – contralateral; SD – standard deviation; COM – center of mass ; GRF – ground reaction force; N - newton; Kg - kilogram; cm - centimetre; m - metre;

362

363   In the SLDJ, similar biomechanical differences in the sagittal plane were again evident

364   between CI and NCI groups on the contralateral side. (Table 7; Figure 2). There was

365   significantly less distance vertically from COM to knee (12%–83%; d = 0.73) and ankle

366   (12%–88%; d = 0.70), longer ground contact times (d = 0.70), less COM stiffness vertically

367   (d = 0.70), and lower reactive strength (d = 0.50) on the contralateral side in the CI group.

368   Further, there was higher, then lower, then higher vertical GRF in the CI group (3%–11%,

369   32%–68%, 86%–99%; d = 0.65, d = 0.69, d= 0.63, respectively). In the sagittal plane, there

370   was significantly increased hip flexion (14%–88%; d = 0.59), increased knee flexion (18%–

371   24% and 64%–92%; d = 0.52 and d =0.58, respectively), increased ankle dorsiflexion (84%–

372   88%; d = 0.52), and increased trunk on pelvis flexion (23%–43%; d = 0.50) in the CI group.

373   In addition, there was significantly higher hip extension moment in (74%–79%; d = 0.61),

374   increased knee extension moment in early and late stance (13% - 18%, and 83%–89%; d =

375   0.60 and d = 0.58, respectively; as well as reduced ankle plantarflexion moment through mid

376   stance (22% - 63%; d = 0.61) in the CI group. In the frontal plane, there was significantly

377   greater internal knee valgus moment (11%–15%; d = 0.58) and ipsilateral thorax on pelvis

378   side flexion (54%–72%; d = 0.52) in the CI group. There were no differences in the

379   transverse plane. The COM to knee, COM Stiffness, vertical GRF (3 to 11% and 33 to 68%)

380   and hip extension moment were selected for the regression model and could predict

381   membership of the CI group with an accuracy of 62.1% (baseline 53.2%), with a sensitivity

382   of 0.51 and specificity of 0.75 (AUC: 0.75).

Table 7. Biomechanical differences on the contralateral side during SLDJ

Variable	Start	End	CI non-ACLR mean (± SD)	95% Cint	NCI non-ACLR mean (± SD)	95% Cint	p-value	Effect Size
				Difference Between Contralateral Injury and Contralateral Matched Cohort on ACLR side - SLDJ				
COM to Knee Vertical (mm/BH)	12	84	0.24 (0.01)	0.24 to 0.25	0.25 (0.01)	0.25 to 0.26	< 0.001	0.73
Contact Time (sec)			0.39 (0.08)	0.37 to 0.41	0.33 (0.05)	0.32 to 0.35	< 0.001	0.70
COM Stiffness (N/Kg/mm)			138.3 (54.8)	122.8 to 153.6	180.1 (56.4)	165.6 to 194.7	< 0.001	0.70
COM to Ankle Vertical (mm/BH)	12	89	0.44 (0.02)	0.43 to 0.45	0.46 (0.01)	0.45 to 0.46	< 0.001	0.7
Vertical GRF (N/Kg)	3	11	9.8 (3.1)	8.9 to 10.7	8.2 (1.5)	7.8 to 8.6	0.002	0.65
	33	68	25.1 (4.5)	23.8 to 26.3	28.2 (3.9)	27.2 to 29.2	< 0.001	0.69
	87	99	4.4 (1.5)	2.3 to 6.5	3.5 (1.1)	1.7 to 5.4	< 0.001	0.63
Hip Extension Moment (Nm/Kg)	74	79	0.3 (0.7)	0.1 to 0.5	-0.2 (0.57)	-0.3 to 0	0.004	0.61
Ankle Plantarflexion Moment (Nm/Kg)	22	63	2.9 (0.6)	2.7 to 3.1	3.4 (0.7)	3.2 to 3.6	< 0.001	0.61
Knee Extension Moment (Nm/Kg)	13	18	1.0 (0.8)	0.7 to 1.3	0.5 (0.67)	0.24 to 0.77	0.020	0.60
	83	89	0.2 (0.5)	0 to 0.5	-0.1 (0.46)	-0.35 to 0.23	0.010	0.58

