A step forward in running-related injuries
Mousavi, Hamed

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General discussion
The scope of this thesis was to gain insight into the epidemiology and etiology of RRIs, the kinematic risk factors associated with running-related lower limb tendinopathy, and the feasibility and effects of running gait retraining using real-time visual feedback on rearfoot eversion.

**RISK FACTORS FOR RUNNING-RELATED INJURIES**

Knowledge about the etiology of sports-related injuries is of fundamental importance to prevent sports injury. It allows clinicians to examine and diagnose risk factors more carefully. These insights also help clinicians and researchers design effective personalized prevention and intervention programs for specific types of injury. Because of the high incidence of RRIs, this knowledge is even more relevant when dealing with runners with or at risk for an injury.

The classical approach toward identifying risk factors for RRIs focuses on single factors such as foot strike patterns and shoe types [1–4]. This approach can be useful for finding an association between a single risk factor and an RRI, yet it is insufficient as it only relates one factor, segment or parameter to an RRI. A single risk factor alone cannot be responsible for injury development but is rather one part of a total complex of etiological factors. This complex etiological model can be characterized by several factors that interact with each other at various levels. Hence prediction of an injury should involve a complex web of risk factors with their existing interactions [2].

The first steps toward establishing the structure of a running injury prevention model is to increase the knowledge about the epidemiology and etiology of RRIs. Reviews investigating the etiology of RRIs acknowledge that these are caused by several risk factors from various categories [5–9]. In Chapter 2 of this thesis we investigated risk factors associated with lower limb injuries in recreational runners. Using a cross-sectional survey, we analyzed the association of potential risk factors with RRIs using multivariate logistic regression. The following factors were shown to be associated with RRIs in terms of etiology: more obsessive passion and motivation to exercise, poor sleep quality, lower perceived health, running over 20 km/week, overweight, having pes planus or cavus, hard-surface running, running in a group, and following a training program. A systematic review and meta-analysis in Chapter 3 additionally describes the most important kinematic risk factors for RRIs. The following kinematic risk factors contributed to lower limb tendinopathies: peak rearfoot eversion, peak knee internal rotation, peak hip adduction, rearfoot eversion, and knee flexion at touchdown. Overall, we explored the effectiveness of 25 potential risk factors as well as kinematic risk factors for RRIs. So far no study has investigated the effect of sleep quality on RRIs, and factors such as passion for running, motivation to run, perceived health, foot arch have been examined to a very limited degree.

**INJURY MODEL**

In the introduction of the thesis we tried to design a complex web of determinants for RRIs and their interactions, based on the model proposed by Bettencourt et al. (2016) [2]. These determinants were retrieved from reviewing previous studies investigating risk factors for RRIs. Based on new findings in this thesis, we tried to further complete this web of determinants for RRIs (Figure 1). We added knowledge about previously unidentified determinants, identified with question marks in the Introduction section Figure 2 (page 13). For other important determinants, we were able to strengthen the evidence based on the results of our studies.

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**Figure 1.** Web of determinants for running-related injuries (updated). The circles at the bottom comprise the web of determinants that is composed of contributing variables with different weights. Variables circled by darker lines have more interactions than variables circled by lighter lines and exert a greater influence on the outcome. Dotted lines represent a weak interaction and thick lines

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TRAINING-RELATED FACTORS
In the conceptual model described by Malisoux et al., training-related factors are considered the primary risk factors for RRIs, while non-training-related risk factors are assumed as effect-measure modifiers which act as complementary factors in the casual mechanism [10]. They concluded that: “Runners do not sustain an RRI only because they are overweight, older, or have had a previous injury. RRI can only occur when people practice running”. This implies that training-related factors are essential factors in the development of RRIs. In line with our survey, several studies emphasized one single aspect of training factors such as speed training [11] and running distance [5,12–17] as a cause for RRIs. However, reviews report conflicting results on training-related factors associated with RRIs [5,6,18]. The main reason for this inconsistency is the classification and/or cut-off point of training-related factors. While some studies consider running distance above 20 km/week as a risk factor [15], others report running above 30 km/week [5,12,13]. Moreover, it seems that the population of runners studied and statistical analyses used are partly responsible for the conflicting results on training-related factors [19,20].

