












Association between foot morphology and dynamic knee valgus during single leg squats in recreational male football players: a cross-sectional study

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ABSTRACT

Purpose. This study examines the relationship between foot morphology, foot type, and dynamic knee valgus in male football players during single-leg squats using biomechanical analyses.

Methods. A cross-sectional study design was adopted. Male football players ($n = 151$) aged between 18 and 30 years belonging to three Malaysian football clubs were recruited. Of these participants, foot type, single-leg squat (SLS) performance, knee alignment using knee frontal plane projection angle (FPPA), and other measures of foot morphology were recorded, including foot length, foot width, truncated foot length, and navicular height. Chi-square tests were used to examine the association between foot type, SLS, and knee alignment. Bipoint serial correlations were used to determine the relationship between foot morphology, SLS, and knee alignment.

Results. A significant association was found between foot type and SLS ($p < 0.05$). During the SLSs, only navicular height ($r_{pb} = 0.154$, $n = 151$, $p < 0.05$) and dorsal height ($r_{pb} = 0.144$, $n = 151$, $p < 0.05$) showed a statistically significant connection in the dominant leg. In contrast, only navicular height in the non-dominant leg ($r_{pb} = 0.169$, $n = 151$, $p < 0.05$) showed a significant correlation with SLSs.

Conclusions. This study established a strong link between foot type and SLS in football players. Specifically, a statistically significant association between navicular and dorsal height in the dominant leg and navicular height in the non-dominant leg. This study emphasises the significance of foot morphology and the dynamic evaluation of knee valgus during functional movements.

Key words: foot anatomy, athletic injury, knee kinematics, unilateral squat, health risk, football

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Introduction

Football is an intermittent sport that requires high levels of agility, endurance, and speed, as well as continuous physical exertion, leading to transient periods of fatigue, especially after high-intensity activities [1, 2]. To be successful in the game, players must engage in high-intensity efforts that include sprinting, fast running, changing direction, and soccer-specific skills such as passing, tackling, and scoring goals [3]. Football players are known to use high levels of aerobic power to cover longer distances and to utilise the anaerobic system for high-intensity sprinting power during games [4]. The average heart rate during a 90-minute game is between 155 and 172 beats per minute [5]. Therefore, sports injuries often occur during soccer training, especially during powerful movements such as jumping, running, and abrupt changes in direction. A total of 88% of muscle injuries occur in a variety of situations, including hamstring injuries associated with running and acceleration [6], calf injuries often occur when accelerating from a standstill or at low speeds [7], and pivoting with sudden changes of direction/deceleration results in an anterior cruciate ligament (ACL) injury [8]. These injuries result in athletes not being able to reach their full potential or delaying their return to competitive sports [9]. According to a meta-analysis of the epidemiology of football player injuries, professional male soccer players experienced an overall incidence of 8.1 injuries per 1000 hours of exposure, with lower extremity injuries being the most common site of injury with an incidence rate of 6.8 injuries per 1000 hours of exposure [10]. To better understand how sports injuries occur, as well as to prevent and treat them, biomechanical analyses were rapidly performed to provide objective measurements [9].

Foot morphology is one of the most common assessments in sports evaluation [11, 12] and includes the anatomical features of the foot, including its dimensions, configuration, arch structure, and alignment, as well as any existing abnormalities [13]. The association between foot morphology and function during functional movement and positioning is well supported by previous studies [13, 14]. Yamauchi et al. [14] showed that differences in arch height between sitting and standing positions significantly influence the force-generating ability of the foot when standing upright [14]. Likewise, Xiao et al. [15] reported that the flexor strength of the first toe was positively correlated with truncated foot length in sitting ($p = 0.004$) and standing ($p = 0.009$), as well as standing foot width ($p = 0.031$). Similarly, the flexor strength of the other toes was asso-

ciated with truncated foot length in sitting ($p < 0.001$) and foot width in standing ($p = 0.020$), and these findings highlight the important role of foot morphology in dynamic movements and weight-bearing activities [15]. Likewise, foot shape and function have been attributed to a greater risk of injury [16]. Foot types, including normal, planus, and cavus feet, as well as different foot postures, such as normal, pronated, and supinated feet, are associated with running-related sports injuries such as football [17]. In high-intensity sports like running, the foot must not only be flexible to absorb ground reaction forces but also withstand deformation and provide a stable support base and lever arm for efficient body propulsion [18]. Additionally, flat feet or a high arch can result in modified loading of the foot during athletic activities, along with diminished static and dynamic postural stability performance, which could further lead to fracture and overuse injuries [19, 20].