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Hip Flexion Angle (º)	14	88	43.8 (9.2)	41.2 to 46.4	38.5 (7.0)	36.8 to 40.4	0.001	0.59
Knee Flexion Angle (º)	18	22	51.8 (8.9)	49.3 to 54.3	47.5 (7.1)	45.7 to 49.4	0.040	0.52
	64	92	40.7 (9.2)	38.2 to 43.3	35.5 (7.7)	33.6 to 37.5	0.003	0.58
Knee Valgus Moment (Nm/Kg)	11	15	0.9 (0.4)	0.7 to 1.0	0.7 (0.3)	0.6 to 0.8	0.030	0.58
Ankle Dorsiflexion (º)	84	88	1.3 (7.4)	-3.6 to 6.2	-2.6 (6.9)	-7.5 to 2.3	0.040	0.52
Thorax to Pelvis Side Flexion (º)	54	72	0.8 (4.9)	-0.5 to 2.2	-1.7 (4.6)	-2.9 to 4.6	0.020	0.52
Thorax to Pelvis Extension (º)	23	43	-2.5 (9.2)	-5.0 to 0.1	2.1 (8.3)	-0.1 to 4.2	0.030	0.51
Reactive Strength (cm/sec)			0.32 (0.12)	0.29 to 0.35	0.37 (0.09)	0.35 to 0.40	0.010	0.50

386

387

388 CI – contralateral injury; NCI – no contralateral injury; start/end - % of gait cycle; ACLR – anterior cruciate ligament reconstruction; SLDJ –single leg drop jump; BH - body height; sec - seconds; COM – center of

389 mass ; GRF – ground reaction force; CInt – confidence interval; SD – standard deviation mm - metre;

390

391 *Difference in asymmetry between groups*

392 Differences in asymmetry of biomechanical variables between limbs between CI and NCI

393 groups are reported in Table 8. There was no significant difference in asymmetry between

394 groups for SLDJ or planned or unplanned CoD. In the DLDJ there was significantly greater

395 asymmetry in the CI group for knee varus angle (91%–100%; d = 0.66), with less knee varus

396 on the contralateral limb.

397

398   Table 8. Differences in asymmetry of biomechanical variables between groups

Difference Between Limbs Between Contralateral Injury and Contralateral Matched Cohort on ACLR side - DLDJ								
Variable	Start	End	CONTRA ACLR side (± SD)	95% Cint	CONTRA Matched ACLR side (± SD)	95% Cint	p - value	Effect Size
Knee Varus Angle (º)	91	100	1.0 (2.9)	0.9 to 1.2	-0.7 (2.1)	-0.6 to -0.8	0.03	0.66

399   CI – contralateral injury; NCI – no contralateral injury; ACLR – anterior cruciate ligament reconstruction; DLDJ – double leg drop jump; CInt – confidence interval; SD – standard deviation;

400

Discussion

This study found there were quadriceps strength and biomechanical differences primarily in the sagittal plane during plyometric tests on the contralateral side 9 months post-surgery for male athletes who experienced contralateral injury after ACLR compared to those who did not at 2 years post-reconstruction. These differences had fair to good ability to predict risk of future contralateral injury and were present despite no difference in LSI between groups and minimal biomechanical asymmetry between groups. Given the higher contralateral ACL injury rate reported in the literature, this study highlights the importance of assessing the contralateral limb and suggests tests and variables that should be targeted during rehabilitation and RTP testing that may play an important role in minimising risk of contralateral ACL injury after ACLR.

