Effectiveness of Anterior Cruciate Ligament Injury Prevention Training Programs

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Background: The objective of this study was to systematically review the literature on anterior cruciate ligament (ACL) injury prevention programs and to perform a meta-analysis to address three questions: First, what is the effectiveness of ACL injury prevention programs? Second, is there evidence for a “best” program? Third, what is the quality of the current literature on ACL injury prevention?

Methods: We conducted a systematic review with use of the online PubMed, MEDLINE, EMBASE, CINAHL (Cumulative Index to Nursing and Allied Health), and Cochrane Central Register of Controlled Trials databases. Search terms were anterior cruciate ligament, knee, injury, prevention, and control. Data on study design and clinical outcomes were extracted independently in triplicate. After assessment of between-study heterogeneity, DerSimonian-Laird random-effect models were used to calculate pooled risk ratios and risk differences. The risk difference was used to estimate the number needed to treat (the number of individuals who would need to be treated to avoid one ACL tear).

Results: The pooled risk ratio was 0.38 (95% confidence interval [CI], 0.20 to 0.72), reflecting a significant reduction in the risk of ACL rupture in the prevention group (p = 0.003). The number needed to treat ranged from five to 187 in the individual studies. Stratified by sex, the pooled risk ratio was 0.48 (95% CI, 0.26 to 0.89) for female athletes and 0.15 (95% CI, 0.08 to 0.28) for male athletes.

Conclusions: Our study indicated strong evidence in support of a significant effect of ACL injury prevention programs. Our pooled estimates suggest a substantial beneficial effect of ACL injury prevention programs, with a risk reduction of 52% in the female athletes and 85% in the male athletes.

Level of Evidence: Therapeutic Level II. See Instructions for Authors for a complete description of levels of evidence.

Approximately 100,000 injuries of the anterior cruciate ligament (ACL) occur per year in the United States, and costs associated with the evaluation, therapy, rehabilitation, and possible loss of funding and scholarships of affected athletes total $625 million to $1 billion annually. 

ACL tears are serious injuries and predispose patients to subsequent osteoarthritis, which in turn causes further pain, immobility, and reduction in quality of life and ability to work. Fifty to ninety percent of untreated patients develop osteoarthritis within ten to fifteen years after the ACL injury.
The current treatment of ACL tears involves reconstruction with use of autogenous or allogeneic grafts. However, despite promising short and intermediate-term outcomes, questions have arisen regarding the long-term efficacy of current treatments of ACL tears with regard to preventing osteoarthritis. Long-term studies have indicated that 41% to 75% of patients undergoing ACL reconstruction still develop osteoarthritis by fourteen years postoperatively; in addition, the rate of graft failure is high, peaking at 20% to 25% in adolescent patients, resulting in knee instability as well as osteoarthritis progression. New treatment options, such as regenerative treatments based on tissue engineering methods, are being developed but are not available for clinical use.

A different approach to the problem of ACL tears involves prevention. Approximately 80% of all ACL tears are noncontact injuries, suggesting that a substantial percentage of tears could be avoided. Indeed, a number of ACL injury prevention programs have been developed and have been shown to reduce ACL injury rates significantly. These programs usually target high-risk groups, such as young female athletes, and aim to improve dangerous motion patterns. For example, a program may aim to improve landing technique from "flat foot" landing with an extended lower extremity to landing with deep hip and knee flexion. However, the effectiveness of these programs has not been comprehensively analyzed and described.

The objective of the present study was to systematically review the literature on programs for prevention of ACL injury in female and male athletes and to perform a meta-analysis to address three questions: First, do ACL injury prevention programs decrease the risk of ligament injuries? Second, is there an indication for a "best" program? Third, what is the validity of these findings?

**Materials and Methods**

This study was conducted in accordance with the PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses) statement.