The occurrence of dynamic knee valgus (DKV) results in displacement of the knee to the medial side beyond the alignment of the foot and thigh [21]. This movement pattern has been identified as a predominant risk factor for acute and chronic lower extremity injuries [22]. When the knee joint is in a valgus or varus position during dynamic movements, its stability is compromised, and it is more susceptible to damage. DKV is often associated with conditions such as non-contact ACL injuries and patellofemoral pain (PFP) [23]. Existing literature indicates that ACL injuries in football players often manifest in the initial phase of knee flexion along with the application of knee valgus loads. In addition, research suggests that within the first 0 to 60 minutes after physical activity, some factors, such as reduced body temperature and insufficient muscle readiness, may contribute to limited knee flexion. This restriction can subsequently lead to an increased occurrence of dynamic valgus and an increased susceptibility to injuries [24]. DKV refers to the synchronised motion involving hip adduction and internal rotation, knee abduction, tibial lateral rotation, and ankle joint eversion, along with foot pronation [25]. This pattern is considered a risk factor for injuries, including ACL trauma and the development of PFP [26]. Moreover, increased valgus angles in the frontal projection plane angle (FPPA) during a single-leg squat (SLS) have also been linked to a higher risk of serious ankle injuries in young athletes [27]. The present study utilised SLS as a functional assessment that simulates athletics motions to evaluate DKV and the risk of lower limb injuries, making it helpful in assessing performance and rehabilitation in football [28].

The increased incidence of injury observed in football players may be attributed to several variables, including foot shape and the occurrence of DKV [29, 30]. The use of biomechanical analysis, such as 3D motion capture or digital foot scanning, facilitates the examination of elements such as foot shape and DKV by enabling detailed visualisation of foot structure and lower limb alignment during movement. Examination of these elements allows for the identification of injury causes and the evaluation of players who are more susceptible to such ailments. This can accelerate the development and increase awareness of preventive measures and early detection techniques that reduce the likelihood of injuries [31].

Previous studies have highlighted the importance of foot morphology and lower limb alignment in influencing lower limb injuries and balancing ability related to athletic performance [32, 33]. The foot morphology, including the arch and metatarsal alignment, affects how forces are distributed across the foot and transmitted to the ankle and knee joints, and such distribution is crucial for maintaining balance and stability during squats [34]. In addition, misalignments such as forefoot varus, rearfoot varus, and tibiofibular varum are associated with excessive pronation, which can exacerbate dynamic valgus by altering the kinematic chain of the lower limb [35]. Individuals with malaligned foot structures were particularly prone to running-related foot injuries [32]. Further, an athlete's ability to maintain single-leg balance has been linked to ankle injuries [36]. More specifically, DKV during a SLS, which is characterised by inward collapse of the knee, is associated with various knee injuries in football players, including ACL injuries and PFP syndrome [37, 38].

Despite the existence of an association between foot morphology and DKV, there is a lack of research examining the correlation between foot morphology and balance ability as demonstrated through SLSs, both of which are important factors related to athletic performance, and none of the earlier studies were conducted on recreational male football players. Considering this research gap, the authors undertook this study to (1) examine the association between foot type (i.e., normal arch, high arch, and flat foot) and SLS performance as well as knee alignment in both dominant and non-dominant legs and (2) examine the relationship between foot morphology (i.e., foot length and width, truncated foot length, height of the navicular, dorsum height at 50% of the foot length) and SLS as well as knee alignment in both dominant and non-dominant legs.

Material and methods

Study design

A cross-sectional study design was adopted to determine the association between foot morphology and DKV during SLSs in male football players.

