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Bilateral differences in coordination variability among injured and uninjured runners: A prospective study

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ABSTRACT

This prospective cohort study aimed to identify bilateral differences in coordination variability (CAV) to determine if limb-specific CAV or CAV asymmetry is associated with running-related overuse injury (RRI) development in recreational runners. Lower limb kinematics were collected at enrollment. Runners were classified as injured (n = 14) or controls (n = 17) based on RRI incidence during a ≥ 6-month follow-up. Pelvis-thigh, knee-shank, knee-ankle, and shank-ankle CAV was quantified bilaterally within thirds of stance using modified vector coding. Wilcoxon Signed-Rank tests compared CAV between limbs within each group, and Wilcoxon Rank-Sum tests compared CAV asymmetry between groups ($\alpha \leq 0.05$). Injured runners displayed elevated injured versus uninjured limb CAV during initial-stance for all couplings ($p < 0.010$,d(effect size) = 0.51–1.31) except pelvis-thigh ($p = 0.060$,d = 0.36). During mid-stance, the injured limb exhibited restricted knee-ankle CAV ($p < 0.010$,d = 0.413) and elevated pelvis-thigh CAV ($p < 0.010$,d = 0.23). Controls also displayed bilateral differences specifically in pelvis-thigh CAV across stance, shank-ankle CAV during initial-stance, in all couplings during mid-stance, and shank-ankle CAV during late-stance ($p < 0.010$–0.025,d = 0.09–0.63). Comparing CAV asymmetry between groups revealed lower asymmetry among injured runners compared with controls for knee-ankle coupling in mid-stance and all couplings except pelvis-thigh during late-stance ($p < 0.010$,d = 0.85–1.87). Injured runners also displayed greater knee-shank CAV asymmetry in mid-stance versus controls ($p < 0.010$,d = 0.85). Logistic regression ($\alpha \leq 0.05$) revealed that between-limb CAV asymmetry did not predict RRI ($p = 0.161$), however, the odds of RRI were > 20% in the limb with either elevated shank-ankle CAV in initial-stance ($p = 0.020$) or elevated knee-ankle CAV in mid-stance ($p = 0.043$) than the contralateral limb. Therefore, limb-specific CAV rather than degree of CAV asymmetry may influence risk of RRI.

1. Background

Research examining the mechanisms of running related overuse injuries (RRI) has been insightful. However, limited prospective evidence and inconsistent results across investigations exists for the relationship between traditional biomechanical metrics and RRI risk (Ceyssens et al., 2019). One reason for this inconsistency may be that the most common RRI, such as patellofemoral pain, iliotibial band syndrome, and anterior knee pain (Taunton et al., 2003; van Gent et al., 2007; Walter et al., 1989; Wen et al., 1997), are not necessarily associated with biomechanics at the injured anatomical location. For example, rearfoot eversion angles in addition to peak hip adduction are suggested to increase susceptibility to RRI like iliotibial band syndrome (Ferber et al., 2010; Milner et al., 2010; Noehren et al., 2007). Additionally, both frontal plane ankle and sagittal plane knee kinematics differ between healthy control runners and runners with knee injuries (Duffey et al., 2000; Miller et al., 2007; Wen et al., 1997), and may be related to Achilles tendinopathy and tibial stress fracture (Hein et al., 2014; Milner et al., 2007). While studying discrete biomechanical metrics are insightful, they may provide limited information about RRI risk factors. Discrete biomechanics, such as peak joint angle magnitudes, cannot provide information about the underlying joint interactions which produce those magnitudes or movements. Therefore, alternative analyses approaches are needed to understand the bi-planar joint interactions that may influence the most common RRIs.

Dynamical systems theorists posit that analyzing gait as relative motions of joints and segments throughout the gait cycle may reduce information loss (Hamill et al., 2012). The proposed injury mechanism involves suboptimal relative motion between mechanically and anatomically related joints and/or segments (e.g., shank internal rotation during knee flexion) that may abnormally stress soft tissue structures. Variability in relative joint and/or segment motions over the gait

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cycle is termed intralimb coupling angle variability or coordination variability (CAV).

CAV (i.e., variability in relative joints and/or segments motions) has successfully identified differences between controls and symptomatic, retrospectively injured, and prospectively injured runners, including cohorts that displayed no differences in discrete kinematics (Baida et al., 2018; Cunningham et al., 2014; Desai & Gruber, 2020; Foch & Milner, 2019; Hamill et al., 2012; Heiderscheit et al., 2002; Hein et al., 2012; Miller et al., 2008). However, it remains unknown if CAV characteristics within the injured limb increase RRI susceptibility in that limb or if bilateral asymmetry plays a role since CAV has mostly been assessed unilaterally. In one of few studies comparing CAV bilaterally, the injured limb of symptomatic runners displayed less transverse plane thigh-leg CAV compared with their uninjured limb and both limbs of healthy runners (Heiderscheit et al., 2002). These findings suggest CAV characteristics may be different in injured and uninjured limbs, and the magnitude of these differences may be relevant to injury risk. To understand if CAV is related to biomechanics of the injured limb, or if asymmetry in CAV also contributes to injury development, it is necessary to prospectively assess CAV bilaterally and examine the degree of bilateral asymmetry present.