The importance of training-related factors for RRIs is also emphasized in the conceptual injury model described by Nielsen et al. [19]. In this model, training load, load capacity, and cumulative load interact with each other when sustaining an injury. Training load is defined and measured by training-related factors and biomechanical factors. Load capacity depends on personal characteristics such as age, sex, running experience, strength, psychological factors, lifestyle, etc. [19]. These factors and their association with RRIs are investigated in our survey and systematic review (Chapters 2 and 3). In fact, these factors interact together to determine cumulative load and load capacity. This cumulative load may expose an athlete to developing an injury if it is greater than the athlete’s normal load capacity, presenting two possible scenarios before an injury occurs [21]: 1) when a runner does multiple running sessions with similar cumulative load but without sufficient recovery between sessions, this may cause the load to exceed the load capacity, ultimately leading to injury; 2) when a runner performs a single session in which the training load gradually increases and finally exceeds the load capacity, this may cause the runner to sustain an RRI. These conceptual injury models highlight the prominent contribution of training load to RRI development, which is directly linked with changes in training-related factors. About 70% of running injuries have a cause related to training-related factors [22,23].

PREVIOUS INJURY
Previous injuries can act as a primary risk factor for a new injury. The role of having previous injuries on the occurrence of new injuries has been demonstrated in several studies [7–9,11,24–27]. Previous injuries may increase the risk of a new injury because of 1) incomplete recovery from an earlier injury, 2) structural abnormalities of the runner’s gait, and 3) adoption of faulty movement patterns to relieve any pain or discomfort caused by an injury. Not all evidence supports the aforementioned theories though. For example, it was reported that about 77% of reinjured runners sustained the new injury on a different place than the previous injury, contradicting the theory of incomplete recovery [28]. Also, errors in gait characteristics have not yet been investigated for the recurrence of RRIs, therefore more insight into understanding the mechanism of sustaining a re-injury following a previous injury may help reduce RRIs. Our survey showed that 20% of runners reporting an actual or recent injury had sustained multiple injuries before. Moreover, prospective studies indicate that previous injuries play an important role in injury recurrence [6–8,11,13,14,29,30].

MENTAL ASPECTS
Obsessive passion and higher motivation to run seem to play a role in injury development by directly affecting training-related factors. While the effects of mental aspects on sports performance, the efficacy of rehabilitation programs, and some sports injuries have been explored extensively [31,32], very little has been published examining the link between mental aspects and RRIs. Our survey showed that an obsessively passionate attitude is associated with most types of running injuries. More importantly, runners who reported multiple injuries had a higher obsessive passion score than those reporting one injury. Our results also showed that obsessive passion is associated with motivation to run. Passion and motivation are two important psychological factors that play an important role in performing an activity [33,34]. Obsessive passion is one aspect of passion that has been described by Vallerand et al. [35] as an attitude in which individuals are unable to fully control their passionate attitude. Obsessive passion for running means that runners keep on running regardless of their ability and loading capacity. They exceed their body tolerance threshold by running too long (distances), too frequently, or too fast. In fact, runners who have an obsessive passionate attitude may ignore any discomfort or mild pain while running,
which in turn predisposes them to injury. This may occur more frequently in novice and recreational runners because they might be less familiar with the normal loading their body can tolerate. A certain level of motivation is necessary to make runners want to run. Motivation can be considered a precursor to obsessive passion [35,36]. Obsessive passion may be a consequence of high motivation. Hence when the motivation is higher than necessary, it can be indicated as obsessive passion. Thus obsessive passion and motivation to run are added to the web of RRI determinants as two mental aspects-related determinants.

SLEEP
Our survey showed that poor sleep quality is associated with increased RRIs. There is convincing evidence that poor sleep quality can play a role in predisposing individuals at risk of injuries such as work-related and falling injuries [37–41], yet few studies have considered sleep as a potential risk factor for sports-related injuries [42–45]. To the best of our knowledge no study has investigated sleep as a risk factor for RRIs. Sleep allows the body to repair and regenerate from the day. Bones, ligaments, tendons, and muscles need this time to recover in order to achieve positive adaptation and in this way prevent injuries. Poor sleep quality can influence the load capacity of runners’ bodies before the start of a running session [21], potentially placing them at a higher risk of sustaining an injury. We found that poor sleep quality is associated with most RRI types. However, based on our survey it is difficult to determine the cause-and-effect relationship between sleep and RRIs. Poor sleep quality can influence training-related factors considered to be primary risk factors for RRIs. Further prospective studies are warranted to determine the effect of poor sleep quality on the development of RRIs. Therefore, sleep is placed in the web of RRI determinants.