**Systematic Search and Strategy**

We conducted a systematic review of the literature with use of the PubMed, MEDLINE, EMBASE, CINAHL (Cumulative Index to Nursing and Allied Health Literature), and Cochrane Central Register of Controlled Trials databases. We searched these electronic databases online for "anterior cruciate ligament OR knee" AND (control OR prevention) AND injury," using these terms as keywords and exploded MeSH (Medical Subject Headings) terms. The search was not restricted by language or year of publication. We then performed a meta-analysis of the controlled trials that were identified, pooling data on the effectiveness of ACL injury prevention algorithms to answer our three study questions.

We included only prospective, controlled studies that directly compared ACL injury prevention programs with no treatment in human subjects. Studies with partially overlapping data were merged to the extent possible; duplicate studies with completely overlapping data were excluded. Studies that did not focus on clinical treatment or outcome, animal studies, studies without any intervention, and studies with a reported attrition of >20% were also excluded. Eligible interventions involved proprioceptive neuromuscular training techniques (e.g., Prevent injury and Enhance Performance [PEP] programs) with or without a balance board, round board, or wobble board.

**Extraction of Relevant Data**

Eligibility of studies was assessed independently in triplicate and crosschecked to avoid errors. Disagreement was resolved by discussion or, if necessary, by the decision of the senior author (P.V.). The bibliographies of all included studies were reviewed for additional relevant studies. Data concerning study design, participant characteristics, and the number of ACL ruptures at the time of final follow-up were abstracted from the included studies in triplicate and crosschecked. All searches were concluded by December 2010.

The level of evidence (I through V), use of randomization (yes/no), use of blinding (yes/no), and reporting of attrition (yes/no) were extracted from the included studies to describe the study quality. Other extracted data involved the type of prevention program, the total number of participants enrolled in the prevention program and in the control group, the number of athletes with suitable follow-up in each group, the number of uninjured athletes and the number of athletes with an ACL tear at the time of follow-up in each group, the duration of follow-up, the type of sport performed, and the sex of the participants.

**Assessment of Validity**

We determined the level of evidence for each included study. The internal validity of each study was further assessed with use of a modified Jadad scale, which assigns one point each for use of randomization, use of blinding, and reporting of attrition (with zero representing the poorest possible result and three points representing the best result).

**Publication Bias**

Another important problem that jeopardizes the validity of a meta-analysis is publication bias, or so-called "file-drawer" bias, leading to the omission of unpublished studies. These studies often remain "in a file drawer" because their results are not statistically significant, resulting in an erroneously high proportion of studies with significant results among published studies. Publication bias among the included studies was assessed graphically with use of a funnel plot and mathematically with use of the Egger weighted regression technique.

**Study Heterogeneity**

The presence of between-study heterogeneity was assessed qualitatively with use of the Cochrane Q test (with a p value of 0.10 being considered significant because of the low power of this test in small samples) and quantitatively with use of the I² index. Meta-regressions were performed to assess the potential sources of such heterogeneity.

**Quantitative Data Synthesis**

The risk difference was used to calculate the number needed to treat (equal to 1 divided by the risk difference)—in this case, the number of participants who have to be enrolled in the prevention program to result in one less ACL tear. (The number needed to harm, rather than the number need to treat, was reported for studies that showed a better outcome in the group that did not participate in the prevention program.) All analyses were performed on an intention-to-treat basis—i.e., participants were included in the analysis according to their initial allocation and their injury status at the time of final follow-up. Such an analysis produces a more conservative result, with a larger p value compared with an as-treated analysis, but it is also more realistic.

Data were pooled to calculate the pooled risk ratio and the pooled risk difference by constructing random-effects models with use of the DerSimonian-Laird method. Such models postulate that the observed heterogeneity among the studies in a meta-analysis is attributable to normally distributed individual effects around a common effect. This assumption was assessed graphically with use of a forest plot.

All calculations were performed with use of Intercooled Stata (version 10; StataCorp, College Station, Texas). A p value of 0.05 was considered significant for the pooled estimates.