To the authors knowledge, the influence of strength and jump performance measures on contralateral ACL injury has not been investigated previously. This study demonstrated no significant difference in LSI for quadriceps and hamstring strength, jump testing, and timed CoD performance between CI and NCI groups. In addition, when combining the achievement of >90% LSI across strength and jump tests it had little influence on the odds of having a contralateral injury (OR: 0.54; 95% CI: 0.02–16.39). Further, few differences in asymmetry of biomechanical variables between groups were evident. The only asymmetry finding was increased asymmetry of knee varus angle in DLDJ at the end of stance. These limited number of findings suggest asymmetry may not be a major factor in subsequent contralateral ACL injury.

424   There were several differences between groups in the sagittal plane on the contralateral side

425   during the double leg and single leg drop jump. The contralateral limb in the contralateral

426   injury group demonstrated differences in plyometric ability and whole-body stiffness

427   compared to the NCI group, as reflected in differences in reactive strength index (but not

428   jump height). In both the double and single leg drop jump, there were longer ground contact

429   times, reduced centre of mass stiffness, and greater drop of the centre of mass vertically

430   relative to the knee and ankle in the contralateral injury group. This was accompanied by

431   increased flexion at the hip, knee, ankle, and thorax and differences in kinetic variables in the

432   sagittal plane with greater, then less, then greater vertical GRF, ankle plantar flexion moment

433   and knee extension moment as well as changes in hip extension moment in the contralateral

434   injury group. This reduction in reactive strength (driven by longer ground contact times) in

435   combination with higher vertical GRF and higher knee extension moments early in stance

436   may be a major contributor to excessive ACL strain and subsequent ACL injury.[12, 18, 33]

437   Greater knee flexion, longer ground contact times, and greater drop of the centre of mass

438   relative to the ankle during DLDJ have also been identified in male athletes who re-rupture

439   their reconstructed knee after ACLR (King et al., in review). These results suggest that

440   plyometric ability or whole-body stiffness may be important risk factors for ACL injury in

441   previously uninjured knees in male athletes but also for reconstructed knees. Given that ACL

442   rupture normally occurs in the first 40 milliseconds after ground contact,[26] greater muscular

443   co-contraction and early rate of force development associated with increased plyometric

444   ability [8, 30] may be important in controlling anterior tibial translation and ACL loading after

445   ACLR. In addition, ACL injury prevention programmes that have been demonstrated to be

446   effective in reducing ACL injury rates have all included various plyometric exercises (drop

447   jumps, tuck jumps, bounding etc) and it may be that this component of these programmes is

448   highly important in contributing to the reduced injury rates.[15, 32, 37]

449

Much of the focus during rehabilitation is to optimise recovery of quadriceps strength on the ACLR side.[39] In this study those who experienced contralateral injury had lower quadriceps strength of the contralateral limb than those that did not. Previous research has reported decrements in quadriceps strength on the contralateral side after reconstruction, and those decrements may influence second ACL injury risk.[57] Quadriceps strength accounts for ~30% of SLCMJ and SLDJ height performance,[7, 11] and its re-development after ACLR may be an important factor in developing plyometric capacity and may be an important factor to consider when minimising ACL injury risk in healthy limbs. In this study, we found no differences in CoD biomechanics between CI and NCI groups. If plyometric ability or whole body stiffness is an important measure in contralateral ACL injury risk for male athletes, it is intuitive that this would be more evident in drop jump tests rather than CoD tests, despite the fact that CoD is a common mechanism of ACL injury.[1]

462

Fewer differences between groups were observed in the frontal and transverse plane compared to sagittal plane of both DLDJ and SLDJ on the contralateral side. There was greater internal knee valgus moment in both tests (earlier stance in SLDJ, later stance in DLDJ) but lower through midstance in the DLDJ in the CI group. The joint moment signals demonstrated a similar pattern: higher moments earlier and later but lower moments in mid-stance in the CI group. These findings are different to previous studies in female athletes in which external knee valgus was identified as a risk factor for primary injury[17] There were lower maximum internal valgus moments in the CI group, which may reflect a reduced ability to resist external valgus moments upon more chaotic dynamic challenges on return to sport. Paterno et al reported knee valgus range of motion and hip rotation impulse as predictors of second ACL injury. This is not replicated in our study potentially due to our

