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SYSTEMATIC REVIEW

Effectiveness of Conservative Interventions After Acute Hamstrings Injuries in Athletes: A Living Systematic Review

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Abstract

Background Hamstrings injuries are common in sports and the reinjury risk is high. Despite the extensive literature on hamstrings injuries, the effectiveness of the different conservative (i.e., non-surgical) interventions (i.e., modalities and doses) for the rehabilitation of athletes with acute hamstrings injuries is unclear.

Objective We aimed to compare the effects of different conservative interventions in time to return to sport (TRTS) and/or time to return to full training (TRFT) and reinjury-related outcomes after acute hamstrings injuries in athletes.

Data Sources We searched CINAHL, Cochrane Library, EMBASE, PubMed, Scopus, SPORTDiscus, and Web of Science databases up to 1 January, 2022, complemented with manual searches, prospective citation tracking, and consultation of external experts.

Eligibility Criteria The eligibility criteria were multi-arm studies (randomized and non-randomized) that compared conservative treatments of acute hamstrings injuries in athletes.

Data Analysis We summarized the characteristics of included studies and conservative interventions and analyzed data for main outcomes (TRTS, TRFT, and rate of reinjuries). The risk of bias was judged using the Cochrane tools. Quality and completeness of reporting of therapeutic exercise programs were appraised with the i-CONTENT tool and the certainty of evidence was judged using the GRADE framework. TRTS and TRFT were analyzed using mean differences and the risk of reinjury with relative risks.

Results Fourteen studies (12 randomized and two non-randomized) comprising 730 athletes (mostly men with ages between 14 and 49 years) from different sports were included. Nine randomized studies were judged at high risk and three at low risk of bias, and the two non-randomized studies were judged at critical risk of bias. Seven randomized studies compared exercise-based interventions (e.g., L-protocol vs C-protocol), one randomized study compared the use of low-level laser therapy, and three randomized and two non-randomized studies compared injections of platelet-rich plasma to placebo or no injection. These low-level laser therapy and platelet-rich plasma studies complemented their interventions with an exercise program. Only three studies were judged at low overall risk of ineffectiveness (i-CONTENT). No single intervention or combination of interventions proved superior in achieving a faster TRTS/TRFT or reducing the risk of reinjury. Only eccentric lengthening exercises showed limited evidence in allowing a shorter TRFT. The platelet-rich plasma treatment did not consistently reduce the TRFT or have any effect on the risk of new hamstrings injuries. The certainty of evidence was very low for all outcomes and comparisons.

Conclusions Available evidence precludes the prioritization of a particular exercise-based intervention for athletes with acute hamstrings injuries, as different exercise-based interventions showed comparable effects on TRTS/TRFT and the risk of reinjuries. Available evidence also does not support the use of platelet-rich plasma or low-level laser therapy in clinical practice. The currently available literature is limited because of the risk of bias, risk of ineffectiveness of exercise protocols (as assessed with the i-CONTENT), and the lack of comparability across existing studies.

Clinical Trial Registration PROSPERO CRD42021268499 and OSF (https://osf.io/3k4u2/).

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Key Points

As exercise-based interventions showed comparable time to return to full training or matches and the risk of reinjuries, no specific strategy needs to be prioritized when rehabilitating athletes with acute hamstrings injuries. Only eccentric lengthening exercises showed limited evidence in allowing a shorter time to return to full training.

Platelet-rich plasma injections did not consistently reduce the time to return to full training or have any effect on the risk of new hamstrings injuries. Therefore, platelet-rich plasma has no current value in clinical practice.

The currently available literature is still limited owing to a risk of bias, poor description, the risk of ineffectiveness of exercise protocols, and a lack of comparability across existing studies. Further studies are clearly warranted to allow stronger conclusions.

1 Introduction

Hamstrings injuries are common across sports involving sprinting or excessive muscle lengthening [1–11], resulting in ~ 17–27 days lost per 1000 h of training and match exposure [1, 5, 10, 12], with players missing up to 80 training sessions and matches per year because of injury [13]. The unavailability of players to compete owing to injury implies a considerable financial burden, for example, a professional soccer player that is absent from competition for 2 weeks because of injury is estimated to cost around €250,000 for clubs participating in the UEFA Champions League [14], while in the Australian Football League the cost of a single hamstrings injury was $A40,021 in 2021 [15]. Reduced player availability may result in a negative impact on team performance [16, 17]. The return to sport still remains a clinical challenge [18, 19], owing to the unacceptably high injury recurrence rate that ranges between 16.0 and 68.0% across different sports [3, 7, 8, 20–22], and frequently occurs within the first 2 months after return to play [23]. Hamstrings reinjuries are most common within 1 year of returning to sport (with a higher risk in the first 2 weeks) and tend to be more severe [20, 24, 25]. The high rate of recurrence suggests that athletes may be returning to sport unprepared and prematurely [26]. Even if the rehabilitation strategies are appropriate, perhaps athletes are rushing back to sports without enough time for proper biological healing [26].

Rehabilitation is the usual treatment for hamstrings injuries, with surgical treatment reserved for more complex and severe injuries [27, 28]. It has been suggested that interventions could be structured according to the specific injury site (i.e., semitendinosus vs biceps femoris, intra-tendon or extra-tendon) [29, 30] and may be mediated by inter-individual and intra-individual anatomic and physiologic variations [31], but experimental studies are still needed to sustain these claims. Rehabilitation strategies mostly rely on exercise-based interventions that often comprise multimodal approaches (including movement pattern improvement, progressive strength and sprint training, and strength endurance) [32, 33], but there is no consensus on which exercise modes are more effective. Although hamstrings injuries treatment relies mainly on exercise-based interventions, other therapies such as platelet-rich plasma (PRP) or corticosteroid injections, sacroiliac manipulation and/or non-steroidal anti-inflammatory drugs can be concomitantly used [32, 33]. However, the use of conservative (i.e., non-surgical) non-exercise-related strategies seems poorly substantiated by scientific evidence [32, 33].

There are some systematic reviews addressing hamstrings injuries recovery [33–35] and assessing criteria for its rehabilitation progress [18]. Since the last systematic review on the effectiveness of acute hamstrings injuries conservative treatment [33], some new studies have been published [36–41], suggesting the need for an update on the topic. Considering that data from systematic reviews may quickly become outdated [42], living reviews provide a regularly updated summary of the most up-to-date evidence [43]. Thus, we performed a living systematic review of conservative rehabilitation strategies after acute hamstrings injuries (excluding complete tears and avulsion injuries) to compare the effects of different interventions in time to return to sport (TRTS) and/or time to return to full training (TRFT) and reinjury-related outcomes.

2 Methods

2.1 Criteria for Administrating and Updating the Review

This living systematic review followed the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) 2020 [44] and Cochrane guidelines [45], and was performed under the guidance of PERSiST [46]. It will be updated annually on 1 January for a period of 5 years after completion of the initial database searches. These updates will be published in a public OSF project (https://osf.io/3k4u2/) and submitted to publication if new large-scale studies are available and/or new findings significantly change the overall results (e.g., a meta-analysis is possible for existing comparisons or new comparisons are available). Any updates or amendments to the protocol will be fully disclosed.

2.2 Eligibility Criteria

Inclusion and exclusion criteria were set according to the Participants, Intervention, Comparator, Outcome and Study design (PICOS) framework.

2.2.1 Participants

We included athletes of all competitive levels and sports with an acute hamstrings muscle injury, regardless of age, sex, race, or health status. Hamstrings muscle injury had to be diagnosed by physical examination (e.g., palpation, strength tests, range of motion [ROM], among others) and/or confirmed through magnetic resonance imaging (MRI) and/or ultrasound within 10 days of initial injury [18, 33]. Studies that comprised individuals with complete hamstrings muscle ruptures (usually assessed as grade 3, depending on the classification system), avulsion injuries, or hamstrings tendinopathy [18] were excluded. Complete ruptures or avulsion injuries usually undergo surgical procedures, while hamstrings tendinopathy is a chronic injury and therefore the rehabilitation procedures may differ from those applied to acute injuries.

2.2.2 Interventions

We included conservative interventions (i.e., avoiding invasive procedures such as surgery) to treat hamstrings muscle injuries (e.g., exercise training, PRPs).

2.2.3 Comparators

Any other conservative intervention (e.g., different exercise protocols, passive control groups and/or placebo) was accepted as a comparator.

2.2.4 Outcomes

We included studies reporting at least one of the primary outcomes: TRTS, TRFT, or occurrence of hamstrings reinjury or new hamstrings injury. Secondary outcomes were defined in the data items but were not used as eligibility criteria.

2.2.5 Study Design

Only original randomized and non-randomized multi-group study designs, with at least ten participants per group [47, 48], published in any language or date, were accepted.