Participants

This study involved the recruitment of recreational players from three private university soccer clubs. The study involved male volunteers between the ages of 18 and 30 who participated in football activities at least once a week for at least a year. The study excluded participants who engaged in other sports, experienced surgery on the lower extremity or injury in the last six months, and had a history of neurological diseases. The sample size determination was based on a pre-existing population of 230 players registered in three clubs affiliated with a private institution in the Klang Valley region of Malaysia. The sample size was calculated to be 150 using Yamane's calculation [39], with a margin of error of 5%. A total of 160 participants took part in the study, of which 151 people met the qualification requirements. A total of nine people were excluded from the study because they had sustained an injury in the previous six months. All participants ($n = 151$) underwent foot type measurements, SLS assessments, knee alignment evaluations using the knee frontal plane projection angle (FPPA), and various foot morphology measurements, including foot length, foot width, truncated foot length, and navicular height. All outcome tests were assessed by a trained musculoskeletal physiotherapist with over 16 years of experience in musculoskeletal assessment and prior training in administering and scoring the SLS, knee alignment, and foot morphology to ensure accuracy and reliability.

Description of measurement procedures

Foot morphology

For the study, participants were instructed to stand barefoot, align their feet parallel, point their toes forward, and hold their trunks without flexion or rotation. Feet morphology characteristics such as the length of the foot, the width of the foot, truncated foot length (perpendicular distance from the first metatarsophalangeal joint to the most posterior aspect of the heel), the height of the navicular, and dorsum height at 50% of the foot length were measured using a digital calliper

(RS PRO capacity 150 mm, Malaysia) revealing that each foot supports 50% of the body weight [40]. Arch height index (AHI) was measured as the ratio of dorsum height at 50% of the foot length and truncated foot length [41]. A planus foot structure is identified when the AHI is 0.345 or less, a normal foot structure when it exceeds 0.345, and a cavus foot structure when it exceeds 0.370.

Single leg Squat Test (SLS)

SLSs were evaluated by having the subject stand on one leg with markers placed at the anterior superior iliac spine (ASIS), midway between the tibial condyles, and midway between the medial and lateral malleolus. Participants were instructed to flex their shoulders to 90 degrees and lower their bodies until they reached 30 degrees of knee flexion. If they did not achieve this, verbal cues were given to adjust the squat depth. Participants were then asked to return to a standing position while maintaining balance on the same leg. This process was repeated three times for both legs. Abnormal reactions such as flailing arms, Trendelenburg signs, or inward collapse of the supporting knee were noted. A positive SLS test was defined as > 2/3 abnormal reactions on either leg [42], and participants with a positive SLS exhibited poor lower limb mechanics and greater dynamic valgus.

Knee frontal plane projection angle (FPPA)

Using 2D video analysis, the knee FPPA was determined using Kinovea software. Participants were recorded while performing SLS using a camera located 2.0 metres in front of them and positioned approximately at the height of their pelvis. Two-dimensional video analysis was then applied to the videos. The knee FPPA was evaluated at the junction of a line formed by the ASIS and the knee marker and a line generated by the knee and the ankle marker. For analysis, neutral alignment was considered 0°, negative values represent valgus alignment, and positive values represent varus alignment [43].

Statistical analysis

Statistical analysis was performed using SPSS software (version 20; SPSS Inc., Chicago, IL, USA). For continuous variables, the mean and standard deviation were calculated, and percentages representing frequencies were used to summarise the categorical data. Chi-square tests were used in the current study to examine

the association between foot type (normal arch, high arch, and flat foot), SLS, and knee alignment. At the same time, bipoint serial correlations were employed to examine the relationship between foot morphology (foot length, foot width, truncated foot length, navicular height, and dorsum height at 50% of the foot length), SLS, and knee alignment. The p-value was set at < 0.05.

Results

Demographic characteristics

In the current study, 151 male recreational football players with an average age of 23.00 ± 2.34 were evaluated. Most participants fell into the normal BMI category with a mean of 22.68 ± 2.77 . Most participants (78.1%) attended training sessions once or twice a week, averaging 1–2 hours per session (82.1%).

Table 1 shows the characteristics of foot type, foot morphology, SLS performance, and knee alignment as measured using the knee FPPA. A notable number of participants (38.4%) had a normal foot type in the dominant leg, while 35.8% and 31.8% of them had flat feet in the dominant and non-dominant legs, respectively. A high percentage of participants demonstrated poor performance during SLSs in both the dominant (54.3%)

Table 1. Characteristics of foot type, SLS performance, knee alignment, and foot morphology between dominant and non-dominant legs