Previous evidence suggests that biomechanical characteristics in either of a runner's limbs may influence RRI risk (Zifchock et al., 2008a), highlighting the need to assess CAV bilaterally. While both injured and healthy runners display bilateral differences in discrete biomechanical metrics like arch height, hip internal range of motion, and peak tibial acceleration (Bredeweg et al., 2013; Gilgen-Ammann et al., 2017; Zifchock et al., 2006; Zifchock et al., 2008a), degree of asymmetry (i.e., magnitude of difference between limbs) was similar between groups (Zifchock et al., 2008a). Zifchock et al. (2008a) found that discrete kinematics like hip internal rotation range of motion could not predict side of RRI, suggesting that discrete kinematics in either limb may influence unilateral RRI. These results indicate RRI risk should be assessed by examining movement bilaterally, which is an underutilized methodology across RRI research. Assessing CAV bilaterally may help explain why unilateral RRI are more common than bilateral RRI despite identical running exposure between limbs (Nielsen et al., 2014).

Paucity of evidence regarding the role of CAV in side-specific RRI development necessitates further investigation of bilateral CAV in prospectively injured and healthy control runners. Therefore, we aimed to determine bilateral differences and degree of asymmetry in lower limb CAV among prospectively injured and control runners and determine whether degree of CAV asymmetry or limb-specific CAV characteristics are associated with RRI risk. We assessed coordination between biomechanical variables like frontal plane ankle, thigh, and pelvis, transverse plane shank, and sagittal plane knee motions due to their relationship with common RRI like iliotibial band syndrome and patellofemoral pain (Noehren et al., 2007; Noehren et al., 2013; Tiberio, 1987). Given that each limb has different functional roles during locomotion (Sadeghi et al., 2000), our first hypothesis was that both injured and healthy runners will display bilateral differences in CAV. Our second hypothesis was that the degree of asymmetry will be similar between groups since limb-specific characteristics, rather than degree of asymmetry, may influence injury risk (Zifchock et al., 2008a). Previous work involving unilateral comparisons between groups suggests injured compared with control runners display greater CAV (Cunningham et al., 2014; Desai & Gruber, 2020; Foch & Milner, 2019; Hein et al., 2012). Extending these findings to a comparison between limbs among injured runners, our third hypothesis was that within injured runners, the injured limb will display greater CAV than the uninjured limb. Finally, our fourth hypothesis was that limb-specific CAV and not degree of CAV asymmetry will predict injury risk, as previously suggested (Zifchock et al., 2006; Zifchock et al., 2008a).

2. Methodology

2.1. Subjects

Fifty-five healthy recreational runners volunteered for this study (Table 1). Inclusion criteria required subjects to be 18–60 years-old, without lower back or lower limb surgery history, had $\geq$ 2-years of running experience, and ran $\geq$ 10 miles/week for $>$ 3-months prior to enrollment. All subjects were uninjured at the time of enrollment. If an injury occurred within the previous 6-months, they were only included if they had resumed normal weekly running volume for $\geq$ 8-weeks prior to enrollment. Subjects pursued their own running program and reported training, pain, and number of modified running days due to pain in a weekly online survey during a minimum 6-month follow-up. Subjects were excluded if they failed to provide weekly responses for $\geq$ 6-months with $>$ 80% compliance ($n = 16$) or had $<$ 5 successful bilateral trials ($n = 8$). The final sample size was thirty-one. Subjects gave written informed consent before enrollment. All procedures were approved by the Indiana University Institutional Review Board.

Subjects were classified as injured or controls based on if they developed an RRI during follow-up. RRI was defined as any running-related musculoskeletal pain in the lower limbs that caused a restriction/stoppage of running (e.g. distance, speed, duration) for $\geq$ 7-days or three consecutive scheduled training sessions, or that required the runner to consult a physician/other health professional (Yamato et al., 2015). Weekly survey responses of RRI occurrence were evaluated by an experienced physical therapist (DPT, PhD) to ensure pain was consistent with an overuse pathology rather than non-running or acute causes of pain/injury.

2.2. Baseline experimental procedure

A three-dimensional gait analysis was conducted at baseline. Retroreflective markers were placed bilaterally on the lower extremity following published standards (Sutherland, 2002). Subjects wore a neutral running shoe provided by the laboratory (One Cushion 3.0, Reebok, Boston, MA, USA). Before data collection, subjects completed a standing calibration trial with arms across their chest followed by practice running trials across an 18 m level runway at 4 m s^{-1} ($\pm$5%) criterion speed. Subjects' average preferred speed (3.71 $\pm$ 0.54 m s^{-1}) was slower than the criterion speed, but nobody reported or showed signs of discomfort or difficulty performing the criterion speed.

Table 1
Group mean (standard deviation) of demographic and running training variables for the injured and control groups. "Average weekly mileage during follow-up" includes the weeks of follow-up until injury for the injured group, and all weeks of follow-up for the control group. *d* is Cohen's d effect size.