FOOT ARCH
The foot is the only part of the human body that contacts the ground during running. As long as the foot is in contact with the ground, the medial foot arch plays an important role in the dispersal of ground reaction force across the foot [46]. A higher or lower medial foot arch can disrupt shock absorption and attenuation, imposing more stress on the foot or other structures or joints [47]. The results of our survey showed that the presence of either a pes planus or a pes cavus are associated with most types of RRIs. More importantly, a sub-analysis of our results showed that about 80% of runners who reported suffering from plantar fascitis had either pes cavus or pes planus. This indeed highlights the effect of an abnormal foot arch on plantar fascia strain. It is also in line with a recently published study [48] that underscored the effect of atypical medial foot arch on RRIs so that runners with supinated and pronated foot postures had 20 and 77 times higher odds of running injuries, respectively, than runners with a normal foot posture [48]. In contrast, two prospective studies conducted in novice runners found no association between atypical foot postures (pronated or supinated foot) with an increased risk of RRI [49,50]. One of these studies [50] included a very small sample size (13 injured vs. 46 non-injured) which restricts the generalizability of their results. It seems that some features such as the foot posture diagnosis method, sample size, studying specific RRIs or RRIs as general, and population studied explain the different results among studies. This, in turn, hampers the direct comparison between studies. According to the results of our study (Chapter 2) together with the study of Morcillo et al. [48] and the theoretical point of view on the role of foot posture on shock absorption and attenuation, foot arch is placed in the web of RRI determinants that interacts mainly with biomechanical factors.

KINEMATIC RISK FACTORS
We conducted a systematic review and meta-analysis to investigate the kinematic risk factors associated with lower limb tendinopathy in runners. These contributing factors include peak rearfoot eversion, rearfoot eversion at touchdown, peak knee internal rotation, knee flexion at touchdown, and peak hip adduction (Figure 2). Rearfoot eversion was the only factor investigated in all types of tendinopathies. Noteworthy is that one single kinematic risk factor may not cause an injury – a complex of kinematic risk factors that logically interact with each other should be considered for injury development [51]. This refers to lower limb kinematic chains or a cluster of kinematic factors. In a kinematic chain, the kinematics in the distal or proximal parts of the chain may play the most important role. Accordingly, any kinematic alterations in these parts can be accompanied by alterations in other proximal or distal joint or segment kinematics. For example, excessive subtalar pronation leads to more knee internal rotation and subsequently more hip internal rotation. This implies that atypical knee internal rotation, which has frequently been reported as a risk factor for knee injuries, might have atypical subtalar pronation as primary cause. In other words, the primary cause of the injury lies in a different segment or joint than the injury area. However, based on our systematic review we can conclude that not all studies that investigated knee internal rotation also examined subtalar pronation. This might be what’s missing in the studies on kinematic risk factors for RRIs. Had rearfoot eversion been considered in these studies, its important role in sustaining RRIs would potentially be more highlighted.
and propulsion [60, 61]. These are in turn attributed to secondary associated conditions such as pain and lower limb overuse injuries. In our systematic review (Chapter 3) we found that atypical rearfoot eversion is associated with lower limb tendinopathies. Greater rearfoot eversion was also reported as a contributing factor for other common RRsIs such as patellofemoral pain syndrome [62] and medial tibial stress syndrome [63–66].

Modification of both static and dynamic atypical rearfoot eversion and/or medial longitudinal foot arch has long been a challenge for researchers and clinicians [67]. Foot orthotics are the most commonly used modification for atypical subtalar pronation; few studies have investigated the effects of non-orthotic interventions on subtalar pronation such as motion control shoes [68], muscle strengthening exercises [69, 70], and taping [71]. These studies mainly assessed static subtalar pronation, and few have examined dynamic subtalar pronation. The value of using orthoses or taping to treat lower limb injuries or modify lower limb biomechanics remains controversial among researchers and clinicians [72]. Some consider these as temporary interventions facilitating prevention or treatment programs, others see them as last resorts.