474 focus solely on male athletes and contralateral second injuries.[41] In SLDJ, there was

475 increased ipsilateral trunk sway over the contralateral limb in the CI group, which is a

476 common ACL injury mechanism,[1] influences knee frontal plane loading,[9, 10] and, in

477 combination with knee valgus movement, is a risk factor for non-contact knee injuries.[16] That

478 a greater number of variables indicated differences in the sagittal than in the frontal plane in

479 this male cohort compared to previous research may be due to the difference gender/sex of

480 our participants. Females are more likely to demonstrate dynamic knee valgus during landing

481 [38, 48] and during ACL injury mechanism.[28] Cumulatively our findings add new literature

482 suggesting physical risk factors for ACL injury may be different between sexes and may

483 require differential approaches to assessment and analysis to achieve sex specificity for ACL

484 injury risk.

485

486 The biomechanical variables identified had fair to good ability to predict CI group

487 membership for DLDJ and SLDJ, therefore targeting these variables during rehabilitation and

488 RTP testing may reduce risk of ACL injury. Higher levels of sensitivity vs. specificity are

489 important for ACLR given the severe consequences of second injury. Lower specificity also

490 reflects previous research demonstrating that as many as 20% of healthy athletes are

491 classified as having the same movement strategies as those who have undergone ACLR,[46]

492 suggesting that movement alone does not account for all risk related to ACLR injury.

493

494 **Limitations**

495 As no previous literature examined biomechanical risk factors for contralateral ACL injury,

496 this study examined variables throughout the kinetic chain in several jump and CoD tests.

497 Although this may increase risk of "over-analysis" or finding differences that are not relevant

498 to the outcome, inclusion of only medium and large effect size differences attempted to

499   identify only those differences of largest magnitude to highlight variables of greatest clinical

500   and research interest despite multiple analyses. We performed multiple comparisons, and one

501   could argue that a multiple comparisons correction should have implemented to reduce the

502   type 1 error. However, as the type I error decreases, the chance of type II errors increases.[19,]

503   [43, 47, 55] Our approach to modelling and resultant conclusions were based on P values in

504   combination with effect sizes, and differences with weak effects were excluded to decrease

505   the type 1 error. Although a strength of the study is that it was carried out on a homogenous

506   cohort (male field sports athletes), findings may not be directly extrapolated to other

507   populations. Therefore, future research with similar analyses in female athletic populations is

508   needed to identify risk factors specific to that cohort as well as potential differences in risk

509   factors for male and female athletes for additional ACL injury after ACLR. In addition,

510   future research verifying the ability of the findings to predict the risk of contralateral ACL

511   injury in a different group of athletes would be valuable to re-enforce the generalisability of

512   the findings. Although the 2 year cut-off for second injury was selected as a threshold for the

513   control NCI group the average time for contralateral injury in the CI group was 23.3 months

514   ± 9.8 meaning many of the injuries happened after the selected threshold and raising the

515   potential for injury in the NCI group after selection. However all on further follow up of the

516   NCI group none had suffered injury at a minimum of 3.5 years post-surgery. To improve on

517   the model, other biomechanical measures such as variability and coordination and resistance

518   to fatigue could be included to assess if they are factors which may lead to contralateral

519   injury. These can be used in combination with anthropometric, surgical, and radiological data

520   which can influence ACL injury to build a comprehensive model of factors influencing

521   second ACL injury risk. Finally, intervention studies are needed to examine the most

522   effective way to change variables identified during rehabilitation and the influence of this on

523   subsequent contralateral ACL injury.