2.3 Information Sources

Initial searches were conducted on 31 August, 2021, and updated on 1 January, 2022, in CINAHL, Cochrane Library, EMBASE, PubMed, Scopus, SPORTDiscus, and Web of Science, without restrictions on language or publication date and no filters applied. Manual searches were conducted by screening the included studies and relevant reviews reference lists. Prospective snowballing citation tracking was performed in Web of Science on 5 October, 2021. Seven external experts (with published research on the topic) were consulted to provide further potentially relevant studies (from which three responded affirmatively as displayed in the Acknowledgements section). The experts accessed our eligibility criteria, but not the search strategy, to avoid biasing their searches. Errata, corrections, corrigenda and/or retractions were sought for the included studies [45] and pre-registered protocols were retrieved when available. If a study had additional and relevant information published in another article, it was used to complement the information.

2.4 Search Strategy and Selection Process

The general search strategy used the following free terms, without filters or limits applied (the full search strategies are displayed in the Electronic Supplementary Material [ESM]): (1) [Ti/Ab] hamstring* OR semitendin* OR semimembran* OR "biceps femoris" OR "femoral biceps" OR "posterior thigh"; AND (2) [Ti/Ab] rehab* OR conserv* OR treat* OR intervention* OR therap* OR manag* OR clinical* OR recover* OR exercis* OR train*; AND (3) [All] injur* OR strain* OR tear* OR ruptur* OR pain OR dysfunction OR trauma; AND (4) [All] athlet* OR sport*. Two authors (JA and SRR) independently screened all database records and performed the manual searches, with disagreements being resolved by a third author (JGC). Automated removal of duplicates was performed using EndNote™ 20.2 for Mac (Clarivate™) and confirmed by manual screening.

2.5 Data Collection

Assessments were planned for the primary outcomes TRTS, TRFT, reinjuries, and new hamstrings injuries. Data on secondary outcomes (pain, strength, strength endurance, power, balance/stability, sprinting, ROM, pre-bilateral and post-bilateral and anteroposterior asymmetries, and adverse effects frequency, type, and severity), study characteristics (e.g., sample size and study design), participant demographics (e.g., age and sex), and sports participation (e.g., sport and competitive level) were also collected. We collected diagnostic characteristics relative to the criteria and methods used as reported by the included studies to determine acute hamstrings injury, imaging techniques applied, number of physicians assessing the images, and specific muscles injured (i.e., semitendinosus, semimembranosus, biceps femoris long head or short head). The programming details of the interventions were defined for exercise-based interventions (e.g., length, weekly frequency, intensity, sets, repetitions, movement

types, and muscle actions) and for PRP-based interventions (e.g., number and timing of injections, specific contents, and related information to the PRP-based procedures). The criteria used for progressing in rehabilitation (e.g., time based and/or goal based) and to decide on TRTS/TRFT, co-interventions, funding sources, and competing interests were recorded. Two authors (JOJ and JGC) independently collected data and a third author (FMC) arbitrated in case of disagreements.

2.6 Risk of Bias of Individual Studies

Parallel randomized studies were judged at low risk, some concerns, or high risk of bias in five domains using Cochrane's Risk of Bias tool, version 2 (RoB 2) [49]: randomization process, deviations from intended interventions (intention-to-treat analysis), missing outcome data, measurement of the outcome, and selection of the reported result. Non-randomized studies were judged at low risk, moderate risk, or critical risk of bias in seven domains using Cochrane's Risk of Bias In Non-Randomized Studies of Interventions (ROBINS-I) [50]: confounding, selection of the participants, classification of interventions, deviations from intended interventions, missing data, measurement of outcomes, and selection of the reported result.

The risk of bias was judged at outcome (grouped according to domains, such as reinjuries) and study levels (presenting the worst-case scenario per study). In the absence of a pre-registered protocol, the risk of bias in selection of the reported result was judged, at least, as has having some concerns (RoB 2) or moderate risk (ROBINS-I). Two authors (JA and SRR) independently judged the risk of bias, while a third author (RA) arbitrated when needed. The overall summaries of risk of bias judgments were plotted by the main outcome.

2.7 Data Management

If multiple measurements were available in the included studies, the information provided in the current review refers to the interventions' endpoint (unless otherwise stated). When data were exclusively provided in figures, two authors (JA and SRR) independently extracted the data using the validated software WebPlotDigitizer version 4.4 [51], and both values are presented in the relevant tables.

2.8 Quality and Completeness of Therapeutic Exercise Program Reporting

This item judged seven domains using the international Consensus on Therapeutic Exercise and Training (i-CONTENT) tool [52]: patient selection, qualified supervisor, type and timing of outcome assessment, dosage parameters (frequency, intensity, time), type of exercise, safety of the exercise program, and adherence to the exercise program. Each domain can be classified as having a low or high risk of ineffectiveness. The specific criteria used to reach the decisions are detailed in the original publication [52]. Two authors (JA and RA) conducted the data collection and a third author (RJF) arbitrated in case of disagreements. If the studies cited other sources to provide relevant information, those publications were viewed.

2.9 Data Synthesis and Analysis

Demographic data were not pooled because of inconsistent and incomplete reporting. Risk-related and continuous variables were treated as risk ratios and mean differences, respectively. Standardized mean differences were planned, but not calculated, as continuous variables used the same units, and we did not pool the data from different studies. Although a pooled quantitative synthesis was not feasible, we computed the between-group mean differences or relative risk for each study within each outcome. Findings were reported narratively because of the very low number of studies per comparison and their clinical heterogeneity precluded us from reliably performing a quantitative synthesis. The planned quantitative analyses can be viewed in the pre-registered protocol (https://osf.io/3k4u2/).

2.10 Certainty of Evidence

Two authors (JA and RA) judged the certainty of evidence using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) [53] and disagreements were resolved by consensus. Four of five GRADE dimensions were judged [54, 55]: risk of bias, inconsistency, indirectness, and imprecision. The risk of publication bias was not judged because of an insufficient number of studies per comparison to perform this analysis. Further details on the criteria for judging certainty of evidence can be viewed in the ESM, and the originally planned assessments are available in the study protocol (https://osf.io/3k4u2/).

3 Results

3.1 Study Selection

Database searches returned 20,644 records, from which 12,311 were duplicates, and additional searches (included studies' reference lists, snowballing citation tracking, expert consultations, and updated database searches) did not yield any new studies. Following the titles and abstracts screening, 19 records required a full-text analysis, from which five were excluded because of not fulfilling participants [56, 57] or outcomes [58–60] eligibility criteria. Fourteen studies were deemed eligible

for inclusion [24, 36–41, 57, 61–67], one study [66] was complemented by previously published information [68], and another [63] had an erratum [69] and a pre-published protocol [70]. Further details on study selection are shown in Fig. 1 and in the ESM.

3.2 Risk of Bias of Individual Studies

Twelve parallel randomized studies were included in the current review [24, 36, 38–40, 61–67], with one study [63] including an erratum [69] and another [66] a letter to the editor [68] that were considered for judging the risk of bias. Nine studies (75.0%) [24, 36, 40, 61–63, 65–67] and three studies (25.0%) [38, 39, 64] were judged at an overall high and low risk of bias for all primary outcomes, respectively. The study-level assessment (based on the worst-case scenario for each study) and the percentages for each domain are displayed in Fig. 2a and b. Two non-randomized studies [37, 41] were judged at an overall critical risk of bias for all primary outcomes (see Fig. 2c). A more detailed description of am outcome-based and domain-based risk of bias judgment is provided in the ESM.

3.3 Study Characteristics and Results

3.3.1 Publication Details, Funding, and Competing Interests

The studies were published between 2004 and 2020, and five (35.7%) had pre-registered and/or pre-published protocols [38, 39, 63, 64, 66]. Studies were performed mostly in Europe (France, Greece, the Netherlands, Russia, Spain, and Sweden) [36, 40, 41, 61, 62, 65, 66], followed by North America (USA) [24, 37, 67], Asia (Malaysia, Qatar) [63, 64], Oceania (Australia) [38], and South America (Brazil) [39], and no study was performed in Africa. Funding sources were reported in nine studies (64.3%) [24, 37, 38, 61–64, 66, 67] and unreported in three [36, 41, 65], with two studies reporting no funding [39, 40]. Eight studies (57.1%) displayed no competing interests [38–40, 61, 62, 64, 67] or none beyond the public funding [63], while three studies (21.4%) did not address this item [24, 36, 65]. Three studies had potentially relevant competing interests [37, 41, 66] although one of them stated the opposite [66]. More detailed information is provided in the ESM.