Both in clinical and research settings, gait retraining focusing on biomechanical factors has been identified as successful and beneficial to prevent and manage injury and/or improve performance [72–76]. Despite its popularity to alter impaired gait patterns, so far no study has investigated the effect of a running gait retraining protocol to modify atypical rearfoot eversion or medial longitudinal arch angle (MLAA). In order to change rearfoot eversion and MLAA, two running gait retraining protocols were introduced in this thesis, i.e. changing foot progression angle (FPA) and changing center of pressure (COP). In Chapter 4 of this thesis we gave runners real-time visual feedback of their FPA while running on an instrumented treadmill, using an advanced 3D motion system, Gait Real-time Analysis Interactive Lab (GRAIL). To change FPA, 5° lower or higher than normal FPA were considered for toe-in and toe-out running, respectively. Runners easily adapted to these conditions, making this a feasible range for changing FPA while running. To change COP, runners were instructed to run on the lateral and medial side of the foot while following their baseline FPA provided on the screen using real-time feedback. Runners were able to successfully adopt these two running gait retraining protocols. Both protocols showed promising results on rearfoot eversion and MLAA, thus making them potential running gait retraining modalities to modify rearfoot eversion and/or MLAA.

In this thesis we tried to investigate unidentified risk factors for RRsIs. There still remain unidentified determinants that play a role in predisposing runners to injury. These factors are most likely subsets of other main determinants like psychological factors, kinetics, and spatiotemporal parameters.

**RRIs DIFFERENCES BETWEEN IRAN AND OTHER COUNTRIES**

Our survey, described in Chapter 2 of this thesis, was the first study that aimed to investigate the epidemiology and etiology of RRsIs in Iranian recreational runners. We hypothesized that because of environmental and cultural differences as well as other attitudes toward running between countries, the epidemiology and etiology of RRsIs may vary among Western countries and Iran. We could not demonstrate these differences when comparing our results with similar epidemiological studies from the Netherlands, Denmark, UK, US, Austria, and Brazil [11, 30, 52–55].

**RUNNING GAIT RETRAINING FOR REARFOOT EVERSION**

Atypical subtalar pronation (rearfoot eversion) is one of the main causes of lower limb-related biomechanical changes such as hip and tibial internal rotation [56], hip and knee adduction [57], hip and knee adduction moment [58], and pelvic anterior tilt [59]. A change in subtalar motion or structure may affect foot stabilization, shock absorption, and propulsion [60, 61]. These are in turn attributed to secondary associated conditions such as pain and lower limb overuse injuries. In our systematic review (Chapter 3) we found that atypical rearfoot eversion is associated with lower limb tendinopathies. Greater rearfoot eversion was also reported as a contributing factor for other common RRsIs such as patellofemoral pain syndrome [62] and medial tibial stress syndrome [63–66].

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Studies in Chapter 4 and 5 show that the foot is more supinated while running on the
lateral side of the foot and in toe-in running, and more pronated while running on the medial side of the foot and in toe-out running. Running gait retraining by changing mediolateral COP had a greater effect on changing peak rearfoot eversion than did running gait retraining by changing FPA (3.3° vs. 2.1°). Current literature on the effect of interventions for atypical rearfoot eversion mainly focused on interventions that reduce peak rearfoot eversion, as greater peak rearfoot eversion is the most common type of atypical rearfoot eversion. Compared to the results of previous studies investigating non-gait retraining on rearfoot eversion, our results are in the same range as those of non-gait retraining studies. A prior systematic review reported that foot orthoses systematically reduce peak rearfoot eversion approximately from 2° to 3.5° [77]. Motion control shoes show a reduction range of 0° to 4° in peak rearfoot eversion relative to neutral shoes [68,78–81].

When comparing the two running gait retraining protocols, we demonstrated that changing COP yields more changes in rearfoot eversion, subtalar pronation, and MLAA than changing FPA. Both running on the lateral side of the foot and toe-in running reduced peak rearfoot eversion, which suggests that the combination of the two may have a cumulative effect in reducing rearfoot eversion and/or MLAA. However, it is not clear whether combining these two protocols is feasible and whether this incurs an extra burden for the runners. More research is needed to shed light on this hypothesis. Another important issue that warrants further study is whether these gait retraining protocols lead runners into developing other RRIs. For example, Chan et al. (2018) investigated a two-week running gait retraining using real-time visual feedback to reduce vertical loading, a risk factor for RRIs. They reported 62% lower risk of injury in the gait retraining group at one-year follow-up; although that group had a lower incidence of planter fasciitis and patellofemoral pain syndrome, they showed more Achilles and calf injuries [73].