524

Conclusion

525 This study highlights that biomechanical analysis of the contralateral limb at 9 months after

527 ACLR could identify movement differences between those who go on to experience a

528 contralateral ACL rupture and those who do not. These variables had a fair to good ability to

529 predict contralateral injury and would not have been identified by evaluating only clinical

530 performance measures. Findings demonstrate lower quadriceps strength, sagittal plane

531 control, and plyometric ability on the contralateral limb in those who experienced subsequent

532 contralateral ACL injury. These was no difference in LSI in performance measures and

533 minimal differences in asymmetry of biomechanical variables. Therefore, this study

534 highlights several factors that may be used in future analysis to model prediction of second

535 ACL injury and target during rehabilitation to reduce contralateral ACL injury after ACLR.

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539 **References**
540

541 **1.** Alentorn-Geli E, Myer GD, Silvers HJ, et al. Prevention of non-contact anterior
542 cruciate ligament injuries in soccer players. Part 1: Mechanisms of injury and
543 underlying risk factors. *Knee Surg Sports Traumatol Arthrosc.* 2009;17(7):705-729.
544 **2.** Babyak MA. What you see may not be what you get: a brief, nontechnical
545 introduction to overfitting in regression-type models. *Psychosom Med.*
546 2004;66(3):411-421.
547 **3.** Burgi CR, Peters S, Ardern CL, et al. Which criteria are used to clear patients to
548 return to sport after primary ACL reconstruction? A scoping review. *Br J Sports Med.*
549 2019;53(18):1154-1161.
550 **4.** Chawla N, Bowyer K, Hall L, Kegelmeyer W. SMOTE: Synthetic Minority Over-
551 sampling Technique. *J. Artif. Intell. Res. (JAIR).* 2002;16:321-357.
552 **5.** Claes S, Verdonk P, Forsyth R, Bellemans J. The "ligamentization" process in
553 anterior cruciate ligament reconstruction: what happens to the human graft? A
554 systematic review of the literature. *Am J Sports Med.* 2011;39(11):2476-2483.
555 **6.** Cohen J. *Statistical Power Analysis for the Behavioral Sciences*; 1988.
556 **7.** Crotty ND, K.; King, E.; Cafferkey., N; McFadden, C; Falvey, E. The Relationship
557 Between Isokinetic Knee Strength and Single- Leg Drop Jump Testing Following
558 Anterior Cruciate Ligament Reconstruction. Paper presented at: Faculty of Sports and
559 Exercise Medicine Annual Conference, 2019; Dublin.

560   **8.**   de Villarreal ES, Izquierdo M, Gonzalez-Badillo JJ. Enhancing jump performance
561   after combined vs. maximal power, heavy-resistance, and plyometric training alone. *J*
562   *Strength Cond Res.* 2011;25(12):3274-3281.

563   **9.**   Dempsey AR, Lloyd DG, Elliott BC, Steele JR, Munro BJ. Changing sidestep cutting
564   technique reduces knee valgus loading. *Am J Sports Med.* 2009;37(11):2194-2200.

565   **10.**   Donnelly CJ, Lloyd DG, Elliott BC, Reinbolt JA. Optimizing whole-body kinematics
566   to minimize valgus knee loading during sidestepping: implications for ACL injury
567   risk. *J Biomech.* 2012;45(8):1491-1497.

568   **11.**   Fischer F, Blank C, Dünnwald T, et al. Isokinetic Extension Strength Is Associated
569   With Single-Leg Vertical Jump Height. *Orthopaedic Journal of Sports Medicine.*
570   2017;5(11):2325967117736766.

571   **12.**   Fleming BC, Renstrom PA, Beynnon BD, et al. The effect of weightbearing and
572   external loading on anterior cruciate ligament strain. *J Biomech.* 2001;34(2):163-170.

573   **13.**   Grindem H, Snyder-Mackler L, Moksnes H, Engebretsen L, Risberg MA. Simple
574   decision rules can reduce reinjury risk by 84% after ACL reconstruction: the
575   Delaware-Oslo ACL cohort study. *Br J Sports Med.* 2016.

576   **14.**   Healy R, Smyth C, Kenny IC, Harrison AJ. Influence of Reactive and Maximum
577   Strength Indicators on Sprint Performance. *J Strength Cond Res.* 2019;33(11):3039-
578   3048.