	Injured	Controls	p-value	*d*
Sex (Male/Female)	M = 2, F = 12	M = 9, F = 8	0.11	0.34
Age (years)	32.07 (10.70)	31.47 (10.15)	0.87	0.06
Height (meters)	1.67 (0.05)	1.73 (0.09)	0.06	0.78
Mass (kilograms)	61.98 (7.45)	67.17 (14.48)	0.42	0.43
Mileage during first week of follow-up (mi·week^{-1})	14.37 (8.50)	16.82 (12.71)	0.52	0.22
Average weekly mileage during follow-up (mi·week^{-1})	13.68 (7.48)	18.23 (11.77)	0.20	0.44
Years of Running Experience	7.44 (5.46)	9.08 (5.50)	0.33	0.29

Nine motion capture cameras (Oqus 400+, Qualisys AB, Göthenburg, Sweden) recorded three-dimensional marker positions at 240 Hz while subjects ran across the runway. Gait speed was measured within the center of the collection volume using two infrared break-beam sensors (TC-Gait, Brower Timing System, Draper, UT, USA) placed 6 m apart. Five successful trials from within this collection volume, consisting of a single stance phase per trial, were retained for analysis bilaterally (Foch & Milner, 2019; Hafer et al., 2017; Hafer et al., 2016; Needham et al., 2014). A trial was successful if subjects ran within ± 5% of criterion speed, maintained speed between timing sensors (i.e. ≤ 50 N difference between peaks of anteroposterior ground reaction force), did not modify their stride to target the force platform (1200 Hz, AMTI, Inc., Watertown, MA, USA), landed on the force platform with their entire foot, and had minimal marker occlusion during data post-processing.

2.3. Data processing

Qualisys Track Manager (Qualisys AB, Göthenburg, Sweden) was used to track three-dimensional marker positions. The positive direction for the global coordinate system axes were defined as: lateral (right of the origin), anterior, and upward (vertical). Visual3D (C-Motion Inc, Rockville, MD, USA) was used to filter raw kinematic data using a 4th-order, zero-lag Butterworth lowpass filter (12 Hz cutoff frequency) and calculate limb kinematics. Per the right-hand rule, knee (sagittal plane) and ankle (frontal plane) angles were calculated with reference to the proximal segment and shank (transverse plane), thigh (frontal plane), and pelvis (frontal plane) angles were calculated relative to the global coordinate system. Accordingly, right iliac crest elevation for the stance limb indicated negative pelvic obliquity, and pelvic drop was positive. The left iliac crest magnitudes were negated to match right side polarity. The maxima (negative pelvic obliquity, thigh adduction, knee extension, shank internal rotation, ankle inversion) and minima (positive pelvic obliquity, thigh abduction, knee flexion, shank external rotation, ankle eversion) were extracted from the stance phase of each trial and subject bilaterally. Averages of each limb were calculated to compare peak joint and segment angle-magnitudes between limbs within groups. Force platform data were used to identify heel-strike and toe-off during stance phase using a 20 N vertical force threshold. Joint and segment angles were time-normalized from initial contact (0%) to toe-off (100%) and divided into three portions: initial-stance (0–33%), mid-stance (34–66%), and late-stance (67–100%). Stance phase data from injured and uninjured limbs for the injured group, and right and left limbs for the control group were exported to MATLAB (Release 2018b, MathWorks, Natick, MA, USA) for circular data analysis.

Vector coding (Needham et al., 2014) was used to quantify CAV at the pelvis, thigh, knee, shank, and ankle. The relative positions of mechanically linked joint and segments, called couples, throughout stance were constructed with time-series angle-angle plots of the proximal structure (horizontal axis) and the distal structure (vertical axis) (Freedman Silvernail et al., 2018). Bilateral pelvis-thigh, knee-shank, shank-ankle, and knee-ankle angle-angle plots (Fig. 1) were created for each subject and trial. Variables were selected to assess the possible coordination patterns associated with common RRIs (Cunningham et al., 2014; Foch & Milner, 2019; Heiderscheit et al., 2002; Miller et al., 2008). The modified vector coding method was applied to this kinematic data using the MATLAB circular statistics toolbox (Berens, 2009). The coupling angle relative to the right horizontal was calculated from the vector constructed between each pair of consecutive data points within each angle-angle plot. Coupling angles (0°–360°) were averaged across trials for each instant of stance. CAV (unit = degrees) for each subject was computed as the circular standard deviation of the coupling angles across trials. A linear average of CAV was computed for each instant of stance across subjects to present the time-series of the group mean variability during the stance phase for each limb and couple. Average CAV within each third of stance was compared between limbs, within groups. If a subject developed bilateral RRI (n = 5), the limb that developed the injury first was classified as injured. Bilateral injuries were sustained 12.4 weeks apart on average.