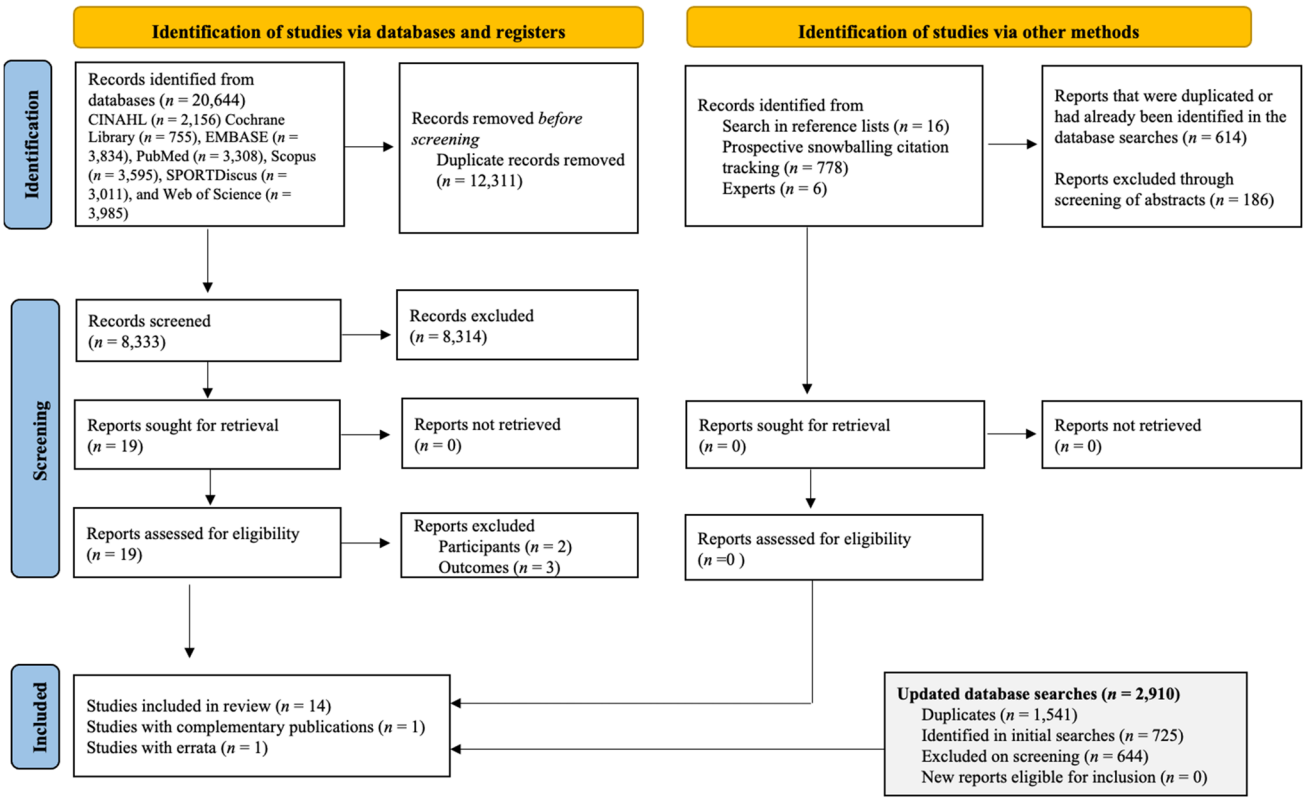

Fig. 1 PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) 2020 flow diagram

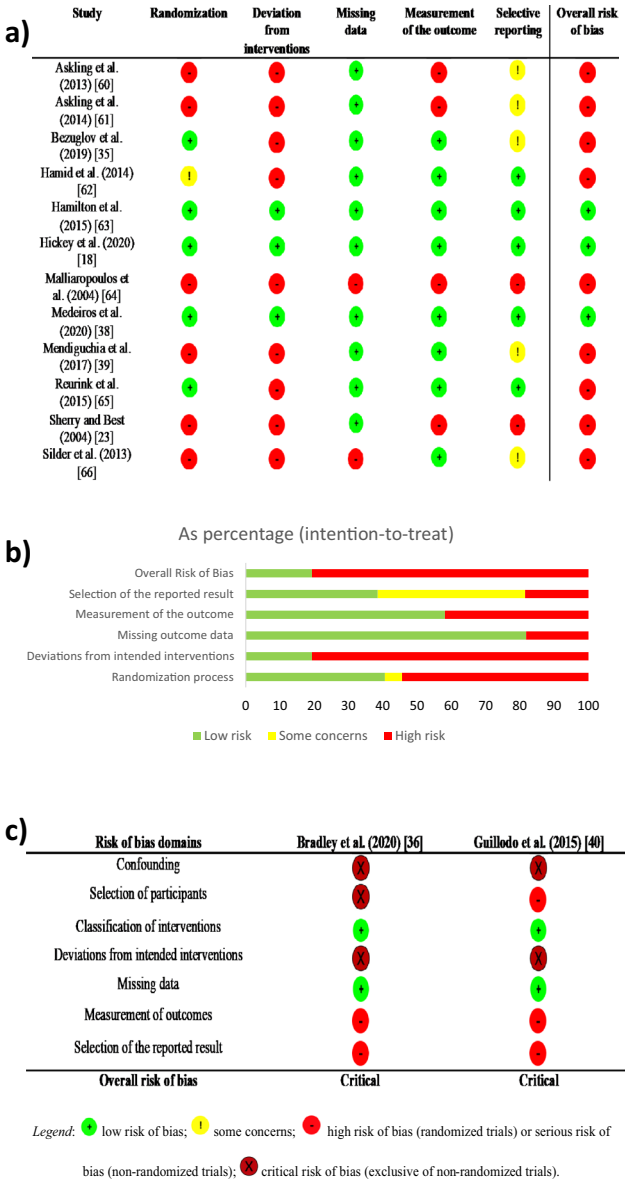

Fig. 2 **a** Risk of bias in randomized trials (study-level assessment); **b** percentage distribution of risk of bias in randomized trials (study-level assessment); and **c** risk of bias in non-randomized trials (study-level assessment)

3.3.2 Participant Demographics

We present here a summary of participant characteristics and further information is available in the ESM. Across the 14 studies, 730 participants were included, with sample sizes that ranged from $n = 24$–90 [39, 64]. Participants' age ranged from 14 to 49 years [24, 63], with 14–49 years [24] and 22–31 years [36] being the widest and narrowest ranges, respectively. Five studies did not provide the age range [38–40, 65, 66] and two studies only provided the average age without a standard deviation [37, 41]. Regarding participants' sex, 654 were male and 72 were female (89.6% and 9.9%, respectively), with four missing values (0.5%). Studies reported the practiced sport for 726 participants, with soccer as the most represented ($n = 346$, 47.7%), followed by track and field ($n = 166$, 22.9%) and American football ($n = 74$, 10.2%). The competitive level ranged from amateur to professional and was unreported in three studies [24, 38, 65]. Table 1 synthesizes the participants' characteristics.

3.3.3 Previous Hamstrings or Lower Limb Injuries

Six studies (42.9%) included participants without any previous hamstrings injuries in the same thigh in the previous 6–12 months [40, 41, 61, 62] or ever [24, 65]. Previous ipsilateral or contralateral hamstrings injuries were presented in five studies [24, 38, 63, 64, 66] and unreported in four studies [36, 37, 39, 67]. Previous lower limb injuries (other than hamstrings injuries) were unreported in nine studies [24, 36, 37, 39, 61–64, 67]. One hundred and thirty-two participants (18.1%) presented previous hamstrings injuries and another seven participants (~ 1%) had previous anterior cruciate ligament reconstruction using hamstrings autografts (further information in the ESM).

3.3.4 Injury Classification and Diagnosis

Studies only included participants with acute hamstrings injuries and adopted a wide range of classification systems. Two studies did not report the type of injury and classification system, but a complete disruption or avulsion were excluded [38, 67]. Participants were diagnosed within 2–10 days post-injury. One study did not report the timeline of diagnosis [37], but it can be assumed that examination took place within 48 h, as the interventions started within 24–48 h after injury. Criteria and methods to determine acute hamstrings injury varied substantially across studies and the criteria were unclear in two studies [36, 64]. When MRI was used to confirm the diagnostic findings [36, 37, 41, 61, 62, 64, 66, 67], it was performed within 2–10 days [36, 67] after the acute injury (information unreported in one study [37]). Two studies used ultrasound in addition to MRI [36, 41], four studies only used ultrasound performed within 2–7 days of injury onset [38, 63, 65], and two studies used no imaging [24, 39]. Detailed accounts are presented in the ESM.

