Asian J Sports Med. 2022 December; 13(4):e129916. https://doi.org/10.5812/asjsm-129916.
Published online 2022 December 6. **Research Article**

Assessing the Association of Shoulder Pain Risk with Physical Fitness in Badminton Players at National Tournament Level

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Received 2022 July 27; **Revised** 2022 October 11; **Accepted** 2022 November 07.

Abstract

Background: Shoulder pain which affects sports performance and activities of daily life, is a common musculoskeletal problem experienced by badminton players.
Objectives: This study aimed to identify the association of shoulder pain with physical fitness in elite university badminton players participating in the national tournament via medical check-ups.
Methods: Physical fitness evaluations were performed among fifty-two 18 - 22 years old university badminton players participating in the national tournament. Handgrip strength, heel buttock distance, angle of straight leg raise, single leg stance, shoulder range of motion, and trunk range of motion were assessed. The prevalence of present shoulder pain was described. Multivariable logistic regression was used to examine the association of present shoulder pain with physical fitness.
Results: Sixteen badminton players (30.8%) sustained present shoulder pain related to badminton. Dominant trunk rotation (adjusted OR: 0.91, 95% CI: 0.84 - 0.99, P-value = 0.028) and single leg stance of the nondominant leg (adjusted OR: 0.97, 95% CI: 0.94 - 1.00, P-value = 0.048) were significantly associated with the presence of present shoulder pain.
Conclusions: Decreased trunk rotation and deficit in single-leg stance balance might be potential risk factors associated with physical fitness for shoulder pain in university badminton players at national tournament level. These findings can help draw the attention of badminton coaches, players, and team members to facilitate physical fitness promotion for badminton pain/injury prevention.

Keywords: Athletes, Racquet Sports, Shoulder Pain, Physical Fitness, Risk Factors

1. Background

Badminton, requiring multi-limb coordination and balance ability of players to transfer body core mass, and simultaneously perform trunk rotation and upper extremity strength and rotation, is one kind of overhead motion sports played by over 330 million people all over the world (1, 2). Due to the characteristics of the sport and the frequency at which overhead motions occur, shoulder injuries and pain are common musculoskeletal problems experienced by badminton players (3-5). Previous studies on the epidemiology of badminton injuries have reported the prevalence of shoulder injuries accounted for 1.4% - 19.0% among 7 - 57-year-old badminton players (5-8). More than half of the badminton players complained of shoulder pain; over one-third of whom continued to play badminton with ongoing pain (3, 4). Pain related to the development of injury is the first stage of injury that is always neglected. Shoulder pain not only reduces upper limb function and negatively impact overhead motion but also disturbs daily living (9, 10). However, studies on shoulder pain in badminton players are scarce. A previous study has demonstrated training hours per day to be a risk factor for shoulder pain in badminton players aged 7 - 12 years (5).

As physical fitness, such as body range of motion, muscle flexibility, and balance ability, affects joint kinematics and kinetics (11, 12), it should be studied to improve shoulder injury prevention as well. Past studies on shoulder range of motion (ROM) have revealed that decreased shoulder internal rotation (IR) and increased shoulder external rotation (ER) on the dominant side were common compared to the nondominant side in healthy badminton players (9, 13, 14). Some studies have revealed that after playing two consecutive matches on the same day, the ER of the nondominant side significantly increased in female badminton players, while the ER of both sides significantly increased in male badminton players. Insufficient shoulder external rotation and glenohumeral internal rotation deficit (GIRD) on the dominant side also have been revealed to increase the likelihood of shoulder injury (15). In badminton, only one previous study has compared shoulder ROM in badminton players with shoulder pain in those without; however, a positive relationship was not found (9).

Badminton overhead motion can be understood as a kinetic chain that transfers energy to the lower limb via the trunk and subsequently through the upper limbs to release it to the shuttlecock. All the parts of the chain are interrelated, where a breakage in one component of the chain can affect shoulder pain and injury (11, 12, 16, 17). In recent years, a positive association between shoulder pain and injury and physical dysfunction of trunk ROM (18, 19), balance ability (16), upper limbs power (20, 21), and muscle flexibility (22) have been reported in other overhead motion sports. Nonetheless, such associations among badminton players are unknown.