Asymmetry within each third of stance was calculated for each subject and coupling relationship using the symmetry angle (Zifchock

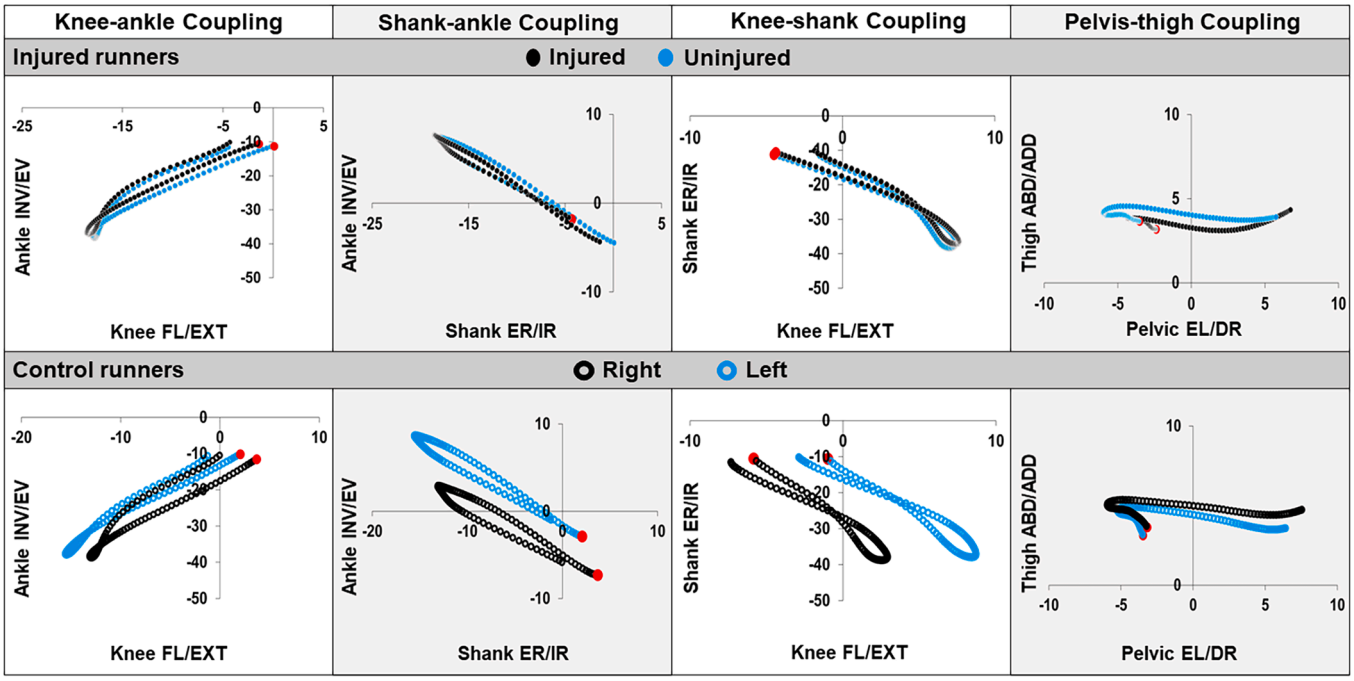


Fig. 1. Bilateral angle-angle plots for both prospectively injured (top row; injured limb - black, uninjured limb - blue) and control (bottom row; right limb – black, left limb - blue) runners for the knee-ankle, knee-shank, shank-ankle, and pelvis-thigh couplings. For each limb within each group, the distal segment or joint angle time-series (units: degrees) is plotted on the vertical axis and the proximal segment or joint angle time-series (units: degrees) is plotted on the horizontal axis. The red dots in each angle-angle plot represents heel-strike. INV/EV – inversion (+ve)/eversion (-ve), FL/EXT – flexion (-ve)/extension (+ve), ER/IR – external rotation (-ve)/internal rotation (+ve), ABD/ADD – abduction (-ve)/adduction (+ve), EL/DR – elevation (-ve)/drop (+ve).

et al., 2008b). The symmetry angle was calculated as a percentage (0% reflects perfect symmetry) using the following equation:

$$SA = \left(45^{\circ} - \arctan\left(\frac{X_{Left\ or\ Injured}}{X_{Right\ or\ Uninjured}}\right)\right) \div 90^{\circ} \times 100$$

where X is the average CAV magnitude for the denoted limb.

2.4. Statistical analyses

A sample size estimate (G*Power Version 3.1.9.4) based on previous studies (Cunningham et al., 2014; Zifchock et al., 2008a) indicated 13–15 subjects in each group was required to obtain 0.80 statistical power ($\alpha < 0.050$) for inter and intra-group comparisons. Shapiro-Wilk tests revealed peak joint and segment angle magnitudes were normally distributed but demographic data and CAV were not. Therefore, Wilcoxon Rank-Sum tests ($\alpha < 0.050$) were conducted, identifying differences between groups in demographics and asymmetry and identify intra-group differences in CAV between limbs for all coupling relationships during each third of stance. Chi square test ($\alpha < 0.050$, Yates correction applied) was conducted to identify differences in sex distribution between groups. Parametric repeated measures t-tests were conducted to identify intra-group differences in peak joint and segment angle magnitudes between limbs.