Characteristics	Dominant leg	Non-dominant leg
Foot type [n (%)]		
flat foot	54 (35.8)	48 (31.8)
normal arch	58 (38.4)	62 (41.1)
high arch	39 (25.8)	41 (27.2)
Performance of SLS [n (%)]		
normal	69 (45.7)	67 (44.4)
abnormal	82 (54.3)	84 (55.6)
Knee FPPA [n (%)]		
valgus	80 (53.0)	83 (55.0)
varus	71 (47.0)	68 (45.0)
Foot morphology (mean \pm SD)		
foot length	252.67 \pm 15.08	251.37 \pm 14.84
foot width	96.70 \pm 5.88	96.50 \pm 5.88
truncated foot length	181.19 \pm 14.43	180.57 \pm 15.59
navicular height	53.67 \pm 7.85	53.32 \pm 7.77
dorsum height at 50% of the foot length	63.55 \pm 6.77	63.44 \pm 6.85

SLS – single-leg squat

FPPA – knee frontal plane projection angle

and non-dominant (55.6%) legs. Likewise, 53% and 55% of participants had valgus knees (53.0%) in both the dominant and non-dominant legs during FPPA, respectively. In addition, the parameters of foot morphology were reported in mean and standard deviation.

Tables 2 and 3 show the association between foot type (normal arch, high arch, and flat feet) and SLS performance and knee FPPA, respectively. When analysing foot type and performance during a SLS, significant associations were found between dominant and non-dominant legs ($p < 0.05$). It was found that players with flat feet performed poorly during SLS, both in the dominant (25.2%) and non-dominant areas (20.5%).

Whereas in the analysis between foot type and knee alignment, there was no significant association in the dominant ($p = 0.430$) and non-dominant legs ($p = 0.317$). A notable number of participants were found to have normal arches with varus knee alignment in the dominant (19.9%) and non-dominant legs (21.3%). Comparably, it was reported that a comparable proportion of participants had valgus knee alignment in their non-dominant legs (19.9%) and dominant legs (18.5%), respectively.

Table 2. Association between foot type and single-leg squat performance in the dominant and non-dominant legs

Foot type	Dominant leg		Non-dominant leg	
	positive SLS <i>n</i> (%)	<i>p</i> -value	positive SLS <i>n</i> (%)	<i>p</i> -value
Flat foot	38 (25.2)		31 (20.5)	
Normal arch	20 (13.2)	< 0.05*	28 (18.5)	< 0.05*
High arch	24 (15.9)		25 (16.6)	

Positive SLS – poor single-leg squat score

* significant at $p < 0.05$

Table 4. Relationship between foot morphology and single-leg squat and knee alignment in the dominant and non-dominant legs

Foot morphology	Dominant leg				Non-dominant leg			
	SLS		knee FPPA		SLS		knee FPPA	
	r_{pb}	<i>p</i> -value	r_{pb}	<i>p</i> -value	r_{pb}	<i>p</i> -value	r_{pb}	<i>p</i> -value
Foot length	0.036	0.660	0.107	0.191	0.101	0.218	0.038	0.640
Foot width	0.007	0.930	0.029	0.728	0.113	0.168	0.012	0.883
Truncated foot length	0.014	0.866	0.044	0.589	0.095	0.246	0.034	0.680
Navicular height	0.154	0.027*	0.100	0.220	0.169	0.038*	0.041	0.617
Dorsum height at 50% of the foot length	0.144	0.035*	0.085	0.299	0.131	0.110	0.043	0.597

SLS – single leg squat, FPPA – knee frontal plane projection angle, * $p < 0.05$

Table 4 shows the relationship between foot morphology with SLS and knee alignment as measured through knee FPPA among football players. In the dominant leg, only the navicular height ($r_{pb} = 0.154$, $n = 151$, $p < 0.05$) and dorsal height ($r_{pb} = 0.144$, $n = 151$, $p < 0.05$) showed a significant relationship during SLS. Whereas, in the non-dominant leg, only navicular height ($r_{pb} = 0.169$, $n = 151$, $p < 0.05$) showed a significant relationship with SLSs. It is also observed that no significant relationship was found between all foot morphology measurements and knee alignment using FPPA in the recreational football players' dominant and non-dominant legs.