579   **15.**   Hewett TE, Lindenfeld Tn Fau - Riccobene JV, Riccobene Jv Fau - Noyes FR, Noyes
580   FR. The effect of neuromuscular training on the incidence of knee injury in female
581   athletes. A prospective study. (0363-5465 (Print)).

582   **16.**   Hewett TE, Myer GD. The mechanistic connection between the trunk, hip, knee, and
583   anterior cruciate ligament injury. *Exerc Sport Sci Rev.* 2011;39(4):161-166.

584   **17.**   Hewett TE, Myer GD, Ford KR, et al. Biomechanical measures of neuromuscular
585   control and valgus loading of the knee predict anterior cruciate ligament injury risk in
586   female athletes: a prospective study. *Am J Sports Med.* 2005;33(4):492-501.

587   **18.**   Hirokawa S, Solomonow M, Lu Y, Lou ZP, D'Ambrosia R. Anterior-posterior and
588   rotational displacement of the tibia elicited by quadriceps contraction. *Am J Sports*
589   *Med.* 1992;20(3):299-306.

590   **19.**   Hopkins WG, Marshall SW, Batterham AM, Hanin J. Progressive statistics for studies
591   in sports medicine and exercise science. *Med Sci Sports Exerc.* 2009;41(1):3-13.

592   **20.**   Irrgang JJ, Anderson AF, Boland AL, et al. Development and validation of the
593   international knee documentation committee subjective knee form. *Am J Sports Med.*
594   2001;29(5):600-613.

595   **21.**   King E, Richter C, Franklyn-Miller A, et al. Whole-body biomechanical differences
596   between limbs exist 9 months after ACL reconstruction across jump/landing tasks.
597   *Scand J Med Sci Sports.* 2018.

598   **22.**   King E, Richter C, Franklyn-Miller A, Wadey R, Moran R, Strike S. Back to Normal
599   Symmetry? Biomechanical Variables Remain More Asymmetrical Than Normal
600   During Jump and Change-of-Direction Testing 9 Months After Anterior Cruciate
601   Ligament Reconstruction. *Am J Sports Med.* 2019;47(5):1175-1185.

602   **23.**   King E, Richter C, Jackson M, et al. Factors Influencing Return to Play and Second
603   Anterior Cruciate Ligament Injury Rates in Level 1 Athletes After Primary Anterior
604   Cruciate Ligament Reconstruction: 2-Year Follow-up on 1432 Reconstructions at a
605   Single Center. *Am J Sports Med.* 2020:363546519900170.

606   **24.**   King E. RC, Franklyn-Miller A., Daniels K., Wadey R., Moran R., Strike S. . Whole
607   body biomechanical differences between limbs persist 9 months after ACL
608   reconstruction across jump/landing tasks. *Scandinavian Journal or Sports Medicine*
609   *and Science (in review).* 2017.