**Source of Funding**

No funding was obtained for this study.
Results

Study Characteristics

Our search strategy identified 909 studies. After exclusion of duplicate studies, studies that did not focus on clinical treatment or outcome, animal studies, and studies without any intervention, nine studies remained eligible for analysis (Fig. 1). The nine included studies were published between 1996 and 2008 in English and German (see Appendix). Five studies focused exclusively on soccer players, two focused exclusively on handball players, and two involved a combination of soccer, basketball, and volleyball players (see Appendix).

The study by Söderman et al. had 22% attrition in the control group and 49% in the prevention group. That study was therefore used only for a sensitivity analysis—i.e., data were pooled with and without that study, and the two pooled estimates were compared to assess the magnitude of the change that resulted from addition of the potentially biased study. The magnitude of this change shows how robust our results were (how resistant they were to flaws in the designs of the individual studies).

Outcomes of the Included Prevention Programs

Caraffa et al. compared 300 Italian soccer players who used a special training program for at least twenty minutes per session for at least thirty days with 300 players who were asked to train as usual. Training was divided into five phases and included the use of a balance board with a focus on proprioceptive training. The authors reported significantly fewer ACL injuries in the intervention group (ten of 300) than in the control group (seventy of 300), and they concluded that proprioceptive training should become standard during preseason training as well as during the actual playing season.

Gilchrist et al. randomly assigned National Collegiate Athletic Association (NCAA) Division I women's soccer teams to a group of 583 athletes who performed special training or to a control group of 852 athletes who performed normal training. The program was used for twelve weeks, with 11.6% attrition overall. The training focusing on stretching, strengthening, plyometrics, agility, and avoidance of high-risk positions depicted on a video, and replacement exercises were also provided to minimize boredom. The overall ACL injury rate was 1.7 times lower in the intervention group than in the control group (p < 0.198). The authors concluded that athletes with a history of ACL injury obtained an especially great benefit from the prevention program.

Heidt et al. randomly selected forty-two of 300 female high school soccer players to participate in the Frappier Acceleration
Training Program, which combines cardiovascular conditioning, plyometric work, sport cord drills, strength training, and flexibility exercises over a seven-week period. The authors observed significantly fewer injuries in the intervention group than in the control group, and they concluded that this type of conditioning can lower the rate of ACL injury in female adolescent soccer players.

Hewett et al.\(^4\) prospectively observed three groups of adolescents: 366 girls on fifteen high school soccer, volleyball, and basketball teams (97, 185, and 84 girls, respectively) participated in a six-week preseason neuromuscular training program; 463 girls on the same fifteen high school soccer, volleyball, and basketball teams (193, 81, and 189 girls, respectively) did not receive the training; and 434 boys (soccer and basketball players) on thirteen teams who did not receive the training served as an additional control population. A total of fourteen serious knee injuries were observed in the 1263 athletes. The girls who underwent the training sustained significantly fewer injuries compared with the girls who did not train, but not compared with the boys who did not train. The authors concluded that before young female athletes participate in sports that entail jumping, pivoting, and cutting, they should undergo a jump training program of proven effectiveness that includes progressive resistance weight training for the lower extremity.

Mandelbaum et al.\(^5\) performed a prospective, nonrandomized cohort study of 1041 female soccer players from fifty-two teams who received a sports-specific training intervention. An age and skill-matched group of 1905 players from the same league served as the control group. The authors conducted a second study with the same design, including 844 players in the intervention group and 1913 in the control group, one year later. A total of 189 players were lost to follow-up. The intervention consisted of education, stretching, strengthening, plyometrics, and sports-specific agility drills. The authors observed an 88% decrease in ACL injuries during the first season and a 74% decrease during the second season compared with the control groups, and they concluded that neuromuscular training programs may have a direct benefit by decreasing the number of ACL tears.