We predicted an association between physical fitness and overload in the shoulder, such that improving physical fitness, i.e., muscle flexibility, shoulder ROM, trunk ROM, and balance ability, can prevent shoulder injury in badminton players. An advanced understanding of what physical dysfunction is possible to increase the occurrence of badminton injury would facilitate badminton injury prevention.

2. Objectives

This study aimed to evaluate the influence of physical fitness on shoulder pain risk among top-level university badminton players in Japan via medical check-ups. Based on the literature, we hypothesized that GIRD, increased shoulder ER, decreased trunk rotation, and weak balance ability are potential risk factors for shoulder pain in university badminton players.

3. Methods

In this study, we recruited badminton players from Japanese universities with twelve top-level badminton teams for investigation from August 2018 to March 2019. This research protocol was reviewed and approved by the ethical committee of the University of Tokyo and was in conformity with the Declaration of Helsinki.

To assess the association between physical fitness and shoulder pain, a self-reported questionnaire and physical fitness tests were used. The questionnaire was modified from previous studies (23, 24) and consisted of basic parameters (gender, age, weight, height, dominant side), duration of badminton playing experience, badminton training hours per day, badminton training days per week, and anamnesis of past injury and shoulder pain. Participants were asked to answer the question "Do you have shoulder pain now?" as well. Inclusion criteria were as follows: (1) playing competitive badminton at a national level tournament; (2) training regularly per week; (3) participants that had completed an informed consent form. Participants were excluded if: (1) they reported current shoulder injury, any shoulder injury within the past year, or past shoulder surgery; (2) the questionnaire had not been completed. The participants were assigned to two groups based on present shoulder pain status.

3.1. Training Volumes

Adequate training volumes not only lessen the likelihood of non-contact injury but improve physical fitness (25); therefore, training volumes were investigated using badminton training hours per day and badminton training days per week. Training hours were defined as the time of physical condition training or badminton motor skills under the supervision of the coach. However, the warm-up and cool-down time were not taken into account as training exposure time.

3.2. Definition of Injury and Pain

To keep consistency in the definitions and enable data across studies to be compared, the definitions of sports injury defined by the International Olympic Committee (26) were used to make the judgment criteria in this study. The definition of pain was any painful somatic discomfort (soreness or ache in body parts, with or without radiating pain) with sustained badminton capacity (27). The definition of an injury was any somatic discomfort sustained during training or match play causing one or more of the three judgment criteria as follows: (1) having to immediately discontinue the current badminton training or match; (2) being unable to participate in subsequent badminton training or matches; and/or (3) needing medical care irrespective of the potential absence from training or match.

3.3. Physical Fitness Tests

Physical fitness tests consisted of a handgrip strength test, heel-buttock distance (HBD) test, straight leg raise (SLR) test, single leg stance test, shoulder ROM evaluation, and trunk ROM evaluation before badminton training. Handgrip strength was examined by a digital hand dynamometer with measuring capacity from 0 - 90.0 kg (a sensitivity of 0.1 kg, N-FORCE, Wakayama, Japan), and ROM was measured by a digital goniometer SA-5468 (measuring range is 0 - 360.0 degree with a sensitivity of 0.1 degree with resolution of 0.05 degree, Suncosmo, Tokyo, Japan).

The physical fitness tests were performed by an orthopedist with over 20 years of experience and a doctoral program candidate of sports medicine. First, handgrip strength (ICC = 0.94 - 0.98) (28) of both sides was measured with the participants in a standing posture. Then, muscle tightness of the thighs (quadriceps femoris and hamstrings) was examined by measuring HBD (ICC = 0.86) (29) and SLR (ICC = 0.93 - 0.97) (30). To evaluate muscle tightness of the quadriceps femoris, the participants lied in a face-down position on a yoga mat. While the participants kept a flat pelvis, the examiner slowly flexed the participants' knee until the heel approached the buttock or discontinued due to tightness or pain in the quadriceps femoris muscles. The distance which was between the buttock and the heel was measured and recorded as HBD. Next, the participants lied in a face-up position, and the examiner raised the participants' one leg slowly while keeping the knee of the leg extended and the other leg flat. As soon as the participants complained about tightness or pain in the hamstring muscles, the test was stopped. The start-stop point angle was measured using the goniometer and recorded as SLR.