For the predictive analysis (RStudio, Version 1.3.959), two initial stepwise regression models (Models 1 and 2) were implemented to select two corresponding best-fit models (Models 3 and 4) for subsequent logistic regression analyses. Model 1 included bilateral CAV magnitudes and model 2 included symmetry angles as RRI predictors. Both models included bilateral data from the injured and control groups. Assumptions for the stepwise multiple regression analysis were met. Forward and backward model selection methods were implemented. The models with the lowest second-order Akaike Information Criteria (AICc) were selected for logistic regression analyses. A logistic regression classification table was constructed to assess model accuracy.

3. Results

The final sample of thirty-one subjects were categorized into injured group (n = 14) and control group (n = 17). No demographical or training related differences were found between groups ($p > 0.050$) (Table 1). Injury distribution by limb side and region is presented in Table 2.

3.1. Intra-group differences between limbs

The control group displayed significant differences between their right and left limbs for peak ankle eversion (left > right; $p = 0.034$), peak shank internal rotation (left > right; $p < 0.010$), and peak shank external rotation (right > left; $p < 0.010$) (Supplemental Content 1). During initial-stance, significant differences between limbs were observed for shank-ankle (right > left; $p < 0.010$) and pelvis-thigh CAV (left > right; $p = 0.002$). During mid-stance, significant differences between limbs were observed for knee-ankle (right > left; $p < 0.010$), shank-ankle (right > left; $p < 0.010$), knee-shank (right > left; $p < 0.010$), and pelvis-thigh (left > right; $p < 0.010$) CAV. During late-stance, significant differences between limbs were only observed for pelvis-thigh (left > right; $p < 0.01$), and shank-ankle (left > right; $p = 0.025$) CAV. No other differences were observed between limbs during initial-stance or late-stance ($p > 0.050$) (Fig. 2, Table 3).

For the injured group, peak joint and segment angle magnitudes were similar between limbs ($p > 0.050$) (Supplemental Content 1). Significant differences were observed between injured and uninjured limbs during initial-stance for knee-ankle (injured > uninjured; $p < 0.010$), shank-ankle (injured > uninjured; $p < 0.010$), and knee-shank CAV (injured > uninjured; $p < 0.010$). Pelvis-thigh CAV was similar between limbs during initial-stance ($p = 0.060$). During mid-stance, significant differences between limbs were observed for knee-ankle (uninjured > injured; $p < 0.010$), and pelvis-thigh (injured > uninjured; $p < 0.010$) CAV. No other differences were observed between limbs during mid-stance ($p > 0.050$). CAV was similar between limbs during late-stance across coupling relationships ($p > 0.050$) (Table 3).

Table 2
Distribution of reported injuries by anatomical region in the lower limb within the injured group. Two subjects sustained three injuries each in the same limb, resulting in an injury count greater than the injured sample size (n = 14). Six subjects developed an injury in their right limb and eight subjects developed an injury in their left limb.

Anatomical region	Number of injuries	Percentage of total injuries (%)
Knee	4	22.22
Shank	2	11.11
Ankle	1	5.55
Hip	5	27.77
Thigh	1	5.55
Foot	4	22.22
Lower back	1	5.55

3.2. Asymmetry: Injured versus controls

Symmetry angle was significantly greater (i.e. more asymmetrical) for the injured versus control group for knee shank coupling during initial ($p < 0.010$), and mid-stance ($p < 0.010$), but significantly less (i.e. less asymmetrical) for mid-stance knee-ankle ($p < 0.010$), late-stance knee-ankle ($p < 0.010$), late-stance knee-shank ($p < 0.010$) and shank-ankle ($p < 0.010$) couplings. Pelvis-thigh symmetry angles were similar between groups for all portions of stance ($p > 0.050$) (Table 4).

3.3. Predictive analysis

Model 1 revealed that the lowest AICc included knee-ankle CAV during initial and mid-stance, and shank-ankle CAV during initial and late-stance, therefore they were included in Model 3. Model 2 revealed the lowest AICc included mid-stance knee-shank and knee-ankle symmetry angles, therefore they were included in Model 4. Model 3 indicated that an increase in knee-ankle CAV during mid-stance decreased the odds of developing a RRI by 20.01% (OR = 0.799, p = 0.043, 95% CI = 0.61–0.96, variance inflation factor (VIF) = 1.17), while an increase in shank-ankle CAV during initial-stance increased the odds of developing a RRI by 23.91% (OR = 1.239, p = 0.020, 95% CI = 1.04–1.51, VIF = 1.36). Knee-ankle coupling during initial-stance and shank-ankle coupling during late-stance were not significantly associated with RRI (knee-ankle: OR = 1.513, p = 0.104, 95% CI = 0.95–2.66, VIF = 1.19; shank-ankle: OR = 0.712, p = 0.079, 95% CI = 0.46–0.99, VIF = 1.28). Model 3 predicted RRI risk with 85.48% accuracy. Model 4 indicated no significant association between RRI and the included symmetry angle variables (knee-shank: OR = 1.168, p = 0.176, 95% CI = 0.94–1.51, VIF = 1.01; knee-ankle: OR = 0.902, p = 0.166, 95% CI = 0.76–1.03, VIF = 1.01).