Petersen et al.\(^6\) conducted a prospective case control study of female handball players to investigate the effect of injury prevention training consisting of balance board exercises and jump exercises. The study included 134 players in the intervention group and 142 players in the control group. The authors found knee injuries to be the second most frequent type of injury after ankle sprains, and they observed five ACL tears in the intervention group compared with nine in the control group. The authors concluded that proprioceptive and neuromuscular training is appropriate for the prevention of knee and ankle injuries among female handball players.

In a second investigation, Petersen et al.\(^7\) compared a handball team that performed proprioceptive and neuromuscular training during the preseason with another team that was trained as usual. The intervention consisted of proprioceptive training, jump training, and information on injury mechanisms. The authors found that the training significantly reduced the risk of ACL tears, and they concluded that prevention strategies should be included in routine handball training programs.

Pfeiffer et al.\(^8\) compared 577 female athletes who underwent a knee ligament injury prevention (KLIP) program with 862 female athletes in a control group. The drills in the KLIP program consisted of running, jumping, and landing in forward and backward directions; the athlete initially landed on both feet and later progressed to landing on a single foot. This program was designed to require less time than the prevention program proposed by Hewett et al.\(^4\). The authors observed no significant difference in the rate of knee injuries between the groups, and they concluded that the rate of noncontact ACL tears will not be lowered by use of the KLIP program.

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**Funnel Plot for ACL Prevention Studies**

Funnel plot showing the eight pooled ACL injury prevention studies. The funnel plot is a tool to graphically assess publication bias by plotting the standard error (se) of the logarithm of the relative risk (RR) against the RR. The vertical dashed line shows the pooled RR, and the diagonal dashed lines show the corresponding 95% confidence interval. Although the studies are somewhat asymmetrically arranged around the pooled effect, all studies lie within the funnel, suggesting a low risk of publication bias. Furthermore, mathematical assessment showed no evidence of publication bias ($p = 0.131$).
Söderman et al.53 conducted a prospective study in which 121 female soccer players were randomized to the intervention group and 100 to the control group. The intervention consisted primarily of exercises involving use of a balance board for ten to fifteen minutes three times per week at home for at least thirty days. The injury rate did not differ significantly between the groups, and the authors concluded that balance board training did not prevent ACL injuries in female soccer players. As mentioned above, this study suffered from massive, differential attrition of participants prior to the follow-up evaluation.

**Publication Bias**

The funnel plot (Fig. 2) was slightly skewed, suggesting that a few negative studies (i.e., studies that showed no significant difference between the groups) are missing from the literature. However, quantitative assessment of this possibility with use of Egger regression showed no significant evidence of publication bias in the included studies (p = 0.131).

**Heterogeneity**

Heterogeneity among the results of the studies was significant (p = 0.011), with an I² index of 64.0%. However, as shown in the forest plot (Fig. 3), the studies were uniformly distributed about a common effect, suggesting that random-effect modeling could be used to pool the individual results.

**Pooled Effect**

The risk differences varied considerably among the individual studies, with the corresponding estimates of the number needed to treat ranging from five to 187 except in the study by Pfeiffer et al.52, which showed a slightly lower risk in the control group (leading to an inversion of the number needed to treat to a number needed to harm [582]) (see Appendix). However, the pooled DerSimonian-Laird random-effect risk ratio was 0.38 (95% confidence interval [CI], 0.20 to 0.72), and the reduction in the risk of ACL rupture in the prevention group was significant (p = 0.003) (Fig. 3).