Static balance ability was evaluated by the time of balance measured by single leg stance test, which has good intra-rater reliability (ICC = 0.88) (16). The participants crossed their forearms over the chest and lifted one thigh to 90° of hip flexion with eyes closed while standing with one leg as long as they could. The test was stopped if any of the criteria happened as follows: (1) the lifted lower limb touched the yoga mat or the stance leg; (2) movement of the stance leg; (3) opening eyes. Three trials on each leg were performed by the participants in which the longest time on each leg was chosen.

In shoulder ROM evaluation (ICC = 0.62) (31), ER and internal rotation (IR) in both the dominant and nondominant shoulders were examined (15, 32). The participants were in a face-up position on a standard examination table, with a straight leg, 90° of shoulder joint abduction, 90° of elbow joint flexion. The scapula was stabilized and the forearm was placed in neutral position by the examiner; then, the forearm was pushed posteriorly (ER) and anteriorly (IR) with the humerus rotation for producing maximum passive ER and IR. The angles of ER and IR on both sides were measured by the second examiner at the point that no more humerus movement would happen without the movement of the scapula. Compared with the non-dominant side, the loss of IR of the glenohumeral joint of the dominant side was defined as GIRD, while increased ROM angle of ER of the glenohumeral joint of the dominant side was defined as ER gain. The total ROM (TROM) of each side was calculated by the sum of ER and IR of the side individually, and the loss of TROM in the dominant shoulder as compared with the contralateral shoulder was defined as TROM loss (20, 33).

Finally, trunk ROM including trunk flexion, extension, and trunk rotation, were examined. The participants, in an upright standing position, bent the trunk forward/backward progressively as far as possible while keeping straight legs, chest out and chin up. Trunk flexion was measured (ICC = 0.93) by the angle between the stop-point of the trunk bending forward and the vertical line (34). Trunk extension was measured (ICC = 0.92) by the angle between the stop-point of the trunk bending backward and the vertical line (34). With regard to the trunk rotation test, the participant in a sitting position with crossed legs on the yoga mat kept the trunk in an upright posture and crossed arms over the chest. Then the participants were asked to rotate the trunk to the dominant/nondominant as far as possible. The start-stop point angles were measured by the examiner using the goniometer and recorded as trunk rotation (ICC = 0.65) (35).

3.4. Statistical Analysis

For sample size calculation, we hypothesized that the prevalence of the participants with risk factors (normal distribution) would be 40% while those without risk factors would be 15% based on previously published data (3, 4, 9). A minimum total sample size (calculated by G*Power) of 47 would have a power of 80% to test the moderate association of present shoulder pain with risk factors (one-tail α of 0.05, R = 0.5).

The Shapiro-Wilk test was used to analyze the normality of baseline parameters, i.e., age, height, weight, body mass index (BMI), badminton playing experience, badminton training days per week, badminton training hours per day, and total hours per week. Due to the normal distribution of the data, independent samples *t*-tests were operated to compare basic parameters between the groups. Categorial variables, analyzed by the χ^2 test, are presented as numbers and percentages. In terms of physical fitness parameters, binary logistic regression analyses were performed to evaluate the association of handgrip strength, HBD, the angle of SLR, times of single leg stance, and shoulder and trunk ROM with the presence of present shoulder pain. We calculated the odds ratios (ORs) and 95% confidence intervals (CIs) of the association between present shoulder pain and physical fitness parameters. Then, the variables with a P-value < 0.2 were screened for identifying potential risk factors of present shoulder pain using multivariable logistic regression analysis (10, 23). For statistical analysis, P < 0.05 was considered significant.