One key question is which runners would benefit from gait retraining to modify rearfoot eversion and MLAA: injured runners with atypical rearfoot eversion, uninjured runners with atypical rearfoot eversion, or both. In other words, can everyone with atypical rearfoot eversion benefit from these running gait retraining modalities? If greater rearfoot eversion and/or pronated feet are diagnosed as causes of pain or injury in a symptomatic runner, gait retraining as part of a treatment plan by changing FPA or COP may be useful to modify rearfoot eversion. This results in relative unloading of the involved tissues and may be helpful toward reducing symptoms, at least in the short term [82].

First it should be considered whether runners can undergo gait retraining by changing FPA or COP, and which gait retraining modality will be the most effective. This can be evaluated by screening lower-limb biomechanics during running in order to answer the following questions: Are FPA and COP values in the normal range? What are the potential effects of changing FPA or COP on known lower limb biomechanical risk factors such as hip internal rotation, adduction, and impact force? Are these biomechanics still in their normal ranges while retraining? How much change in FPA or COP is required to reach optimal rearfoot eversion? Clinicians and researchers should have clear answers to these questions prior to the gait retraining. For example, implementing gait retraining by changing FPA (e.g. toe-in running) for a runner with greater rearfoot eversion who runs toeing-in is not only impractical, it also imposes an extra burden on the knee and ankle joints [83]. Another issue is whether long-term running gait retraining in uninjured runners or in injured runners with atypical rearfoot eversion aimed to prevent (re)injury should be recommended. In that case, long-term running gait retraining by changing FPA or COP is thought to be useful if atypical rearfoot eversion or MLAA is considered to be causing or contributing to injury. So the main goal of a gait retraining program is to minimize specific mechanical loads on involved tissues by means of an altered gait pattern. At the outset it should be possible to determine which kinematic and kinetic variable will be influenced by gait retraining, namely how much mechanical load would be imposed on the involved joints and tissues by changing FPA or COP. The next step is to take factors such as individual differences, age, and running level – essential factors when tailoring a gait retraining program – into account.

FROM THE LAB TO THE FIELD
Transition of running gait retraining from the lab to the field also needs consideration. Running is a fast repetitive motion, encumbering real-time feedback on a special biomechanical parameter such as FPA and COP outside the lab. Current approaches to give feedback on FPA mainly need a 3D motion capture system, which limits running gait retraining to the lab setting. This hampers the transition of gait retraining to the field. Previous studies present valid tools using insole- or shoe-embedded sensors to give real-time feedback on FPA [84,85] and COP during walking [86–88]. These tools can be applied inside and outside the lab to modify FPA or COP to a given quantity in order to alter rearfoot eversion and MLAA. Further research is required, as the usability of these tools has not been validated during running. Another potential way to modify rearfoot eversion out of the lab is to provide real-time feedback on rearfoot eversion itself while changing FPA or shifting the plantar pressure during running. A recent study investigated the validity of rearfoot eversion measures during running derived...
Also more research is needed to 1) obtain insight into potentially negative implications of changing FPA and mediolateral COP on foot, ankle, knee, and hip biomechanics during running, 2) investigate how effective modification of FPA or mediolateral COP is in bringing about changes in runners with atypical rearfoot eversion or MLAA, and 3) research how effortful and natural these two gait retraining modalities are when executed by individuals with atypical rearfoot eversion or MLAA.

Hip rotation is another kinematic factor that has the potential to be retrained in order to alter rearfoot eversion. Internal hip rotation has a positive association with rearfoot eversion [91], therefore a small external hip rotation may reduce rearfoot eversion during running.

According to the results of our systematic review (Chapter 3) showing that atypical rearfoot eversion is a contributing factor to RRIs, we suggest that modifying atypical rearfoot eversion leads to injury prevention. Future studies need to investigate whether the modification of atypical rearfoot eversion using these running gait retraining protocols indeed has an effect on RRIs or pain improvement when managing RRIs.