### Pooled Effect of ACL Prevention Program

**Risk Ratio of ACL Rupture**

<table>
<thead>
<tr>
<th>Study</th>
<th>RR (95% CI)</th>
<th>Events, Treatment</th>
<th>Events, Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caraffa et al. (1996)</td>
<td>0.14 (0.08, 0.27)</td>
<td>10/300</td>
<td>70/300</td>
</tr>
<tr>
<td>Gilchrist et al. (2008)</td>
<td>0.57 (0.24, 1.35)</td>
<td>7/583</td>
<td>18/852</td>
</tr>
<tr>
<td>Heidt et al. (2000)</td>
<td>0.77 (0.10, 5.98)</td>
<td>1/42</td>
<td>8/258</td>
</tr>
<tr>
<td>Hewett et al. (1999)</td>
<td>0.51 (0.10, 2.59)</td>
<td>2/366</td>
<td>5/463</td>
</tr>
<tr>
<td>Mandelbaum et al. (2005)</td>
<td>0.18 (0.08, 0.42)</td>
<td>6/1885</td>
<td>67/3818</td>
</tr>
<tr>
<td>Petersen et al. (2002)</td>
<td>0.33 (0.01, 7.68)</td>
<td>0/18</td>
<td>1/18</td>
</tr>
<tr>
<td>Petersen et al. (2005)</td>
<td>0.59 (0.20, 1.71)</td>
<td>5/134</td>
<td>9/142</td>
</tr>
<tr>
<td>Pfeiffer et al. (2006)</td>
<td>1.49 (0.30, 7.38)</td>
<td>3/577</td>
<td>3/662</td>
</tr>
<tr>
<td>Overall</td>
<td>0.38 (0.20, 0.72)</td>
<td>34/3905</td>
<td>181/6713</td>
</tr>
</tbody>
</table>

Fig. 3

Forest plot showing the findings of the meta-analysis. The study by Caraffa et al. analyzed all ACL tears, and the other seven pooled primary studies analyzed only noncontact ACL tears. The risk ratio (RR) is plotted on a logarithmic scale on the x axis, and the dashed vertical line and the diamond represent the pooled RR. The sizes of the squares for the included studies represent the sizes of those studies, and the horizontal lines and the width of the diamond represent the associated 95% confidence intervals (CIs). A significant treatment effect is indicated if the CI does not include the solid vertical line denoting the absence of an effect.
Stratified by sex, the pooled risk ratio was 0.48 (95% CI, 0.26 to 0.89) for female athletes and 0.15 (95% CI, 0.08 to 0.28) for male athletes. The reduction in the number of ACL tears was significant in both female athletes (p = 0.021) and male athletes (p < 0.001).

Inclusion of the probably biased study by Söderman et al.53 changed the pooled DerSimonian-Laird random-effect risk ratio from 0.38 to 0.45 (95% CI, 0.23 to 0.89), which was still consistent with a significant reduction in the risk of ACL rupture in the prevention group (p = 0.021).

Meta-Regression
Meta-regression of the effect of individual variables on the pooled risk ratio (i.e., on the effect of preventive treatment) showed no effect of a focus on balance board use (p = 0.712), use of video assistance (p = 0.914), duration of follow-up (p = 0.437), or the year of publication (p = 0.358). The regression showed that conducting prevention programs during the preseason compared with the playing season reduced the risk of ACL injury by 19.1%, but this difference was not significant (p = 0.691).

Study Quality
The mean Jadad score for the included studies was one point (95% CI, 0.43 to 1.57 points). Only three of the nine studies used a randomized design, and only two used blinded outcome assessment. One of the studies with the highest Jadad score (two points), which was also the only study with an a priori sample size calculation, was the study by Söderman et al.53 that had to be excluded because of selection bias.

Discussion
Summary of Evidence
The authors’ conclusions regarding the effectiveness of ACL injury prevention programs differed among the included manuscripts. Caraffa et al.,54 Heidt et al.,57 Petersen et al.,50,51 and Hewett et al.46 reported positive effects with injury prevention programs involving various training methods, resulting in significantly lower rates of ACL injury. Gilchrist et al.46 and Mandelbaum et al.49 concluded only that there might be an advantage to training, without making definite recommendations. In contrast, Pfeiffer et al.45 and Söderman et al.53 concluded that a twenty-minute plyometric-based exercise program twice a week22 or training involving the use of balance boards for ten to fifteen minutes three times a week for at least thirty days55 would not significantly reduce the risk of ACL injury in female high school athletes in noncontact sports, but these authors did not clearly pinpoint the reason for the difference between these findings and those of prior studies.