4. Results

Of the recruited 52 badminton players (26 males and 26 females), one male badminton player with lacking data on present shoulder pain report was excluded, while 51 badminton players met the eligibility criteria. Based on the definitions of pain and injury, 51 badminton players without current shoulder injuries were divided into two groups based on their present shoulder pain. Sixteen players with present shoulder pain (8 male and eight female players) were divided into the pain group, while 35 players without present shoulder pain (17 male and 18 female players) were divided into the pain-free group. The basic parameters of the players are presented in Table 1. No significant differences in basic parameters existed between the pain group and the pain-free group.

The ORs and 95% CIs of crude analysis using binary logistic regression on the association between physical fitness tests and the presence of present shoulder pain are listed in Tables 2 and 3. Participants with present shoulder pain showed a significantly increased SLR degree of the dominant leg compared to those without present shoulder pain (90.7° vs. 82.4°, OR: 1.06, 95% CI: 1.00 - 1.11, $P < 0.05$). The other variables of physical fitness showed no significant association with present shoulder pain.

Ultimately, variables with a p-value < 0.2, including SLR of both sides, the balance of the nondominant leg, GIRD, trunk extension, and dominant trunk rotation were screened and analyzed using multivariable logistic regression analysis. In the model, dominant trunk rotation (adjusted OR: 0.91, 95% CI: 0.84 - 0.99, $P = 0.028$) and balance of the nondominant leg (adjusted OR: 0.97, 95% CI: 0.94 - 1.00, $P = 0.048$) were significantly associated with the presence of present shoulder pain (Figure 1).

5. Discussion

This is the first study to detect the association between physical fitness and shoulder pain risk using physical fitness tests of medical check-ups among Japanese university badminton players at the top level. The first newly unique findings in this study were that decreased dominant trunk rotation and deficit in single leg stance balance were significantly associated with shoulder pain.

Badminton forehand overhead stroke, similar to the overhead motion of other overhead sports such as baseball, is played with a full overhead throwing motion requiring players to perform weight shift, trunk rotation, and upper limb rotation through the kinetic chain (36). The trunk as an engine for force development is a major part of the kinetic chain motion (11, 37). Regarding research on shoulder symptoms in overhead sports players by trunk ROM evaluation, previous studies of baseball players demonstrated decreased trunk rotation (19) and improper trunk rotation (11, 12) as risk factors for shoulder injuries. A study of softball players reported that restricted flexibility of forward trunk rotation was a risk factor for shoulder injuries (18). In this study, a significant association was detected between decreased dominant trunk rotation and the incidence of present shoulder pain, indicating that decreased dominant trunk rotation might be a potential risk factor for shoulder pain.

As for balance ability using single leg stance, previous studies of volleyball players revealed that decreased balance ability was negatively related to the occurrence of shoulder pain and disability (38). A study of overhead players consisting of lacrosse players, softball players, swimmers, football players, water polo players, baseball players, field throwing athletes, and basketball players, reported that players with weak single-leg stance time were more vulnerable to sustaining shoulder symptoms (39). We also found a similar result that in badminton players with weak single leg stance time were more likely to present with shoulder pain.

For overhead motion, the trunk plays a vital role in transferring energy of the kinetic chain from lower limbs to upper limbs (2, 37). The shoulder, as the central location in the kinetic chain, suffers from the high loads, and as a funnel for forces, is regularly the victim of a deficit in any part of the kinetic chain. The decreasing energy production of the trunk by 20% can result in increased stress on the shoulder joint by up to 34% (11). Additionally, balance ability is crucial for maintaining the body's center of gravity, especially for badminton players who need to adjust for the transfer in the center of gravity from one leg to the other leg quickly during an overhead stroke (2). A weak single-leg stance indicates weak balance ability, which represents weakness of trunk control (11, 16). Balance control is essential to safely execute coordinated and smooth neuromuscular movement involving the movement of body parts or the whole body (40). The mechanics of the forehand overhead motion are complex and generate tensile load in the shoulder joint via dissipating excess momentum (11, 37). Weak balance ability as well as decreased trunk rotation, can result in abnormal kinetic chain transfer of energy. The abnormal kinetic chain coordination could alter proper techniques, which could change the load in the shoulder joint or result in upper-limb deviation, ultimately causing shoulder injuries and pain (12, 18).