The biceps femoris (even if the injured long or short head was not always reported) represented 61.8–87.5% [39, 41], the semitendinosus 6.9–21.7% [37, 67], and the semimembranosus 7.0–26.5% [41, 62] of all injuries. In the two studies that classified sprinting versus stretching-type injuries and reported the specific muscles injured, the biceps femoris long head and the semitendinosus corresponded to

Table 1 Participant characteristics (mean ± standard deviation unless otherwise stated)

Study (year)	Sample size	Age and sex	Previous injuries	Sports and competitive level
Askling et al. (2013) [61]	Initial sample: $n=75$ Dropouts: none	Global: NR L-protocol: 25 ± 5 years (median: 24, range: 16–37) C-protocol: 25 ± 6 years (median: 25, range: 15–37) Male ($n=69$, 92.0%) and female ($n=6$, 8.0%) In each group: 8.0% female, 92.0% male	*Hamstrings* None in the same leg in the previous 6 months *Lower limb (non-hamstring)* NR	Soccer, mainly (unreported percentage) from the two highest divisions in Sweden. Elite vs non-elite (unclear if this refers to the division): $n=67$ (89.3%) vs $n=8$ (10.7%)
Askling et al. (2014) [62]	Initial sample: $n=56$ Dropouts: none	Global: NR L-protocol: 21 ± 4 years (median: 19, range: 15–29) C-protocol: 19 ± 3 years (median: 18, range: 15–29) Male ($n=38$, 67.9%) and female ($n=18$, 32.1%). In each group: 32.0% female, 68.0% male	*Hamstrings* None in the same leg in the previous 6 months *Lower limb (non-hamstring)* NR	Track and field ($n=46$ sprinters and $n=10$ jumpers). Ranked among the top 20 in each discipline indoors and/or outdoors
Bezuglov et al. (2019) [36]	Initial sample: $n=40$ Dropouts: none	Global: 27 ± 3.3 years (range: 22–31) PRP: NR Placebo: NR Male individuals	*Hamstrings* NR *Lower limb (non-hamstring)* NR	Soccer: Russia Football Premier League and Russian Football National League
Bradley et al. (2020) [37]	Initial sample: $n=69$ Dropouts: NR	Global: NR PRP group: 28.8 years (SD or range: NR) Non-PRP group: 25.7 years (SD or range: NR) Only male individuals	*Hamstrings* NR *Lower limb (non-hamstring)* NR	Single American football team from the National Football League
Guillodo et al. (2015) [41]	Initial sample: $n=34$ Dropouts: NR	Global: NR PRP group: 26.3 ± 3.7 years (range: NR) Non-PRP group: 28.8 ± 7.4 years (range: NR) Only male	*Hamstrings* None in the same leg in the previous 12 months *Lower limb (non-hamstring)* Participants were excluded if presenting a history of direct impact at the site of injury	Running ($n=2$), basketball ($n=2$), soccer ($n=27$), handball ($n=1$), Thai boxing ($n=1$), weightlifting ($n=1$) Non-league ($n=1$), district ($n=6$), regional ($n=18$), national ($n=5$), international ($n=4$)
Hamid et al. (2014) [63]	Initial sample: $n=28$ Dropouts: $n=4$ ($n=2$ in each group)	Global median and IQR: 21.00, 8.50 (range: 17–49) PRP: 20.00, 6.50 Non-PRP: 21.00, 8.50 Male ($n=24$, 85.7%). Female ($n=4$, 14.3%)	*Hamstrings* Not directly reported, but previous hamstrings injury was included as a covariate *Lower limb (non-hamstrings)* NR	Track and field ($n=12$), soccer ($n=9$), other ($n=7$, hockey, netball, basketball, rugby, tennis, shot put) National level ($n=15$), state level ($n=3$), club level ($n=2$), school level ($n=8$)

Table 1 (continued)

Study (year)	Sample size	Age and sex	Previous injuries	Sports and competitive level
Hamilton et al. (2015) [64]	Initial sample: $n=90$ Dropouts: $n=5$ lost to primary outcome analysis; $n=4$ lost at 2-month follow-up; $n=7$ lost at 6-month follow-up	Global: NR PRP: 26.6 ± 5.9 years (median 26.3, range: 21.2–31.4) PPP: 25.6 ± 5.8 years (median 24.9, range: 22.1–29.3) No injection: 25.5 ± 5.7 years (median 24.3, range: 20.7–29.4) Only male	*Hamstrings* Supposedly, it was an exclusion criterion, but the authors report previous hamstrings injuries in all groups: PRP ($n=19$, 63.3%), PPP ($n=15$, 50.0%), and non-injection ($n=15$, 50.0%) *Lower limb (non-hamstrings)* NR	Athletics ($n=4$), basketball ($n=2$), decathlon ($n=1$), soccer ($n=66$), futsal ($n=8$), handball ($n=3$), hockey ($n=2$), physical coach football ($n=1$), squash ($n=1$), volleyball ($n=1$), weightlifting and bodybuilding ($n=1$) Professional athletes ($n=87$), "competitive" athletes ($n=3$)
Hickey et al. (2020) [18]	Initial sample: $n=43$ Dropouts: none	Global: NR Pain-free group: 27.4 ± 5.2 years. Range: NR Pain-threshold: 24.9 ± 5.3 years. Range: NR Only male	*Hamstrings* Pain-free: $n=16$ (72.7%) had a previous hamstrings injury Pain-threshold: $n=14$ (66.7%) had a previous hamstrings injury *Lower limb (non-hamstrings)* None with other causes of posterior thigh pain (e.g., hamstrings tendinopathy, low back pain)	Australian rules football ($n=32$), other ($n=11$). Competitive level: NR
Malliaropoulos et al. (2004) [65]	Initial sample: $n=80$ Dropouts: NR	Global: 20.5 ± unreported years. Range: NR One daily session: 20.6 ± 3.7 years. Range: NR Four daily sessions: 20.3 ± 3.3 years. Range: NR Male ($n=52$, 65.0%). Female ($n=28$, 35.0%)	*Hamstrings* None *Lower limb (non-hamstring)* Free medical history for hamstrings, lumbar spine, or lower-extremity injuries	Presumably, track and field (as this Federation provided the ethics approval). Competitive level: NR
Medeiros et al. (2020) [39]	Initial sample: $n=24$ Dropouts: $n=2$ ($n=1$ *per* group)	Global: NR LLLT: 30.4 ± 7.1 years. Range: NR Placebo: 28.0 ± 7.4 years. Range: NR Only male	*Hamstrings* NR *Lower limb (non-hamstrings)* NR	Soccer ($n=14$), futsal ($n=5$), American football ($n=2$), track and field ($n=2$), rugby ($n=1$) Amateur
Mendiguchia et al. (2017) [40]	Initial sample: $n=54$ Dropouts: $n=6$	Global: NR Individualized: 24.0 ± 4.4 years. Range: NR General: 22.9 ± 6.0 years. Range: NR Only male	*Hamstrings* None in the same leg in the previous 6 months *Lower limb (non-hamstrings)* None who had experienced extrinsic trauma to the posterior thigh or chronic hip, knee, leg, ankle, foot, or lumbopelvic injuries	Semiprofessional soccer

Table 1 (continued)

Study (year)	Sample size	Age and sex	Previous injuries	Sports and competitive level
Reurink et al. (2015) [66]	Initial sample: $n=80$ Dropouts: none for primary outcome analysis. $n=7$ dropouts at 1-year follow-up	Global: NR PRP: 28 ± 7 years. Range: NR Placebo: 30 ± 8 years. Range: NR PRP: Male ($n=39$, 95.1%) and female ($n=2$, 4.9%) Placebo: male ($n=37$, 94.9%) and female ($n=2$, 5.1%)	*Hamstrings* PRP: $n=27$ (65.9%). Ipsilateral: $n=24$ (58.5%) Placebo: $n=23$ (59.0%). Ipsilateral: $n=18$ (46.2%) *Lower limb (non-hamstring)* Previous ipsilateral hamstrings anterior cruciate ligament-graft harvesting (no injury but of importance): PRP group: $n=5$ (12.2%) Placebo group: $n=2$ (5.1%)	Soccer ($n=57$), field hockey ($n=12$), track and field ($n=4$), American football ($n=3$), fitness ($n=2$), cricket ($n=1$). [1 missing in the placebo group] PRP: competitive ($n=30$, 73.2%) and recreational ($n=11$, 26.8%) Placebo: competitive ($n=29$, 74.4%) and recreational ($n=10$, 25.6%) Unclear definition of recreational and competitive
Sherry and Best (2004) [24]	Initial sample: $n=28$ Dropouts: $n=4$ ($n=3$ in intervention, $n=1$ in comparator)	Global: NR PATS: 23.2 ± 11.1 years. Range: 15–49 years STST: 24.3 ± 12.4 years. Range: 14–49 years PATS: Male ($n=9$, 69.2%) and female ($n=4$, 30.8%) STST: male ($n=9$, 81.8%) and female ($n=2$, 18.2%)	*Hamstrings* None with chronic hamstrings injuries nor previous hamstrings injuries in the same leg STST: $n=2$ had a previous contralateral hamstrings injury PATS: $n=1$ had a previous contralateral hamstrings injury *Lower limb (non-hamstrings)* None currently with other lower limb injuries	Multi-sports ($n=11$), softball ($n=3$), triathlon ($n=1$), tennis ($n=1$), sprinter/jumper ($n=4$), soccer ($n=4$) Competitive level: NR
Silder et al. (2013) [67]	Initial sample: $n=29$ Dropouts: $n=4$ ($n=3$ in intervention, $n=1$ in comparator)	Global: 24 ± 9 years. Range: 16–46 years PATS: 25.4 ± 10.2 years. Range: 16–46 years PRES: 22.3 ± 7.9 years. Range: 16–44 years PATS: Male ($n=11$, 68.7%) and female ($n=5$, 31.3%) PRES: male ($n=12$, 90.9%) and female ($n=1$, 9.1%)	*Hamstrings* NR *Lower limb (non-hamstrings)* NR	Sports requiring high-speed running. No further information provided. None was professional

IQR interquartile range, *NR* non-reported, *LLLT* low-level laser therapy, *PATS* progressive agility and trunk stabilization, *PPP* platelet-poor plasma, *PRES* progressive running and eccentric strengthening, *PRP* platelet-rich plasma, *SD* standard deviation, *STST* hamstrings stretching and strengthening

85.0–94.0% [61, 62] and 76.0–100.0% [61, 62] of sprinting-type injuries, respectively. The specific muscles injured were not reported in five studies [24, 40, 64–66].