To allow further generalizability of our results and practical applications, studies are needed to investigate the reproduction of the above running gait retraining protocols outside the lab. This can be done using wearable devices designed to give real-time feedback on FPA or COP.

No threshold exists to determine the extent to which rearfoot eversion and MLAA should be considered atypical or normal during running. Unfortunately, the lack of normative data and not having adopted an accurate definition of rearfoot eversion has hindered progress in this respect. Decision-making on whether rearfoot eversion is a risk factor is based on statistical differences between injured and non-injured runners. The classification of rearfoot eversion into atypical and normal would at least help clinicians and researchers identify individuals more prone to injury. And yet it appears difficult to classify rearfoot eversion and generalize a cut-off value with a one-size-fits-all approach. Future research should address this issue.

**PRACTICAL IMPLICATIONS FOR CLINICIANS AND RUNNERS**

This thesis contributes to a better understanding of risk factors for RRIs, knowledge which is useful for runners, coaches, and clinicians. Our findings may have implications for the prevention and management of RRIs. The following recommendations should be considered for prevention/management of RRIs or gait retraining to modify rearfoot eversion.
Clinicians, coaches, and runners should be aware of the important role of sleep for injury prevention/recovery. Research shows that less than six hours of sleep per night substantially increases the risk of injury. Runners are advised to get enough sleep (> 6 hours). Developing a healthy sleep routine (e.g. going to bed early, not using electronic devices 30 minutes before bedtime) can be helpful in this respect.

CONCLUSION
This thesis adds new information to the complex web of determinants of RRIs and explores the role of running gait retraining in changing rearfoot eversion and MLAA. Mental aspects and sleep quality seem to play a role and need to be incorporated in the prevention and management of RRIs. Atypical rearfoot eversion or MLAA can be changed by modifying FPA or COP during running. These running gait retraining protocols should be considered as an alternative for commonly prescribed interventions such as orthotic therapy or motion control shoes to modify atypical rearfoot eversion or MLAA.

1 Clinicians should be aware of the role of kinematic chains during locomotion. Proximal abnormal kinematics often have a distal cause, which implies the modification of distal kinematics at first. For example, excessive rearfoot eversion is accompanied by excessive tibial internal rotation and hip internal rotation, which are contributing factors in the development of iliotibial band syndrome and patellofemoral pain syndrome.

2 Clinicians should assess rearfoot eversion, hip adduction, and knee internal rotation and flexion as kinematic risk factors contributing to lower limb tendinopathy. 2D motion analysis smartphone applications can be used to measure these kinematics as alternatives to 3D motion analysis systems, which are more expensive and difficult to operate.

3 Clinicians should be aware of the role of abnormal foot arch when dealing with RRIs, especially for runners with plantar fasciitis. Eighty percent of runners who reported plantar fasciitis had pes planus. Measures such as navicular drop and Staheli index can be used to identify abnormal foot posture. There is however conflicting evidence on the association between static and dynamic foot posture [92,93]. Although it is common in clinical practice to make a decision on dynamic rearfoot eversion by measuring static rearfoot eversion, clinicians should keep in mind that static assessment of foot posture might not properly predict dynamic foot posture. Interventions such as orthoses [70], exercise programs [69], and gait retraining modalities (this thesis) may be considered for modifying abnormal foot arch.

4 Be alert to avoid excessive change of the FPA in gait retraining. It is important to select the applicable degree of change based on individual lower limb biomechanics, as individual differences may affect the response to the FPA change and the extent of potential change. We found that a 5° FPA deviation from normal running is an achievable and feasible change of FPA, yet this change may strongly vary per individual. Excessive change of FPA or mediolateral shifting of COP in running gait retraining has the potential to increase the stress to lower leg musculoskeletal structures, thereby even increasing injury risk.

5 Runners should be more aware of the role of obsessively passionate attitude and the risk for sustaining RRIs, and clinicians should counsel runners on increasing this awareness. Runners are advised to take their body tolerance into account and reduce the training load by adapting their training schedule or temporarily stop running when they feel any discomfort or pain. Continuing to run without any adaptation in training load while feeling pain is one of the main causes of overuse injuries, which are the most prevalent type of RRIs.


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