Based on the above findings, we speculated that decreased trunk rotation and deficit in single-leg stance balance might lead to shoulder pain among university top-level badminton players who perform overhead motions repetitively. Additionally, this study showed no associa-

Table 1. Basic Parameters of the Participants in Pain-Free and Pain Groups [a]

Demographic	Pain Free (n = 35)	Pain (n = 16)	P-Value
Gender			0.93
Male	17 (48.6)	8 (50.0)	
Female	18 (51.4)	8 (50.0)	
Age (y)	19.6 ± 1.1	20.1 ± 1.3	0.23
Height (cm)	165.2 ± 7.1	165.7 ± 8.4	0.83
Weight (kg)	60.1 ± 7.2	60.3 ± 7.6	0.90
BMI (kg/m^2)	22.0 ± 1.6	21.9 ± 1.5	0.93
Badminton experience (y)	11.0 ± 2.4	11.4 ± 2.9	0.60
Days (per week)	5.2 ± 0.5	5.2 ± 0.7	0.82
Hours (per day)	3.3 ± 0.5	3.3 ± 0.5	0.78
Total (min per week)	1039.1 ± 161.8	1016.3 ± 178. 3	0.65

Abbreviation: BMI, body mass index.
[a] Values are expressed as mean ± SD.

Table 2. Binary Logistic Regression Analyses of Variable Factors of Physical Fitness Associated with Present Shoulder Pain [a]

Variables	Pain Free (n = 35)	Pain (n = 16)	OR (95% CI)	P-Value
Hand grip strength (kg)				
Dominant	36.8 ± 9.9	40.0 ± 8.7	1.04 (0.97 - 1.10)	0.27
Nondominant	31.1 ± 8.4	33.9 ± 8.5	1.04 (0.97 - 1.12)	0.27
HBD (cm)				
Dominant	1.4 ± 3.0	2.3 ± 4.2	1.08 (0.91 - 1.27)	0.39
Nondominant	1.3 ± 3.0	2.6 ± 5.1	1.09 (0.93 - 1.26)	0.28
SLR (°)				
Dominant	82.4 ± 11.6	90.7 ± 14.3	1.06 (1.00 - 1.11)	0.04 [b]
Nondominant	81.4 ± 11.6	89.6 ± 17.7	1.04 (0.997 - 1.09)	0.067 [b]
Balance (s)				
Dominant	43.3 ± 30.1	53.9 ± 48.3	1.01 (0.99 - 1.02)	0.34
Nondominant	45.9 ± 37.3	26.5 ± 26.7	0.98 (0.96 - 1.00)	0.085 [b]

Abbreviations: OR, odds ratio; CI, confidence interval; HBD, heel buttock distance; SLR, straight leg raising.
[a] Values are mean ± SD.
[b] P-value < 0.2.

tion between shoulder pain and training hours which is inconsistent with the previous studies that revealed training hours per day as a risk factor for shoulder pain in 7 - 12 years-old badminton players (5). The significant differences in age, which means the different physical maturation levels might contribute to the different results, which also indicates that physical fitness is a more important factor than overuse. Given the findings of our studies, not only in badminton players but in other overhead motion sports players who require multi-limb coordination, physical fitness should be focused on. If shoulder pain occurs, players, coaches, physicians, and physiotherapists should evaluate trunk rotation and balance ability so that prevention programs can be implemented to decrease the risks to shoulder injuries as early as possible. Moreover, this study could be used for reference and be extended to further find physical risk factors for improving injury prevention in other sports.