3.3.5 Interventions, Comparators, and Co-interventions

Seven randomized studies compared different therapeutic exercise-based interventions, particularly the L-protocol (focused on the lengthening phase of the hamstrings actions) versus the C-protocol (focused on the hamstrings actions shortening phase) [61, 62], pain-free versus pain-threshold exercise [38], single versus four stretching daily sessions [65], multimodal individualized exercise versus a general exercise program [40], progressive agility and trunk stabilization (PATS) versus hamstrings stretching and strengthening (STST) [24], and PATS versus progressive running and hamstrings eccentric strengthening (PRES) [67]. A single randomized trial compared low-level (LLLT) to placebo laser therapy [39]. Three randomized studies compared PRP to placebo injections [36, 66] or no injection [63], one trial compared all these three conditions [64], and the two non-randomized trials compared PRP injections to no injection [37, 41]. A complete description is reported in Tables S4 and S5 of the ESM.

The intervention length was not predetermined in any study and rehabilitation was progressive and stepwise depending on goal-based criteria to progress (which could be assessed through TRTS and/or TRFT). Commonly, daily [36] and weekly [24, 61–64, 67] assessments were performed, or even prior to every rehabilitation session [38, 39]. Follow-up (when existing and described) ranged from 4 to 12 months after return to full sports training [24, 41, 61, 62, 66, 67], but was unclear in two studies [37, 65]. All studies included therapeutic exercise as intervention or co-intervention (the details of each intervention and comparator, including information dosage, is shown in the ESM).

3.3.6 Quality and Completeness of Therapeutic Exercise Program Reporting

The completeness and quality of exercise and physical rehabilitation protocols were appraised for all studies as either interventions or co-interventions (Fig. 3). Overall, only three studies (21.4%) were judged with a low risk of ineffectiveness in all seven domains [38, 39, 64]. The remaining 11 studies (78.6%) had a high risk of ineffectiveness in two [40, 63, 66, 67], three [24, 61, 62], four [65], five [36, 41], or six domains [37]. A detailed analysis is provided in the ESM.

3.3.7 Primary Outcomes

Eleven studies (78.6%) assessed TRFT [24, 36, 38, 40, 41, 61–66], with one study assessing both TRTS and TRFT (but the information for the latter was unclear [37]), and two studies focusing only on TRTS [39, 67]. Terminology varied, sometimes even within the same study (e.g., return to play, full return to sports, return to full training, return to full participation in the training process). Eleven studies (78.6%) assessed reinjuries and/or new injuries, from which six studies reported reinjury rates < 5.0% [36, 37, 39, 41, 61, 62]. Details are presented in the ESM.

3.3.8 Secondary Outcomes

Few studies reported pre-intervention to post-intervention changes in strength and ROM [39, 67], bilateral asymmetries [66, 67], and pain [36, 66]. Overall, no between-group differences could be detected for secondary outcomes. Adverse effects (beyond new hamstrings injuries or reinjuries) were unreported in six studies (42.9%) [24, 39, 40, 61, 62, 65]. In the remaining studies, there were either no adverse effects to report or these were mostly minor and/or isolated cases. A detailed account is provided in the ESM.

3.4 Narrative Synthesis

3.4.1 Studies Comparing Therapeutic Exercise-Based Interventions

Therapeutic exercise-based interventions were diverse, with only a few comparisons available for each program. Two studies compared the L-protocols and the C-protocols [61, 62], with one study [62] also including a running and stationary cycling program. The L-protocol compared with the C-protocol showed faster TRFT (28 ± 15 days vs 51 ± 21 days [61]; 49 ± 26 days vs 86 ± 34 days [62]), but data were compromised because of a risk of selection (randomization) and detection bias. All negative-MRI participants were purposely allocated to the L-protocol, with implications for the recovery time: in one study [61], negative-MRI participants had an average TRFT of 6 days, and four of the 11 soccer players recovered within 5 days of injury and did not even perform the L-protocol. In the other study [62], the negative-MRI participants returned after 15 days, compared with 45 days for the other participants. Moreover, the assessors were unblinded to the intervention and the authors explicitly stated that this knowledge could have influenced the Askling H test, which determined discharge to return to sport. Therefore, the evidence from these two studies is associated with important methodological problems that could have influenced the results. One reinjury (0.8%) [61] and two reinjuries (3.6%) were registered [62] in the C-protocol, and none in the L-protocol.

Two studies analyzed the PATS [24, 67], with one comparing PATS to PRES (based on running and eccentric strengthening) [67]. Both intervention and comparator were

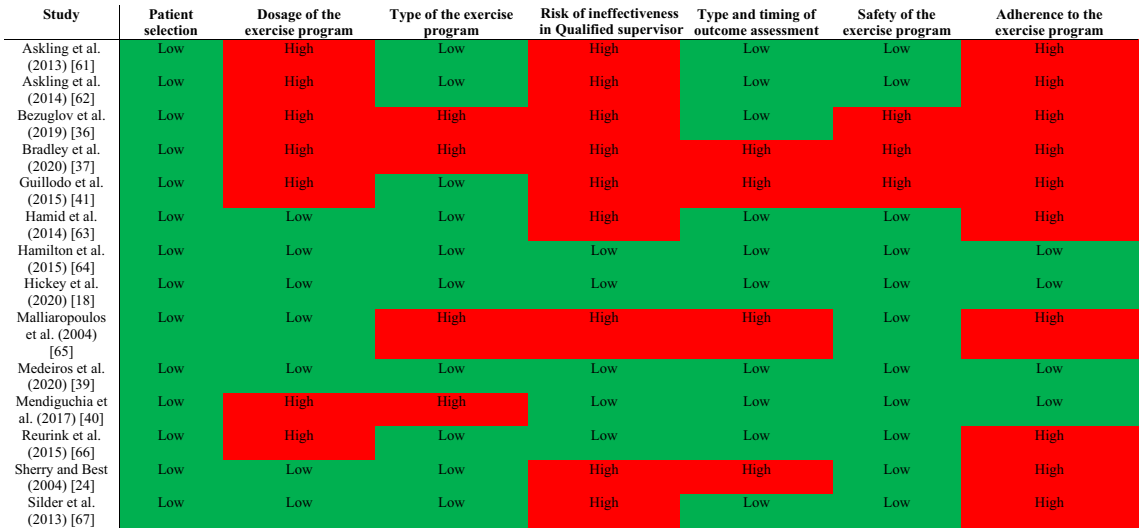

Fig. 3 Risk of ineffectiveness in qualified supervisor

home based and performed daily (with only one weekly supervised session guaranteed and poor adherence-related measures). No differences were detected in TRTS between PATS and PRES groups, but one versus three reinjuries (6.3 vs 23.1%) were registered in the PATS and PRES groups, respectively. The other study [24] compared PATS to STST (based on hamstrings stretching and concentric, eccentric, and isometric strengthening), again in a mostly home-based setting with very poor control of adherence. The PATS group had a shorter TRFT (22.2 ± 8.3 days versus 37.4 ± 27.6 days), but a closer analysis raised concerns, as 72.0% of participants in the PATS groups had a grade 2 injury versus only 36.0% of participants in the STST group. These baseline differences suggest problems with the randomization process. Furthermore, the authors planned an intention-to-treat analysis, but instead performed a per-protocol analysis, suggestive of bias due to selective reporting. This study also presented an outlier value of reinjuries in the STST group ($n = 7$, 63.6%) versus a single reinjury (7.7%) in the PATS group.

A single study compared one versus four daily sessions of hamstrings static stretching [65]. The single daily session group took longer to return to training than the other group (15.1 ± 0.8 days vs 13.3 ± 0.7 days) and, although this difference was statistically significant, in absolute values there was only a 2-day difference in recovery time. Reinjuries were not reported, and the study [65] was judged at a high risk of bias in all domains and a high risk of ineffectiveness in several i-CONTENT domains (type of exercise program, qualified supervisor, type and timing of outcome assessment, and adherence to the exercise program).

One study compared an individualized and multifactorial criteria-based algorithm to a general rehabilitation protocol including a running-based program and the L-protocol [40], with no description of the general rehabilitation components or the running program specifications. There were no differences in TRFT, but there were fewer reinjuries in the individualized group versus the general rehabilitation group ($n = 1$, 4.0% vs $n = 6$, 25.0%). Finally, one study applied a strength-based exercise program (combined with running) performed at different pain-threshold intensities (0 and ≤ 4 out of a ten-point scale) [38]. No differences were found in TRFT between groups and two reinjuries were registered in each group (9.1% and 9.5% in the pain-free and pain-threshold groups, respectively).