610   **25.**   King E. RC, Franklyn-Miller A., Daniels K., Wadey R., Moran R., Strike S. .
611   Biomechanical but not timed performance asymmetries persist between limbs 9
612   months after ACL reconstruction during planned and unplanned change of direction. .
613   *Journal of Biomechanics (In Press).* 2018.
614   **26.**   Koga H, Nakamae A, Shima Y, et al. Mechanisms for noncontact anterior cruciate
615   ligament injuries: knee joint kinematics in 10 injury situations from female team
616   handball and basketball. *Am J Sports Med.* 2010;38(11):2218-2225.
617   **27.**   Kristianslund E, Krosshaug T, van den Bogert AJ. Effect of low pass filtering on joint
618   moments from inverse dynamics: implications for injury prevention. *J Biomech.*
619   2012;45(4):666-671.
620   **28.**   Krosshaug T, Nakamae A, Boden BP, et al. Mechanisms of anterior cruciate ligament
621   injury in basketball: video analysis of 39 cases. *Am J Sports Med.* 2007;35(3):359-
622   367.
623   **29.**   Kyritsis P, Bahr R, Landreau P, Miladi R, Witvrouw E. Likelihood of ACL graft
624   rupture: not meeting six clinical discharge criteria before return to sport is associated
625   with a four times greater risk of rupture. *Br J Sports Med.* 2016.
626   **30.**   Kyrolainen H, Avela J, McBride JM, et al. Effects of power training on muscle
627   structure and neuromuscular performance. *Scand J Med Sci Sports.* 2005;15(1):58-64.
628   **31.**   Lynch AD, Logerstedt DS, Grindem H, et al. Consensus criteria for defining
629   'successful outcome' after ACL injury and reconstruction: a Delaware-Oslo ACL
630   cohort investigation. *Br J Sports Med.* 2015;49(5):335-342.
631   **32.**   Mandelbaum BR, Silvers Hj Fau - Watanabe DS, Watanabe Ds Fau - Knarr JF, et al.
632   Effectiveness of a neuromuscular and proprioceptive training program in preventing
633   anterior cruciate ligament injuries in female athletes: 2-year follow-up. (0363-5465
634   (Print)).
635   **33.**   Markolf KL, Burchfield DM, Shapiro MM, Shepard MF, Finerman GA, Slauterbeck
636   JL. Combined knee loading states that generate high anterior cruciate ligament forces.
637   *J Orthop Res.* 1995;13(6):930-935.
638   **34.**   Marshall BM, Franklyn-Miller AD, King EA, Moran KA, Strike SC, Falvey EC.
639   Biomechanical factors associated with time to complete a change of direction cutting
640   maneuver. *J Strength Cond Res.* 2014;28(10):2845-2851.
641   **35.**   Marx RG, Stump TJ, Jones EC, Wickiewicz TL, Warren RF. Development and
642   evaluation of an activity rating scale for disorders of the knee. *Am J Sports Med.*
643   2001;29(2):213-218.
644   **36.**   Moudy S, Richter C, Strike S. Landmark registering waveform data improves the
645   ability to predict performance measures. *J Biomech.* 2018.
646   **37.**   Myklebust G, Engebretsen L Fau - Braekken IH, Braekken Ih Fau - Skjølberg A,
647   Skjølberg A Fau - Olsen O-E, Olsen Oe Fau - Bahr R, Bahr R. Prevention of anterior
648   cruciate ligament injuries in female team handball players: a prospective intervention
649   study over three seasons. (1050-642X (Print)).
650   **38.**   Norcross MF, Lewek MD, Padua DA, Shultz SJ, Weinhold PS, Blackburn JT. Lower
651   extremity energy absorption and biomechanics during landing, part I: sagittal-plane
652   energy absorption analyses. *J Athl Train.* 2013;48(6):748-756.
653   **39.**   O'Malley E. RC, King E., Moran R., Strike S., Moran K. and Franklyn-Miller A. .
654   Countermovement jump and isokinetic dynamometry as measures of rehabilitation
655   status following anterior cruciate ligament reconstruction. *Journal of Athletic*
656   *Training, In Press.* 2017.
657   **40.**   Paterno MV, Rauh MJ, Schmitt LC, Ford KR, Hewett TE. Incidence of contralateral
658   and ipsilateral anterior cruciate ligament (ACL) injury after primary ACL
659   reconstruction and return to sport. *Clin J Sport Med.* 2012;22(2):116-121.