Healthy overhead athletes regularly present with soft-tissue and bony adaptations of the dominant upper limbs because of the repetitive loading of overhead motion. These changes, such as humeral retroversion and soft-tissue laxity or tightness, are seen in changes in shoulder ROM, resulting in posterior shoulder tightness, i.e., GIRD, and anterior shoulder laxity, i.e., ER gain, and are regularly related to shoulder injury (41, 42). A variety of overhead sports studies have studied shoulder ROM. Previous studies of overhead sports, such as tennis, baseball, and handball, revealed that GIRD and insufficient ER gain significantly increased the likelihood of shoulder injury (15, 20, 24, 43). In contrast, other studies of baseball and softball revealed that GIRD and ER gain were not risk factors for shoulder injury (32, 44). In this study, we hypothesized that GIRD and ER gain are potential risk factors for shoul-

Table 3. Binary Logistic Regression Analyses of ROM Associated with Present Shoulder Pain [a]

ROM (°)	Pain Free (n = 35)	Pain (n = 16)	OR (95% CI)	P-Value
IR				
Dominant	75.8 ± 12.5	81.3 ± 19.5	1.03 (0.98 - 1.07)	0.23
Nondominant	88.2 ± 13.2	88.6 ± 13.8	1.00 (0.96 - 1.05)	0.92
ER				
Dominant	116.1 ± 7.9	117.5 ± 12.5	1.02 (0.95 - 1.08)	0.64
Nondominant	110.7 ± 8.2	113.4 ± 12.5	1.03 (0.97 - 1.10)	0.36
TROM				
Dominant	191.9 ± 15.7	198.7 ± 25.5	1.02 (0.99 - 1.05)	0.25
Nondominant	198.9 ± 15.0	202.0 ± 21.0	1.01 (0.98 - 1.05)	0.54
TROM loss	7.0 ± 12.4	3.2 ± 12.9	0.98 (0.93 - 1.03)	0.33
GIRD	12.4 ± 11.7	7.3 ± 9.8	0.96 (0.91 - 1.01)	0.14 [b]
ER gain	5.4 ± 8.2	4.0 ± 8.6	0.98 (0.91 - 1.05)	0.58
Trunk flexion	92.2 ± 14.4	94.6 ± 15.3	1.01 (0.97 - 1.05)	0.59
Trunk extension	36.2 ± 5.9	39.6 ± 11.3	1.06 (0.98 - 1.14)	0.17 [b]
Trunk rotation				
Dominant	73.5 ± 10.6	67.9 ± 10.3	0.95 (0.90 - 1.00)	0.09 [b]
Nondominant	72.1 ± 8.3	69.6 ± 7.0	0.96 (0.89 - 1.04)	0.31

Abbreviations: OR, odds ratio; CI, confidence interval; IR, internal rotation; ER, external rotation; TROM, total range of motion; GIRD, glenohumeral internal rotation deficit.

[a] Values are mean ± SD (standard deviation).

[b] P-value < 0.2.

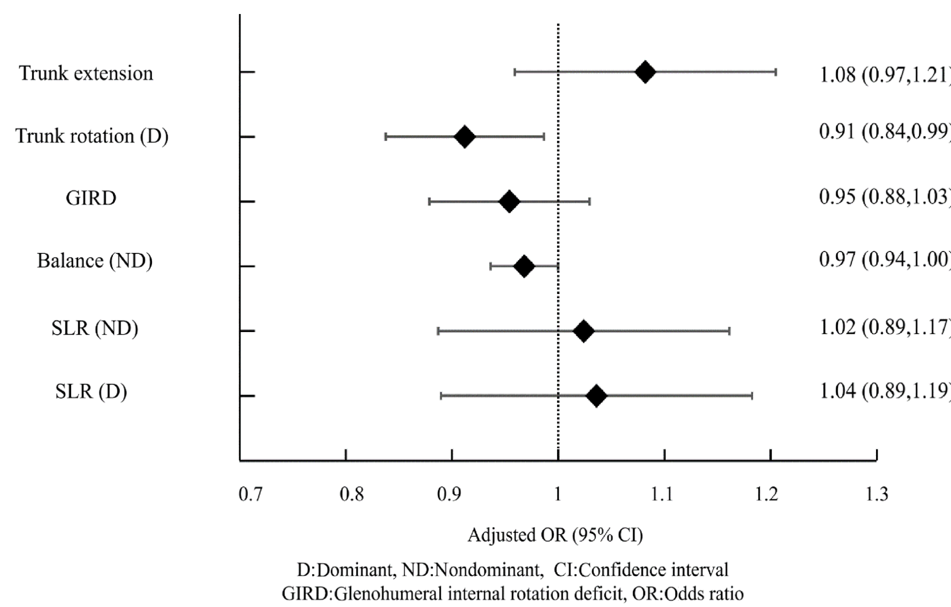

Figure 1. Multivariable logistic regression analysis of factors associated with the incidence of present shoulder pain.