In summary, few studies have assessed each exercise program type (e.g., PATS and L-protocol), relevant heterogeneity was observed regarding their study populations, diagnosis and criteria for progressing in rehabilitation, and methodological problems associated with these studies were detected. Currently, the available evidence does not allow us to confidently assume or suggest a superiority of one exercise program over another in terms of TRTS/TRFT or reinjuries.

3.4.2 Studies Comparing PRP Injections to Placebo or Control

Two randomized studies compared PRP to placebo injections [36, 66], one contrasted PRP with no injection [63], and another compared the three conditions [64]. Because the three studies comparing PRP to placebo injections [36, 64, 66] were very heterogeneous (regarding participants, injury diagnosis, injection contents and dosages, and co-interventions), a quantitative pooled synthesis was not accomplished. Most studies applied a single PRP injection [36, 63, 64] and

one study [66] applied two injections 5–7 days apart, with dosages varying from 3 to 8-mL single applications [36, 63] to 1-mL injections in three sites [64, 66]. Injection platelet count varied from unreported [63, 64, 66] to 700,000 per 1 mL [36] and activation agents varied from none [63, 64] to 20 µL per mL of plasma [36] (or were unreported [66]). Placebo injections also varied in content (0.9% NaCl [36], isotonic saline solution [66], platelet-poor plasma [64]), quantity (1–2 [36, 64, 66]), dosage (8 mL or 3 × 1 mL [36, 64, 66]), activating agents (unreported [36, 66] and no agent used [64]), and number of injection sites (single to three locations [36, 64, 66]).

A shorter TRFT was observed in the PRP group compared with the placebo group (11.4 ± 1.2 days vs 21.3 ± 2.7 days) in one study [36] and no reinjuries were registered; information was insufficient to assess baseline differences between groups. Another study showed a faster TRFT in the PRP group than in the platelet-poor plasma group (median 21 vs 27 days and interquartile range 16–33 vs 19–33) [64]. Both groups sustained two reinjuries (6.7% and 8.0%) at the 2-month follow-up, with an additional reinjury in the platelet-poor plasma group at the 6-month follow-up. Last, there were no differences in TRFT between PRP and placebo injections in a third study [66]. In this study, at the 1-year follow-up, 10 and 11 players (27.0% and 30.0%), respectively, in the PRP and placebo groups sustained a reinjury.

One study reported faster TRFT (26.7 ± 7.0 vs 42.5 ± 20.6 days) when comparing PRP to no injection groups [63], but there were important baseline differences between the groups (particularly the fact that 42.9 vs 78.6% of participants had reinjuries and 57.1 vs 78.6% of them had biceps femoris injuries, respectively). A study with three groups (PRP, placebo, no injection) showed a faster TRFT with PRP injection versus placebo (platelet-poor plasma) [64]; however, the same study reported no differences between PRP and the group taking no injections. This study [64] also reported two reinjuries in each group at the 2-month follow-up (with an additional reinjury in the no injection group at the 6-month follow-up).

The two non-randomized cohort studies compared PRP to no injection [37, 41]. One study [37] applied one to three leukocyte-poor PRP injections and both groups engaged in poorly defined physiotherapy and physical therapy protocols. There were no differences in the TRTS and in the number of days off, and each group sustained one reinjury. The authors mentioned lost games, but this may have been affected by match scheduling or coaching decisions. The other non-randomized cohort trial [41] compared a single PRP injection to no injection, with both groups engaging in unclear physiotherapy protocols and exercise programs with undisclosed dosage. There were no differences in TRFT and there were no reinjuries to report. Both non-randomized studies were judged at high risk of ineffectiveness and at critical risk of bias. Overall, the evidence on PRP injections is contentious and they may not result in a faster TRTS/TRFT or reduced reinjury rates than placebo injections or no injection.

3.4.3 Single Study Assessing Low-Level Laser Therapy

One study compared three weekly sessions of LLLT (60 s and 30 J per site, 850-nm wavelength, and continuous frequency) to placebo LLLT (with the device turned off), both supplemented by a rehabilitation exercise program focused on hamstrings strength, trunk stabilization, and agility [39]. There were no differences between the groups in TRTS, TRFT was not assessed, and no reinjuries were reported. Lack of imaging techniques (such as MRI or ultrasound) to confirm diagnosis may have resulted in the inclusion of low-grade or unequal injuries, potentially influencing recovery time. Conversely, the study [39] was judged at low risk of bias in all domains and at low risk of ineffectiveness in all i-CONTENT domains.

3.5 Certainty of Evidence

Three studies reported TRTS [37, 39, 67], 11 studies referred to TRFT [24, 36, 38, 40, 41, 61–66], and 12 studies identified reinjuries or new injuries [24, 36–41, 61, 62, 64, 66, 67]. The reduced number of studies for each comparison (one to three studies), the high risk and critical risk of bias, the serious inconsistency, and the high imprecision resulted in a very low certainty of evidence for all outcomes and comparisons analyzed. Therefore, no current recommendation can be provided based on existing evidence (Table 2 synthesizes the main findings, including the GRADE judgments).

4 Discussion

The high incidence of hamstrings injuries and their associated financial costs and performance losses [14–17] require effective rehabilitation protocols to facilitate return to sport and reduce the reinjury risk. We systematically reviewed 14 studies ($n = 730$) that assessed the impact of different conservative rehabilitation strategies to treat acute hamstrings injuries on the TRTS/TRFT and reinjuries.

4.1 What Does the Current Literature Tell Us?

Based on the existing evidence, it is unclear which conservative approaches are more effective in allowing a faster TRTS/TRFT or reducing the reinjury risk. Our results support the findings of a previous systematic review [33] where the authors did not find any effect of the PRP interventions and reported limited evidence for exercise-based interventions. In our systematic review, we included six new studies

Table 2 Synthesis and certainty of evidence regarding the effects of conservative interventions on time to return to sport, time to return to full training, and reinjuries

Outcome	Study (year)	Intervention	Comparator	Estimate MD/RR (95% CI)	RoB	i-Content	Grade
Time to return to sport (3 studies)	Silder et al. (2013) [67]	PATS ($n=13$) 25.2 ± 6.3 days	PRES ($n=12$) 28.8 ± 11.4 days	3.60 (−3.94 to 11.14)	-	+ + + - + + -	Very low certainty[a,b,c]
	Bradley et al. (2020) [37]	PRP ($n=30$) 22.5 ± 20.1 days	No injection ($n=39$) 25.7 ± 20.6 days	3.20 (−6.68 to 13.08)	X	+ - - - - - -	Very low certainty[a,b,c]
	Medeiros et al. (2020) [39]	LLLT ($n=11$) 23.1 ± 9.1 days (12–41 days)	Placebo LLLT ($n=11$) 23.8 ± 12.6 days (11–45 days)	0.70 (−9.08 to 10.48)	+	+ + + + + + +	Very low certainty[a,c]
Time to return to full training (11 studies)	Askling et al. (2013) [61]	L-protocol ($n=37$) 28.0 ± 15.0 days (8–58 days)	C-protocol ($n=38$) 51.0 ± 21.0 days (12–94 days)	23.00 (14.58 to 31.42)	-	+ - + - + + -	Very low certainty[b,d,e]
	Askling et al. (2014) [62]	L-protocol ($n=28$) 49.0 ± 26.0 days (18–107 days)	C-protocol ($n=28$) 86.0 ± 34.0 days (26–140 days)	37.00 (20.78 to 53.22)	-	+ - + - + + -	
	Hickey et al. (2020) [18]	Pain-free exercise ($n=22$) 15 days[f] (95% CI 13 to 17)	Pain-threshold exercise ($n=21$) 17 days[f] (95% CI 11 to 24)	2.00 (−4.47 to 8.47)	+	+ + + + + + +	Very low certainty[a,c]
	Malliaropoulos et al. (2004) [65]	4 ×/day stretching ($n=40$) 15.1 ± 0.8	1 ×/day stretching ($n=40$) 13.3 ± 0.7	−1.80 (−2.13 to −1.47)	-	+ + - - - + -	Very low certainty[a,b,e]
	Mendiguchia et al. (2017) [40]	Individualized, multifactorial criteria-based algorithm ($n=24$) 25.5 ± 7.8 days	General rehabilitation, running-based program, and L-protocol ($n=24$) 23.3 ± 11.7 days	−2.20 (−7.98 to 3.58)	-	+ - - + + + +	Very low certainty[a,b,c]
	Sherry and Best (2004) [24]	PATS ($n=13$) 22.2 ± 8.3 days (10–35 days)	STST ($n=11$) 37.4 ± 27.6 days (10–95 days)	15.20 (−1.45 to 31.85)	-	+ + + - - + -	Very low certainty[a,b,c]
	Bezuglov et al. (2019) [36]	PRP ($n=20$) 11.4 ± 1.2 days	Placebo ($n=20$) 21.3 ± 2.7 days	9.90 (8.56 to 11.24)	-	+ - - - + - -	Very low certainty[c,h,i]
	Reurink et al. (2015) [66]	PRP ($n=41$) 42 days[f] (IQR 30–58) (19–105 days)[g]	Placebo ($n=39$) 42 days[f] (IQR 37–56) (14–149 days)	0.00 (−8.22 to 8.22)	-	+ - + + + + -	
	Hamilton et al. (2015) [64]	PRP ($n=28$) 21 days[f] (IQR 16–33)	Placebo (PPP) ($n=30$) 27 days[f] (IQR 19–33)	6.00 (−0.38 to 12.38)	+	+ + + + + + +	
	Guillodo et al. (2015) [41]	PRP ($n=15$) 50.9 ± 10.7 days	No injection ($n=19$) 52.8 ± 15.7 days	1.90 (−7.77 to 11.57)	X	+ - + - - - -	Very low certainty[b,c,i]
	Hamid et al. (2014) [63]	PRP ($n=12$) 26.7 ± 7.0 days	No injection ($n=12$) 42.5 ± 20.6 days	15.80 (2.77 to 28.83)	-	+ + + - + + -	
	Hamilton et al. (2015) [64]	PRP ($n=28$) 21 days[f] (IQR 16–33)	No injection ($n=27$) 25 days[f] (IQR 20–30)	4.00 (−1.93 to 9.93)	+	+ + + + + + +	
New hamstrings injuries or reinjuries (12 studies)	Askling et al. (2013) [61]	L-protocol ($n=37$) 0/37 (0.0%)	C-protocol ($n=38$) 1/38 (2.6%)	0.34 (0.01 to 8.14)	-	+ - + - + + -	Very low certainty[b,c]
	Askling et al. (2014) [62]	L-protocol ($n=28$) 0/28 (0.0%)	C-protocol ($n=28$) 2/28 (7.1%)	0.20 (0.01 to 3.99)	-	+ - + - + + -	
	Hickey et al. (2020) [18]	Pain-free exercise ($n=22$) 2/22 (9.1%)	Pain-threshold exercise ($n=21$) 2/21 (9.5%)	0.96 (0.15 to 6.17)	+	+ + + + + + +	Very low certainty[a,c]