Discussion

The current study examined the association between foot type (normal arch, high arch, and flat feet) with positive SLS test performance and knee alignment using FPPA, as well as the association between foot morphology with positive SLS test performance and knee alignment using FPPA in 151 recreational football players. Regarding dominant and non-dominant legs, about half of the participants showed poor

Table 3. Association between foot type and knee alignment in the dominant and non-dominant legs

Foot type	Dominant knee FPPA			Non-dominant knee FPPA		
	valgus <i>n</i> (%)	varus <i>n</i> (%)	<i>p</i> -value	valgus <i>n</i> (%)	varus <i>n</i> (%)	<i>p</i> -value
Flat foot	28 (18.5)	26 (17.2)		27 (17.9)	21(13.9)	
Normal arch	28 (18.5)	30 (19.9)	0.430	30 (19.9)	32 (21.3)	0.317
High arch	24 (15.9)	15 (9.9)		26 (17.2)	15 (9.9)	
Total	80 (53.0)	71 (47)		83 (55.0)	68 (45.0)	

FPPA – knee frontal plane projection angle

SLS test performance and had valgus knees during FPPA. Also, a significant association was found between foot type and positive SLS test performance. There was no significant association between foot type and knee alignment (valgus or varus). Likewise, there was no significant relationship between all foot morphology measurements and knee alignment during FPPA. Moreover, foot morphology measurements such as foot length, foot width, and truncated foot length, except navicular height, failed to show a significant relationship with SLS. Notably, the dorsum height at 50% of the foot length is significantly related to SLS only in dominant legs.

Besides, the results showed a significant association between foot type and positive SLS test performance in dominant and non-dominant legs. Especially, recreational football players with flatfoot demonstrated poor SLS test performance irrespective of the dominance of the leg. This observation might be due to the abnormal foot posture, which affects the lower limb biomechanics during weight-bearing activities and has been associated with hip, knee, and lower back pain [44]. Foot posture might be a factor in the performance of SLSs, indicating an association between proximal musculoskeletal dysfunction, weight-bearing biomechanics, and foot posture [44]. A study by Ugalde et al. [42] on female soccer players also found that those with a supple planus foot type had decreased hip muscle activation and increased vertical ground reaction forces, which could impact dynamic stability and neuromuscular control during SLS. Foot type may influence the mechanics of SLS, potentially leading to greater DKV, a known risk factor for lower extremity injury [42]. Conversely, a recent study observed that foot posture was unrelated to healthy people who passed and failed the SLS test for medial knee deviation [44]. Tourillon et al. [45] stated that individuals with flatfoot generally exhibit increased flexibility in the midfoot, which helps them absorb ground reaction forces more effectively. However, this increased flexibility comes at the cost of reduced stability and rigidity in the foot, leading to decreased power generation and less efficient force transfer. In contrast, individuals with highly arched feet have a rigid foot structure, resulting in increased generation of peak forces and reduced absorption of ground reaction forces. This condition, in turn, can contribute to accelerated shortening of the calf muscles [45]. Variations in foot structure, such as flat or high arches of the feet, can alter force distribution and affect balance and stability during squatting [46]. Here, stability during SLSs indicates an athlete's ability to maintain control during dynamic

movements, which is essential for their performance [47]. Moreover, the altered mechanical axis of the foot in individuals with flat feet significantly influences the activation of the abductor hallucis muscle, which supports the medial arch during SLSs [48]. Thus, rehabilitation programs should incorporate exercises that promote correct foot alignment and abductor hallucis muscle activation to improve functional performance during activities like SLSs [49].

Concerning lower limb kinematics, foot posture is a key factor in DKV incidence [50]. A recent study found that subjects with pronated feet demonstrated a significantly higher degree of DKV than those with non-pronated feet during stair descent using 2D video analysis [51]. Conversely, the current study revealed no significant association between foot type and knee alignment (valgus or varus) using 2D video analysis of FPPA in both dominant and non-dominant legs among recreational football players. In line with the current finding, a previous study on male adolescent athletes found no statistically significant differences in hip and knee kinematics in all directions when considering different foot positions [52]. On the other hand, Kim et al. [51] stated that flat feet associated with medial tilting of the tibia can increase DKV while performing single-limb activities, namely squatting, landing, and stair descent [51]. A recent study observed that the FPPA was significantly higher in persons with a pronated foot and medial arch support than their counterparts [50]. The clinical significance of knee alignment is closely connected to foot type. Individuals with high arches may be more prone to varus knee alignment, while those with low arches may tend towards valgus knee alignment [53]. This highlights the importance of taking foot biomechanics into account when assessing and managing knee-related issues. Moreover, altered active and passive stabilising components of the hip, along with malalignment of the foot, can impact dynamic knee position while performing weight-bearing tasks [54].