Pooling the results from the individual studies showed strong evidence for a significant, positive effect of prevention programs. Furthermore, the pooled risk ratio of 0.38 indicated that athletes in the prevention programs had a 62% reduction in the risk of ACL rupture compared with athletes in the control groups. Stratification by sex showed that female athletes actually benefited less than male athletes, with a risk reduction of 52% compared with 85% in male athletes. The substantial magnitude of this protective effect was supported by the estimates of the number needed to treat; the number of participants who would need to be enrolled in a prevention program to result in one less ACL tear ranged from five to 187, which is fairly small considering the size of an average high school or varsity team. Of note, two of the studies, by Caraffa et al.46 and by Söderman et al.53, included all ACL injuries rather than focusing on noncontact ACL tears, which could bias our finding. However, the outcomes reported in those two studies did not deviate from those of the other included studies.

Although we attempted to identify a “best” training program to avoid ACL injury, we were unable to find conclusive evidence supporting any one specific type of intervention because of the considerable heterogeneity of the included studies. Despite this heterogeneity, there is agreement among the results of the successful trials that an ACL injury prevention program should include at least ten minutes of exercises three times per week, with a focus on neuromuscular training, as a bare minimum. However, we found no evidence supporting the superiority of balance board exercises, video assistance, or new protocols over older ones.

In general, the scientific quality of the included studies was low, with only two study designs having appropriate blinding (Petersen et al.50 and Pfeiffer et al.52) and only three having adequate randomization (Gilchrist et al.46, Heidt et al.47, and Söderman et al.53). Matched-pair analysis was performed in only three studies: groups were matched with regard to age and number of training units by Caraffa et al.54; with regard to age, height, weight, muscle flexibility, balance and postural sway of the lower extremities, and the number of years in soccer training by Söderman et al.53; and with regard to age and athletic skill by Mandelbaum et al.49. Finally, only one study included an a priori power analysis53, and this study was biased by very high and differential drop-out rates of 49% in the intervention group and 22% in the control group.

Limitations
Our study has potential shortcomings. As with all systematic reviews and meta-analyses, the validity of our findings depends on the validity of the primary studies. Although the overall quality of the included studies was low, such low study quality grades are not unusual for surgical and musculoskeletal trials. Furthermore, the fact that the pooled estimates changed only modestly (by 18%) after inclusion of the biased study by Söderman et al.53 showed that our findings were quite robust.

Another shortcoming is the heterogeneity of the results of the included primary studies. Although this heterogeneity was normally distributed about a common effect, and thus pooling with use of a random-effect model is allowed, the heterogeneity prevented us from identifying determinants of the success of preventive training. Once more studies involving the same type of prevention are available, subgroup analyses can be conducted to assess determinants of the outcome. It is
worth noting that most studies (five of nine) focused exclusively on soccer players, and this might therefore be a source of bias in the present study. However, such bias would result in clustering in the forest plot (Fig. 3), with soccer studies on one side and handball studies on the other. Instead, the forest plot showed a uniform distribution of all studies about the pooled relative risk.

Conclusion
In conclusion, our study produced strong evidence in support of a significant effect of ACL injury prevention programs. Our pooled estimates suggested a substantial beneficial effect of ACL prevention programs, with a 52% reduction in the risk of an ACL tear in female athletes but an 85% reduction in male athletes. Although the current literature was found to be of average quality, sensitivity analyses suggested that our findings are robust. However, we are not able to recommend a specific type of prevention program on the basis of the current published evidence.

Appendix
Tables showing the characteristics of the included studies and the estimates of the number needed to treat are available with the online version of this article as a data supplement at jbjs.org.

References