Table 2 (continued)

Outcome	Study (year)	Intervention	Comparator	Estimate MD/RR (95% CI)	RoB	i-Content	Grade
	Mendiguchia et al. (2017) [40]	Individualized, multifactorial criteria-based algorithm ($n=24$) 1/24 (4.2%)	General rehabilitation, running-based program, and L-protocol ($n=24$) 6/24 (25.0%)	0.17 (0.02 to 1.28)	-	+ - - + + + +	Very low certainty[a,b,c]
	Sherry and Best (2004) [24]	PATS ($n=13$) 1/13 (7.7%)	STST ($n=11$) 7/11 (63.6%)	0.12 (0.02 to 0.84)	-	+ + + - - + -	Very low certainty[a,b,c]
	Silder et al. (2013) [67]	PATS ($n=13$) 1/13 (7.7%)	PRES ($n=12$) 3/12 (25.0%)	0.31 (0.04 to 2.57)	-	+ + + - + + -	Very low certainty[a,b,c]
	Bezuglov et al. (2019) [36]	PRP ($n=20$) 0/20 (0.0%)	Placebo ($n=20$) 0/20 (0.0%)	1.00 (0.02 to 48.01)	-	+ - - - + - -	Very low certainty[c,d,h]
	Reurink et al. (2015) [66]	PRP ($n=37$) 10/37 (27.0%)	Placebo ($n=36$) 11/36 (30.6%)	0.89 (0.43 to 1.82)	-	+ - + + + + -	
	Hamilton et al. (2015) [64]	PRP ($n=26$) 2/26 (7.7%)	Placebo [PPP] ($n=28$) 3/28 (10.7%)	0.72 (0.13 to 3.96)	+	+ + + + + + +	
	Bradley et al. (2020) [37]	PRP ($n=30$) 1/30 (3.3%)	No injection ($n=39$) 1/39 (2.6%)	1.30 (0.08 to 19.95)	X	+ - - - - - -	Very low certainty[b,c,d]
	Guillodo et al. (2015) [41]	PRP ($n=15$) 0/15 (0.0%)	No injection ($n=19$) 0/19 (0.0%)	1.25 (0.03 to 59.60)	X	+ - + - - - -	
	Hamilton et al. (2015) [64]	PRP ($n=26$) 2/26 (7.7%)	No injection ($n=29$) 3/29 (10.3%)	0.74 (0.13 to 4.11)	+	+ + + + + + +	
	Medeiros et al. (2020) [39]	LLLT ($n=11$) 0/11 (0.0%)	Placebo LLLT ($n=11$) 0/11 (0.0%)	1.00 (0.02 to 46.41)	+	+ + + + + + +	Very low certainty[a,c]

CI confidence interval, *IQR* interquartile range, *LLLT* low-level laser therapy, *MD* mean difference, *PATS* progressive agility and trunk stabilization, *PPP* platelet-poor plasma, *PRES* progressive running and eccentric strengthening, *PRP* platelet-rich plasma, *RoB* risk of bias, *RR* risk ratio for sustaining a reinjury or new injury, *STST* hamstrings stretching and strengthening

[a]Automatically judged at very low certainty because of a single study being available for this comparison

[b]Downgraded by two levels because of a high risk of bias in all the studies and/or due to critical risk of bias

[c]Downgraded by two levels if there was also no clear direction of the effects

[d]Downgraded by one level because of clinical and/or statistical heterogeneity

[e]Downgraded by one level because of < 800 participants for the comparison

[f]Median value

[g]One participant still had not returned at day 182 and this player was censored from the analysis

[h]Downgraded by one level because of a high risk of bias in more than half of the studies

[i]Downgraded by two levels because of clinical and statistical heterogeneity

i-CONTENT: first row, from left to right: risk of ineffectiveness in patient selection, dosage of the exercise program, type of the exercise program, and qualified supervisor. Second row, from left to right: risk of ineffectiveness in type and timing of outcome assessment, safety of the exercise program, and adherence to the exercise program. + indicates a low risk of ineffectiveness, - indicates a high risk of ineffectiveness

Risk of bias: + indicates a low risk of bias, - indicates a high risk of bias, X indicates a critical risk of bias

[36–41] and excluded two studies that did not meet the eligibility criteria for population [56] and outcomes [58]. In contrast to the previous systematic review [33], we considered that the reduced number of studies for each comparison and their clinical heterogeneity advised against performing a meta-analysis; we thus avoided pooling data from different studies and reported the between-group differences for each study and described them in a narrative manner.

When comparing different exercise-based interventions, it is unclear which exercise modalities are more effective (although there is some support for eccentric training) and even less is known concerning dose–response relationships, which aligns with the main findings of the previous review [33]. Also aligned with this review [33], the effectiveness of PRPs and placebo injections remains unclear. Independent of participants' age, sex, sport background, or injury characteristics (e.g., severity, anatomical location, and etiology), no recommendations on the best rehabilitation strategy can be provided based on current knowledge for TRTS/TRFT and reinjuries.

The literature has devoted considerable attention to the incidence of hamstrings injuries and reinjuries [3, 4, 7, 12] as well as to their financial and performance-related costs [14–17]. The literature has also extensively focused on the primary prevention of hamstrings injuries [5, 71–76], but their number continues to grow [2, 77], and thus we assumed that many studies would be found focusing on rehabilitation strategies. However, only 14 studies fulfilled eligibility criteria (12 randomized and two non-randomized with 730 participants), with a maximum of three studies per comparison. Most randomized studies (75.0%) were judged at high risk of bias, both non-randomized studies (100.0%) were judged at critical risk (i.e., above serious risk), and 78.6% of the exercise programs were judged at high risk of ineffectiveness. These findings corroborate the poor reporting of exercise interventions in the context of hamstrings injury rehabilitation that was recently highlighted by a scoping review [78]. The GRADE judgments denoted very low confidence in the existing published data.

These findings emphasize it is not possible to determine which are the most effective conservative interventions for recovery after acute hamstrings injuries. Studies have focused mostly on exercise-based interventions and on comparing PRP to placebo or no injection (with exercise as a co-intervention). The benefits of adding PRP to exercise interventions remain unclear (conflicting findings) and the most appropriate exercise modalities and dosages are not yet known. Although rehabilitation should be customized to individual needs, it is unknown whether the most appropriate conservative interventions may vary depending on injury mechanism, injury classification and severity, type of sport, competitive level, sex, age, or other individual characteristics. Although it has been hypothesized that the specific injury location, especially if affecting the intramuscular tendon, may change the length of recovery [29, 30, 79], the evidence is still preliminary and it is unclear how conservative interventions could be adapted.

Very recent clinical practice guidelines [80] maintained that moderate-level evidence supports faster TRTS/TRFT with interventions focusing on eccentric training, added to stretching, general strengthening, stabilization, and progressive running programs. Likewise, the guidelines [80] reported moderate-level evidence in support of PATS in addition to stretching, general strengthening, and "functional" exercises to reduce reinjury risk after an acute hamstrings injury. The results of our systematic review do not fully support either of these claims and, with the scarce and limited available data, no recommendations can be made on which is the best rehabilitation strategy for acute hamstrings injuries.