In this study, foot morphology measurements such as length of the foot, width of the foot, and truncated foot length showed no significant relationship with SLSs in the dominant and non-dominant legs of recreational football players. Nonetheless, a prior study stated that the structural elements of the foot, including length, width, and circumference, correlate positively with the power of the muscles responsible for ankle movement. Foot morphology may influence ankle joint strength and performance, which is critical for maintaining balance and control during a SLS [55]. Besides, this study observed that dorsum height at 50% of the foot

length demonstrated a significant relationship with SLS in dominant legs. Also, navicular height presented a significant relationship only with SLS in both dominant and non-dominant legs. In line with this finding, Murley et al. [56] stated that arch height significantly influences the morphometry of the lower limb muscles and tendons [56]. Notably, it is described that people with flatfoot seemed to have thick tibialis anterior and peroneus longus muscles. Such muscle and tendon thickness variations can impact the frontal and sagittal plane motion control during SLS [56]. Hence, it is mandatory to understand the relationship between foot morphology and neuromuscular control while framing active rehabilitation workouts for people with ACL injuries [57].

Moreover, this study found no significant relationship between all foot morphology measurements and knee alignment using FPPA in recreational football players' dominant and non-dominant legs. Similar to this finding, Ohi et al. [58] noticed that foot parameters like rearfoot angle, navicular height, and navicular height/foot length had no significant relationship with the corrected anatomical axis angle (AAA) measuring frontal plane knee alignment in medial knee osteoarthritis cases. Meanwhile, the corrected AAA was related to the calcaneal angle concerning the floor and hallux valgus. These outcomes indicated the presence of an association between altered foot posture and frontal plane knee alignment [58]. Furthermore, a previous study stated that long-term exposure to play and sustained heavy loading can worsen foot morphology and lead to an increase in knee misalignment, which, in turn, increases the risk of injury and can force players to stop playing [12]. In summary, it is recommended that coaches and sports medicine professionals thoroughly examine and evaluate the foot type, foot morphology, and knee alignment of football players. This comprehensive assessment not only improves the understanding of the dynamics of the musculoskeletal system but also serves as a crucial preventive measure and significantly reduces the risk of injuries.

To effectively evaluate the outcomes, it is necessary to examine possible limitations in the research design, such as a limited sample size or the absence of influencing factors. This study did not apply corrections for multiple comparisons, such as the Bonferroni correction, which may increase the risk of false positives. Also, this study is constrained to male football players from three clubs affiliated with a private institution in a specific region of Malaysia. Further research should be conducted with a larger sample size evaluating either the female gender or both genders of football players

across Malaysia to better generalise the results. Moreover, future studies should use three-dimensional motion analysis to understand foot morphology and lower extremity biomechanics better. In the future, researchers can reveal the association between foot morphology and DKV during SLS in various populations, such as athletes and patients with osteoarthritis. Besides, neuromuscular parameters associated with DKV can be explored using electromyography analysis of the lower extremities among football players.

Conclusions

This study concludes that there is a strong correlation between foot shape and the ability to perform SLSs in recreational male football players. In particular, significant correlations were found between navicular and dorsal height in the dominant leg and navicular height in the non-dominant limb. Furthermore, the existence of a relationship between foot shape and the ability to perform SLSs has significant implications for training and rehabilitation in male recreational soccer players. By improving foot mechanics and dynamic stability through targeted exercises and functional assessments, soccer players can improve their SLS performance, reduce the risk of injury, and improve overall lower limb function. The results of the study also highlighted the importance of considering foot morphology to prevent lower limb injuries. The therapist should consider strategies such as modifying footwear and implementing related exercises to enhance efficiency during the sport and avoid injuries.

Ethical approval

The research related to human use has complied with all the relevant national regulations and institutional policies, has followed the tenets of the Declaration of Helsinki, and has been approved by the Faculty of Research and Ethics Committee, INTI International University, Malaysia (approval No.: INTI-IU/FHLS-RC/BPHTI/1NY12023/018).

Informed consent

Informed consent was obtained from all individuals included in this study.

Conflicts of interest

The authors state no conflicts of interest.

Disclosure statement

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