660 **41.** Paterno MV, Schmitt LC, Ford KR, et al. Biomechanical measures during landing and
661   postural stability predict second anterior cruciate ligament injury after anterior
662   cruciate ligament reconstruction and return to sport. *Am J Sports Med.*
663   2010;38(10):1968-1978.
664 **42.** Peduzzi P, Concato J, Kemper E, Holford TR, Feinstein AR. A simulation study of
665   the number of events per variable in logistic regression analysis. *J Clin Epidemiol.*
666   1996;49(12):1373-1379.
667 **43.** Perneger TV. What's wrong with Bonferroni adjustments. *Bmj.* 1998;316(7139):1236-
668   1238.
669 **44.** Pinczewski LA, Lyman J, Salmon LJ, Russell VJ, Roe J, Linklater J. A 10-year
670   comparison of anterior cruciate ligament reconstructions with hamstring tendon and
671   patellar tendon autograft: a controlled, prospective trial. *Am J Sports Med.*
672   2007;35(4):564-574.
673 **45.** Ramsey J. *Functional data analysis.* : John Wiley and Sons; 2006.
674 **46.** Richter C, King E, Strike S, Franklyn-Miller A. Objective classification and scoring
675   of movement deficiencies in patients with anterior cruciate ligament reconstruction.
676   *PLoS One.* 2019;14(7):e0206024.
677 **47.** Rothman KJ. No adjustments are needed for multiple comparisons. *Epidemiology.*
678   1990;1(1):43-46.
679 **48.** Russell KA, Palmieri RM, Zinder SM, Ingersoll CD. Sex differences in valgus knee
680   angle during a single-leg drop jump. *J Athl Train.* 2006;41(2):166-171.
681 **49.** Salmon L, Russell V, Musgrove T, Pinczewski L, Refshauge K. Incidence and risk
682   factors for graft rupture and contralateral rupture after anterior cruciate ligament
683   reconstruction. *Arthroscopy.* 2005;21(8):948-957.
684 **50.** Schairer WW, Marx RG, Dempsey B, Ge Y, Lyman S. The Relation Between
685   Volume of ACL Reconstruction and Future Knee Surgery. *Orthopaedic Journal of
686   Sports Medicine.* 2017;5(7 suppl6):2325967117S2325900298.
687 **51.** Sward P, Kostogiannis I, Roos H. Risk factors for a contralateral anterior cruciate
688   ligament injury. *Knee Surg Sports Traumatol Arthrosc.* 2010;18(3):277-291.
689 **52.** Undheim MB, Cosgrave C, King E, et al. Isokinetic muscle strength and readiness to
690   return to sport following anterior cruciate ligament reconstruction: is there an
691   association? A systematic review and a protocol recommendation. *Br J Sports Med.*
692   2015;49(20):1305-1310.
693 **53.** van Melick N, van Cingel RE, Brooijmans F, et al. Evidence-based clinical practice
694   update: practice guidelines for anterior cruciate ligament rehabilitation based on a
695   systematic review and multidisciplinary consensus. *Br J Sports Med.*
696   2016;50(24):1506-1515.
697 **54.** Walden M, Hagglund M, Magnusson H, Ekstrand J. Anterior cruciate ligament injury
698   in elite football: a prospective three-cohort study. *Knee Surg Sports Traumatol
699   Arthrosc.* 2011;19(1):11-19.
700 **55.** Wasserstein RL, Lazar NA. The ASA Statement on p-Values: Context, Process, and
701   Purpose. *The American Statistician.* 2016;70(2):129-133.
702 **56.** Webster KE, Feller JA, Lambros C. Development and preliminary validation of a
703   scale to measure the psychological impact of returning to sport following anterior
704   cruciate ligament reconstruction surgery. *Phys Ther Sport.* 2008;9(1):9-15.
705 **57.** Wellsandt E, Failla MJ, Snyder-Mackler L. Limb Symmetry Indexes Can
706   Overestimate Knee Function After Anterior Cruciate Ligament Injury. *J Orthop
707   Sports Phys Ther.* 2017;47(5):334-338.

708   **58.**   Wiggins AJ, Grandhi RK, Schneider DK, Stanfield D, Webster KE, Myer GD. Risk
709   of Secondary Injury in Younger Athletes After Anterior Cruciate Ligament
710   Reconstruction: A Systematic Review and Meta-analysis. *Am J Sports Med.* 2016.
711   **59.**   Wright RW, Magnussen RA, Dunn WR, Spindler KP. Ipsilateral graft and
712   contralateral ACL rupture at five years or more following ACL reconstruction: a
713   systematic review. *J Bone Joint Surg Am.* 2011;93(12):1159-1165.
714