Notwithstanding the limitations discussed above and the very low certainty of evidence, some clinical findings may *temporarily* guide clinical practice: (1) adding eccentric lengthening exercises seems superior to conventional stretching and strengthening exercises for returning sooner to full training [61, 62], but these findings are from a single research group and require confirmation by replication studies; (2) no intervention was superior in reducing the reinjury risk, thus no intervention should be prioritized over any other for purposes of secondary prevention; and (3) PRP did not consistently allow a faster TRFT or reduce the reinjury risk and therefore seems to add no value in accelerating recovery from hamstrings injuries.

4.2 Are We Comparing the Same Things?

Our systematic review highlighted extensive heterogeneity in intervention and comparators (including mode, dosage and supervision of the exercise programs, and content and dosages of PRP and placebo injections) and outcome registration. Even within a single group of the same study, the ranges of TRTS/TRFT exhibited extreme interindividual variation, which may be partially related to interindividual variations in hamstrings anatomy and physiology [31], but also to age. Indeed, the age range within a single study was as wide as 14–49 years [24]. As older players are at a higher risk of injury than their younger counterparts [81, 82], investigating and comparing samples with large age variations may affect the results. Moreover, because women comprise only a minority of the studied samples (~10%), it is currently unclear if there are relevant sex-related differences that can affect the recovery process and/or the risk of reinjury.

The competitive level was not reported uniformly across studies, a problem that creates difficulty performing between-study comparisons and to which a recent solution has been proposed [83]. Still, it could be easily identified

that the competitive level in the included studies ranged from amateur practitioners to professional athletes. Comparing rehabilitation processes between very distinct competitive levels is tricky, as there are other factors that can come into play, such as higher motivation from professional players or their easier access to high-quality resources and rehabilitation. The pressure on an early return to competition may be superior at the highest levels, considering the performance and financial stakes. Of note, nearly 50% of research on the topic is focused on soccer, followed by track and field (~ 22%) and American football (~ 10%), with only scarce information on return to sports and reinjury risk being available for other sports.

With regard to secondary outcomes, nearly nothing is known about how effective these interventions are for other relevant variables such as strength, ROM, bilateral and anteroposterior asymmetries, balance, power, speed, endurance, and adverse effects. Even exercise-based interventions largely neglected these outcomes or assessed them as solely post-intervention values. Recent clinical practice guidelines further underline the need to evaluate the ability to walk, run, and sprint [80].

The included studies also varied considerably with respect to injury classification systems, diagnostic and inclusion criteria, criteria for returning to sport, and assessments timing, contributing to clinical heterogeneity and making between-study comparisons very difficult, as had been previously pinpointed elsewhere [84]. The sheer diversity of classification systems denotes a lack of agreement and consistency across studies and may contribute to increasing the heterogeneity of findings, which is further exacerbated by mixing grade I and II injuries and MRI-positive with MRI-negative participants. The absence of imaging in some studies, although justified by the authors, cannot completely rule out avulsion or complete rupture, which was an exclusion criterion of our review.

Different sports have specific physical demands and may require different rehabilitation protocols. Perhaps the time has come for a complete and more definitive international consensus on the classification of hamstrings injuries, diagnostic criteria, and criteria for return to full training. Finally, more than half of the studies mixed participants with and without previous hamstring injuries, which represents a relevant confounder for the results of the interventions, as the history of a hamstrings injury greatly increases the risk of having a reinjury [75, 82, 85, 86].

4.3 Room for Improvement: Priorities for Future Research

Although men are up to 60.0% more likely to sustain hamstrings injuries than women [3, 87, 88], they comprise 90% of the research sample. With the rapid increase in female sports participation [89, 90], further research on hamstrings injuries rehabilitation focusing on women is needed. We further identified several features that require more detailed reporting in future studies: (1) explicitly report previous hamstrings injuries or their absence, as well as surgeries involving hamstrings autografts; (2) different hamstrings muscles may be injured differently (mechanisms, consequences, recovery) and proper reporting of which muscles were injured is advised; (3) provide means and standard deviations (or medians and interquartile ranges, when appropriate) for participants' age and preferably also the range; (4) use the i-CONTENT tool [52] to more completely report on the exercise-based interventions; (5) openly monitor and report adverse effects; and (vi) assess pre-intervention to post-intervention changes in secondary outcomes (such as strength and ROM), providing measures of assessment reliability and reporting the smallest worthwhile changes.

Future research should strive to reduce the risk of bias by following simple procedures: (1) pre-register or pre-publish the research protocols; (2) describe how randomization was achieved, explicitly state whether allocation sequence was concealed and attempt to guarantee balanced baseline values for the most relevant variables (e.g., using minimization techniques when randomizing the participants); (3) attempt to equate the intervention and comparator dosages; (4) ensure proper supervision and monitoring of adherence and/or compliance; in largely home-based interventions, strategies such as regular texting, daily logs, and video calls may help to improve compliance; (5) blind the outcome assessors to eliminate the risk of detection bias; and (6) provide data on the inter-assessor reliability of outcome measurement or, when applicable, measures of error for the used devices (e.g., coefficient of variation, typical error of measures).

Research on conservative intervention to treat acute hamstrings injuries in athletes has been continuing at a slow pace. There is a clear need for more homogeneous studies to allow comparisons and achieve a valid pooled estimate of TRTS/TRFT and reinjuries. To reliably compare the reinjury risk across different conservative interventions, studies with a very large sample size are needed, but these studies are not easy to conduct in real-world club-based sports. We need combined efforts from several clubs implementing the same conservative strategies to increase the comparability and statistical power before clinical practice guidelines can be reliably established. Because we are performing a living systematic review, future updates will reveal changes to the status quo.

4.4 Limitations

The inclusion of non-randomized trials may be interpreted as a weakness of our systematic review, but these trials were analyzed separately from randomized trials and so we

provide a more complete picture without mixing the findings from two fundamentally different study designs. Furthermore, randomized trials are not always feasible, especially with high-level athletes. As previously mentioned, some studies lacked imaging to confirm diagnosis, and thus complete rupture or avulsion could not be completely ruled out. Despite planned at the protocol stage, we opted to not perform a meta-analysis or network meta-analysis because of the wide clinical heterogeneity in populations, interventions, comparators, and other methodological features of the studies (including how the outcomes were assessed), which precluded us from confidently pooling the data from different studies and is coherent with Cochrane's guidelines [45]. Still, to provide useful information, we calculated the between-group mean differences and relative risks for each study within each outcome and provide a narrative summary that is supported with a best evidence synthesis using the GRADE framework.

5 Conclusions

No single intervention or combination of interventions proved superior in achieving a faster return to sports or reducing the reinjury risk. Exercise-based interventions seem comparable and no specific strategy needs to be prioritized when rehabilitating athletes with acute hamstrings injuries. Only eccentric lengthening exercises showed limited evidence (very low certainty) in allowing a shorter TRFT. Platelet-rich plasma did not consistently reduce the TRFT or the reinjury risk and, at the moment, has no value in clinical practice. The use of passive interventions (LLLT) also did not yield any clinical value when added to exercise-based rehabilitation. The currently available literature is limited owing to the risk of bias, the high risk of ineffectiveness of exercise protocols (especially due to poor or uncontrolled adherence, absence of proper supervision, and incomplete information to assess dosage of the prescribed exercise program), and the lack of comparability across existing studies. Future studies should strive to overcome these limitations and provide a pool of evidence that allows meaningful comparisons and stronger clinical directions to be achieved. Our living review will be attentive and update the knowledge synthesis on an annual basis.

Registration and Protocol The protocol was created (https://osf.io/3k4u2/) and pre-registered (https://osf.io/dxe2t) as an OSF project (public since 30 August, 2021), and also pre-registered in PROSPERO (CRD42021268499, attributed on 22 August, 2021). Changes to the original protocol: (1) an age-related inclusion criterion was removed following a suggestion from one of the external experts before submission of the manuscript. This did not, however, change the studies included in the review, as none of those studies had been excluded based on that criterion; (2) the remaining changes were properly identified in the methods (e.g., absence of quantitative synthesis).

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Conflicts of Interest/Competing Interests José Afonso, Jesús Olivares-Jabalera, Ricardo Fernandes, Filipe Manuel Clemente, Sílvia Rocha-Rodrigues, João Gustavo Claudino, Rodrigo Ramirez-Campillo, Cristina Valente, Renato Andrade and João Espregueira-Mendes have no competing interests.

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Consent to Participate Not applicable.

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Authors' Contributions JA and RA were responsible for the initial drafting of the article, which was reviewed and edited by all authors. All authors were involved in the conception, design, and interpretation of data. All authors read and reviewed the manuscript critically for important intellectual content and approved the final version to be submitted. Specific contributions pertaining data selection, extraction, and analysis are detailed in the methods section. All authors read and approved the final manuscript.

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