4. Discussion

We compared bilateral measures of CAV within and between prospectively injured and control runners. Associations of limb-specific characteristics and degree of asymmetry with RRI were also tested. Congruent with hypothesis one, both injured and uninjured runners displayed differences in bilateral CAV. Contrary to hypothesis two, however, degree of asymmetry was different between groups, though it did not significantly predict injury risk thereby confirming hypothesis four. Per previous investigations (Zifchock et al., 2006; Zifchock et al., 2008a), our results suggest movement patterns specific to the injured limb affect RRI risk but the degree of asymmetry observed did not. Therefore, degree of asymmetry in CAV observed among injured and

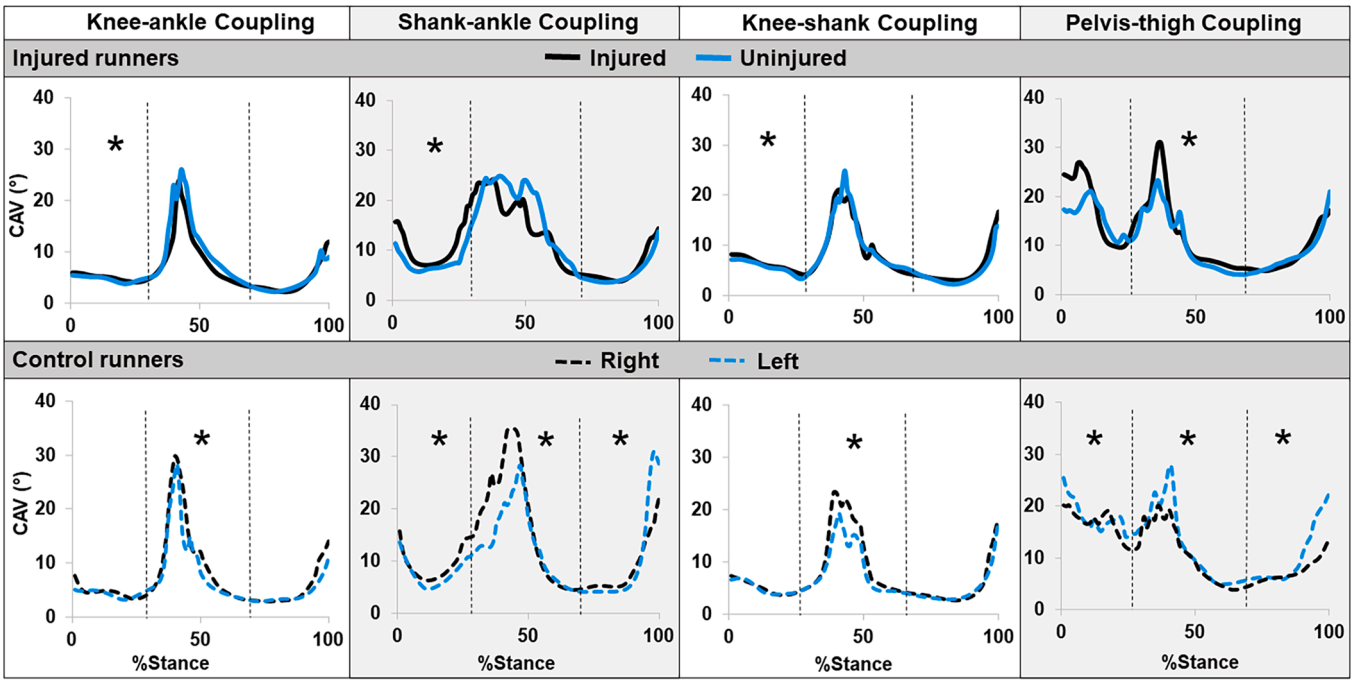


Fig. 2. Bilateral linear average coordination variability (CAV, units: degrees) for both prospectively injured (top row; injured limb - black, uninjured limb - blue) and control (bottom row; right limb – black, left limb - blue) runners for the knee-ankle, knee-shank, shank-ankle and pelvis-thigh couplings. CAV is plotted on the vertical axis and stance phase represented as a percentage of total stance time is plotted on the horizontal axis. The vertical dashed lines in each plot indicate thirds of stance phase: initial stance (0%–33%), mid-stance (34%-66%), and late-stance (67%-100%). * indicates a statistically significant difference ($p < 0.05$) between limbs within the group and within the given portion of the stance phase.

Table 3
Mean coordination variability(standard deviation) for each coupling relationship during the initial, mid, and late portions of the stance phase. * indicates significant differences between limbs ($p < 0.05$). *d* is Cohen's d effect size.