der pain among university badminton players at national tournament level, but the findings showed no significant association of ER gain and GIRD with the increased risks of shoulder pain. A possible explanation is that the university badminton players with national tournament level in this study have experienced adequate prior badminton playing exposure so that the musculoskeletal system has adapted to the overhead motion.

As far as we know, our current study discovered that decreased trunk rotation and deficit in single-leg stance balance might be potential risk factors of shoulder pain in badminton for the first time. According to the findings of our studies, injury prevention strategies should focus on physical fitness, such as increasing trunk rotation and balance ability through neuromuscular training programs. So far, in current prevention programs, there were no studies of injury prevention measures on reducing pain and injuries related to badminton. Such neuromuscular prevention methods have been revealed to have an effect on improving physical fitness and lessening the occurrence of shoulder injury in other athletes. For example, plyometric training facilitated the balance ability of handball players (45). A core-muscle-training program, including bench and side bench, has been shown to enhance trunk ROM in basketball players (46). A prospective intervention study of baseball players showed that a prevention program comprising stretching, balance training, and dynamic mobility can decrease shoulder symptoms and enhance overhead motion performance (22). In addition, foam rolling can improve core function and balance in recreational sports participants (47). Further research is necessary to identify the risk factors for badminton shoulder injuries, such as improper techniques and deficits in physical fitness, that could inform prevention programs and expand the understanding of badminton injuries.

Several limitations in this study should be acknowledged. First, this study is a case-control study. Therefore, whether decreased trunk rotation and deficit in single leg stance balance were the cause or the result of shoulder pain was not identified. A prospective study should be performed to verify the cause and effect in the future. Second, as well as previous studies of physical fitness among elite badminton players (13, 48), this study had a small number of badminton players. Thus, the recruitment of more elite badminton players would be preferable for a stronger power to examine the strong association of shoulder pain with risk factors in future studies. Third, decreased ER strength has been demonstrated to be a risk factor for shoulder injury among handball players (20). Likewise, weakened posterior shoulder musculature, that is, weak muscle strength, increases the risk of throwing-related pain in baseball players (49). However, in our studies, we did not assess the shoulder rotation strength of badminton players. Finally, core stability and dynamic balance ability have been studied in a variety of overhead sports studies (50-54), and future studies are supposed to adopt such measures to confirm more risk factors for badminton injury.

5.1. Conclusions

Among Japanese university badminton players at national tournament level, decreased trunk rotation and deficit in single-leg stance balance might be potential risk factors which increase likelihood to sustain shoulder pain. These findings can help badminton players maintain and facilitate targeted physical fitness for badminton pain/injury participation.

Acknowledgments

We really appreciate BWF for conducting sports science research. We gratefully acknowledge Senshu University and Waseda University for collaborating with us on data collection.

Footnotes

Authors' Contribution: Study concept and design, Kazuhiro Imai; Acquisition of data, Eiji Watanabe; Analysis and interpretation of data, Xiao Zhou; Drafting of the manuscript, Xiao Zhou; Critical revision of the manuscript for important intellectual content, Kazuhiro Imai; Statistical analysis, Xiao Zhou; Administrative, technical, and material support, Xiao-Xuan Liu, Zhuo Chen; Study supervision, Eiji Watanabe.

Conflict of Interests: The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

Ethical Approval: This study was approved by the Ethical Committee of the Graduate School of Arts and Sciences, the University of Tokyo, Japan (Notification Number 602-2 July 26, 2018)

Funding/Support: This study was supported in part financially by the Badminton World Federation (BWF) (development.bwfbadminton.com/sport-science/bwf-research/research-grants-application#1529297797577-2c2fa038-3581).

Informed Consent: Participants had filled out an informed consent form.

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