Coupling	Injured				Controls			
Initial Stance	**Injured (°)**	**Uninjured (°)**	**p-value**	***d***	**Right (°)**	**Left (°)**	**p-value**	***d***
Knee-Ankle	5.48 (0.54)	4.58 (0.77)	<0.010*	1.31	4.50 (0.93)	4.41 (0.54)	0.957	0.12
Shank-Ankle	12.57 (6.31)	9.52 (3.63)	<0.010*	0.58	10.18 (4.30)	7.91 (2.58)	<0.010*	0.63
Knee-Shank	6.41 (1.39)	5.72 (1.23)	<0.010*	0.51	5.16 (1.13)	5.08 (1.01)	0.271	0.07
Pelvis-Thigh	17.37 (6.12)	15.61 (3.30)	0.060	0.36	16.25 (2.68)	17.48 (2.77)	0.002*	0.44
Mid-stance	**Injured (°)**	**Uninjured (°)**	**p-value**	***d***	**Right (°)**	**Left (°)**	**p-value**	***d***
Knee-Ankle	9.56 (5.82)	12.16 (6.43)	<0.010*	0.41	12.06 (7.79)	10.00 (7.0)	<0.010*	0.27
Shank-Ankle	16.66 (6.90)	18.06 (6.63)	0.502	0.20	18.67 (10.15)	14.65 (6.19)	<0.010*	0.47
Knee-Shank	11.56 (6.17)	11.31 (5.92)	0.264	0.04	11.71 (6.41)	9.13 (4.93)	<0.010*	0.44
Pelvis-Thigh	11.96 (8.08)	10.27 (6.23)	<0.010*	0.23	10.24 (5.70)	12.22 (7.58)	<0.010*	0.30
Late Stance	**Injured (°)**	**Uninjured (°)**	**p-value**	***d***	**Right (°)**	**Left (°)**	**p-value**	***d***
Knee-Ankle	3.79 (1.84)	3.84 (1.54)	0.304	0.03	4.72 (3.38)	4.17 (2.01)	0.943	0.16
Shank-Ankle	5.79 (2.62)	5.69 (2.56)	0.100	0.04	7.22 (3.93)	7.78 (7.14)	0.025*	0.09
Knee-Shank	4.52 (3.13)	4.50 (2.48)	0.070	0.01	4.53 (2.98)	4.64 (2.42)	0.112	0.04
Pelvis-Thigh	8.06 (4.05)	7.97 (4.06)	0.648	0.02	7.12 (2.40)	9.84 (5.60)	<0.010*	0.62

control runners may be natural and functional, as suggested previously (Sadeghi et al., 2000). Rather than degree of asymmetry, injured limb characteristics like greater initial-stance shank-ankle and mid-stance knee-ankle CAV reflect increased and decreased odds of RRI development, respectively.

The present study provides insight towards the biomechanics potentially associated with RRI apart from running exposure because weekly mileage was similar between injured and control runners during follow-up (Table 1), and identical between injured and uninjured limbs within the injured group. RRI development may therefore have been influenced by injured limb specific characteristics among injured runners, with 16.7% greater initial-stance shank-ankle CAV in the injured compared with the uninjured limb increasing injury odds by 23.9%. Future investigations could examine how interactions between weekly mileage and bilateral CAV influences RRI risk in a specific limb.

Present results indicate that the relationship between CAV to RRI may vary with portion of stance, as also suggested previously (Hein et al., 2012). For instance, and per hypothesis three, injured runners displayed greater CAV in their injured compared with uninjured limb during initial stance. We observed that greater CAV during initial-stance may increase RRI risk whereas greater CAV during mid-stance may decrease RRI risk. Initial-stance and mid-stance impose different demands on the musculoskeletal system, therefore the implications of greater CAV for RRI during each portion may be dissimilar. Initial-stance involves high impact forces related to heel-strike that cause significant accelerations of body segments, particularly the shank (Nigg et al., 1995). Further, the foot and subtalar joint rapidly transition from an inverted position at heel-strike to eversion motion during initial-stance, transmitting rotational torques between the foot and shank segments (Stiehl, 1991). Therefore, greater shank-ankle CAV, as observed in the injured limb of injured runners in this study, may reflect limited neuromuscular control of impact-related segmental accelerations and

Table 4
CAV asymmetry presented as a mean (standard deviation) percentage difference in CAV magnitudes between limbs. Asymmetry magnitudes we calculated by comparing the injured versus uninjured limbs for the injured group and right versus left limbs for the control group. Asymmetry was computed using the symmetry angle method (Zifchock et al., 2008b). *indicates significant differences between limbs ($p < 0.05$). *d* is Cohen's d effect size.

Coupling	Injured (%)	Controls (%)	p-value	*d*
Initial-stance				
Knee-ankle	14.84 (2.53)	14.58 (2.00)	0.644	0.11
Shank-ankle	16.68 (3.17)	17.32 (3.84)	0.574	0.18
Knee-shank	14.60 (1.91)	12.39 (1.34)	<0.010*	1.33
Pelvis-Thigh	11.77 (9.07)	16.97 (12.20)	0.184	0.27
Mid-stance				
Knee-ankle	14.59 (2.08)	17.54 (1.98)	<0.010*	1.45
Shank-ankle	18.33 (4.49)	19.21 (2.46)	0.969	0.24
Knee-shank	18.43 (2.19)	16.43 (2.46)	<0.010*	0.85
Pelvis-Thigh	14.02 (8.90)	12.57 (7.00)	0.623	0.37
Late-stance				
Knee-ankle	13.91 (1.57)	15.85 (2.00)	<0.010*	1.07
Shank-ankle	13.02 (2.09)	15.16 (2.65)	<0.010*	0.89
Knee-shank	12.93 (1.34)	15.71 (1.61)	<0.010*	1.87
Pelvis-Thigh	9.76 (8.72)	15.63 (11.49)	0.117	0.29

distribution of rotational torques across soft tissue structures unequipped to manage this degree of variability. Hence, RRI risk may increase. The relationship between impact-related segmental accelerations and coordination variability, however, is yet unexplored. Also unknown is the way in which neuromuscular control of movement such as muscle activation is related to CAV. Assessing CAV in relation to both neuromuscular control and impact-related segmental accelerations is an interesting avenue for future research to identify coordination strategies used by the body in response to impact loading.

While greater CAV during initial-stance may reflect heightened injury risk due to the mechanical environment created by rapid joint motion transitions, greater CAV during mid-stance may be desirable given greater weight-bearing demands. Greater knee-ankle CAV during mid-stance may reflect adequate flexibility of available coordination patterns including mechanically linked knee, shank, and ankle motions that contribute to optimal shank rotation. Optimal shank rotation may enable the accommodation of large weight-bearing loads. It may also enable manageable stress distribution over a larger rather than concentrated region of soft tissue structures around the knee, like the iliotibial band, which may occur with limited knee-ankle CAV. Coordination differences between controls and runners experiencing iliotibial band syndrome (Foch & Milner, 2019; Hein et al., 2012; Miller et al., 2008) along with our findings suggest prospective, injury and stance-portion specific coordination analyses combined with imaging or musculoskeletal modeling techniques is necessary to gain insight on specific RRI mechanisms.

Per Wilcoxon rank-sum tests, mean symmetry angles were significantly different between injured and control groups (Table 4). However, logistic regression (model 4) revealed these differences did not predict RRI risk. Since t-tests assess differences in group means while logistic regression assesses the association of a variable to an outcome, these opposing results are plausible. Thus, despite significant differences in group means, symmetry angle did not change the odds of developing RRI and may therefore be less meaningful to RRI risk compared with individual limb CAV characteristics which significantly increased the odds of RRI.

5. Limitations and future scope

This study highlights potential implications of CAV for RRI risk. However, this analysis does not reveal the specific neuromotor processes controlling segmental coordination and variability and so the underlying causes of CAV cannot be inferred. Although we included coordination patterns assessed when analyzing the most common, specific injury types (Cunningham et al., 2014; Foch & Milner, 2019; Heiderscheit et al., 2002; Miller et al., 2008), we cannot infer the role of bilateral CAV in a specific injury type since runners in our sample developed injuries across anatomical locations (Table 2). Consistent with previous investigations, five overground stance phases per limb were used to compute CAV (Hafer et al., 2016; Needham et al., 2014). Wyatt et al. (2021) suggested eleven stance phases are required for stable mean CAV computations. Thus, mean CAV magnitudes in the present study may be underestimated, affecting the ability to detect statistically significant relationships between CAV and injury risk. However, observing statistically significant differences in bilateral CAV magnitudes and between CAV and RRI in the predictive analysis suggests that five trials established sufficiently stable CAV means in our sample. To corroborate this observation, the results of an Intraclass Correlation Coefficient analysis (ICC (3,1)) (Koo and Li, 2016) assessing the reliability of our mean CAV calculated with five trials is presented in Supplemental Content 2.

Logistic regression models 2 and 4 included CAV magnitudes from both limbs per subject yielding 62 data points per predictor variable whereas models 1 and 3 had one set of data points per subject (i.e. symmetry angles) yielding 31 data points per predictor. Fewer data points per predictor for models 1 and 3 may have reduced the predictive power yielding fewer significant observations compared with models 2 and 4. However, since the study was sufficiently powered, the likelihood of a type two error is reduced.

Sex-based differences were not tested because sex distribution was statistically similar between the injured and control groups. Nonetheless, we conducted an exploratory sex-based analysis (Supplemental Content 3) though the obtained results may have limited validity given an insufficient sample size. Sex-based differences for bilateral and multiplanar CAV measures should be explored in future studies with larger sample sizes.

The CAV calculation may result in statistical artifact when vector magnitudes are small (Stock et al., 2018). While future research should address this potential limitation, it is premature to modify vector coding calculations because approaches to address this limitation are developing and need to be validated with large experimental data sets (van Emmerik, 2020).

6. Conclusion

Present findings suggest limb-specific shank-ankle and knee-ankle CAV may influence RRI risk rather than degree of asymmetry, which was not associated with prospective RRI in this study. Based on these findings, it is important that future studies assessing RRI risk investigate CAV bilaterally. To further understand the relationship between bilateral CAV and RRI, bilateral CAV must be assessed with regards to specific injury type and potential interactions with training related variables like weekly running mileage, while also accounting for possible sex-based differences.

CRediT authorship contribution statement

Gauri A. Desai: Conceptualization, Data Curation, Writing - original draft, Visualization, Investigation, Validation, Formal analysis, Methodology. **Allison H. Gruber:** Conceptualization, Funding acquisition, Writing - review & editing, Methodology, Supervision, Resources, Project administration and Software.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jbiomech.2021.110938.

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