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Chronic diseases and allergies are risk factors predictive of a history of Medial Tibial Stress Syndrome (MTSS) in distance runners: SAFER study XXIV

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ABSTRACT

Background: Medial Tibial Stress Syndrome (MTSS) is one of the most common causes of exercise-associated lower leg pain in distance runners.

Aim: To identify risk factors predictive of a history of MTSS in distance runners entering the Two Oceans Marathon races (21.1 km and 56 km).

Design: Cross-sectional study.

Setting: 2012 to 2015 Two Oceans Marathon races (21.1 km and 56 km).

Participants: Consenting race entrants.

Methods: 106,743 race entrants completed an online pre-race medical screening questionnaire. 76,654 consenting runners (71.8%) were studied. 558 verified MTSS injuries were reported in the previous 12 months. Risk factors predictive of a history of MTSS were explored using uni – & multivariate analyses: demographics (race distance, sex, and age groups), training/racing history, history of chronic diseases, allergies, and medication use.

Results: Independent risk factors predictive of a history of MTSS (adjusted for sex, age group, and race distance) were a higher chronic disease composite score (PR = 3.1 times increase risk for every two additional chronic diseases; $p < 0.0001$) and a history of allergies (PR = 1.9; $p < 0.0001$). Chronic diseases (PR > 2) predictive of a history of MTSS were: symptoms of CVD (PR = 4.2; $p < 0.0001$); GIT disease (PR = 3.3; $p < 0.0001$); kidney/bladder disease (PR = 3.3; $p < 0.0001$); nervous system/psychiatric disease (PR = 3.2; $p < 0.0001$); respiratory disease (PR = 2.9; $p < 0.0001$) a history of CVD (PR = 2.9; $p < 0.0001$); and risk factors of CVD (PR = 2.4; $p < 0.0001$) (univariate analysis). Average running speed was associated with higher risk of MTSS.

Conclusion: Novel independent risk factors predictive of a history of MTSS in distance runners (56 km, 21.1 km) were multiple chronic diseases and a history of allergies. Identifying athletes at higher risk for MTSS can guide healthcare professionals in their prevention and rehabilitation efforts.

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Running; Medial Tibial Stress Syndrome (MTSS); shin pain; shin "splints"; epidemiology; risk; ultramarathon

Introduction

Regular moderate – to high-intensity physical activity for >150 min/week can reduce the burden of non-communicable diseases (NCDs) and is associated with a decrease of up to 40% in all-cause mortality compared with nonparticipation [1–4]. Participation in mass community-based endurance events such as distance running has increased in popularity [5–7]. This trend is reported for recreational and competitive runners and more runners opt to participate in longer distance races [5,8].

Increased training and years of running is associated with higher risk of running-related injuries [7,9,10]. The nature of endurance running makes these athletes particularly susceptible to musculoskeletal injuries and more specifically lower leg injuries [11,12]. A common lower leg running related injury is exercise-induced pain along the distal posteromedial border of the tibia with pain on palpation over a length >5 centimeters [13]. This syndrome has historically been referred to as "shin splints," "medial tibial syndrome," "tibial stress syndrome," and "soleus enthesopathy" or "soleus syndrome" [14–16]. All these syndromes are now collectively referred to medial tibial stress syndrome (MTSS), and this is the nomenclature adopted in this study [15,16]. MTSS is a clinical syndrome that causes localized pain across the distal two-thirds of the postero – medial tibia at the muscle-tendon junction [15,16] and the pathology is therefore not only bony but also involves the muscle-tendon-bone interface [16]. MTSS is reported to be the cause of 15–35% of lower extremity injuries affecting recreational and competitive runners [14,16–21].

Risk factors associated with MTSS in runners have been reported in several reviews and meta-analyses [14–16,17,22]. The etiology of MTSS is multifactorial and several intrinsic risk factors associated with MTSS have been identified []. These are an increased BMI and several lower limb biomechanical factors

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Supplemental data for this article can be accessed here.

such as increased navicular drop, foot pronation, greater hip external rotation range of motion (ROM), higher pelvic tilt in the frontal plane, peak internal rotation of the hip, and greater ankle plantar-flexion ROM [15,21]. Although there is some consensus that these intrinsic biomechanical risk factors are associated with MTSS, there are inconsistent findings that other intrinsic factors such as sex, age, years of running, training-related factors, and lifestyle factors are associated with MTSS [13–17,21]. As far as we are aware, there are no data on other potential risk factors for MTSS such as race distance (half marathon, marathon, ultramarathon), weekly training distance, underlying chronic medical conditions, or use of prescription medication use.

We recently showed that a history of chronic disease and allergies is associated with increased risk of any gradual onset injuries in cyclists [22], trail runners [23], and distance runners [24]. For distance runners we reported that all chronic diseases risk factors assessed in this study (any risk factor for cardiovascular diseases, any history of cardiovascular disease, any symptoms of cardiovascular disease, any endocrine disease, any respiratory disease, any GIT disease, any nervous system disease, any kidney/bladder disease, any hematological disease, any cancer) were associated with gradual onset injuries [24]. However, the relationship between a history of chronic disease and allergies and specific running-related injuries such as MTSS has not been documented. A clear understanding of the relationship of these risk factors in specific running-related injuries, such as MTSS, is important to plan intervention strategies and for clinical decisions on time to recovery during rehabilitation. Prevention remains the most critical aspect in the management of this common injury [25].

The purpose of this study is to identify demographic, training-related and chronic disease related risk factors predicting a history of MTSS in distance runners entering the Two Oceans Marathon races (21.1 km and 56 km).

Methods

Study design and ethical concerns

This descriptive cross-sectional study forms part of a series of ongoing SAFER (Strategies to reduce Adverse medical events For the ExerciseR) studies. Ethics approval was obtained from Research Ethics Committees prior to the onset of the study (Research Ethics Committees of the Faculty of Health Sciences (REC009/2011) and (433/2015)).

Participants and demographics

All race entrants of the 21.1 km & 56 km Two Oceans Marathon for each year from 2012–2015 completed an online medical screening questionnaire as a prerequisite for registration. Of the 106,743 race entrants, 76,654 (71.8%) gave consent that their data may be used for research purposes.

Online pre-race medical questionnaire

The online pre-race medical screening questionnaire for the Two Oceans Marathons consisted of a series of self-reported questions specifically developed to provide clinical information for medical staff on race day. The questionnaire is based on guidelines by the European Association for Cardiovascular Prevention and Rehabilitation (EACPR) for cardiovascular evaluation on distance runners [26,27]. We previously described the development of the questionnaire in detail [27] and provided details of the questionnaire [28].

Gradual onset injuries are classified as injuries "that lack a definable sudden, precipitating event as the onset of injury (e.g. a tendinopathy induced by repetitive movement)" [29]. In this study, we asked race entrants to answer the following specific question related to running injuries: "Do you or did you suffer from any symptoms of a running injury (muscles, tendons, bones, ligaments, or joints) in the past 12 months or currently?" [29] Runners were asked to only report injuries that were "severe enough to interfere with or require treatment e.g. use medication, or require you to seek medical advice from a health professional)?"

All entrants were also requested to complete specific questions related to their demographics, (sex, race distance, age), training history (years of recreational running, average weekly training/running distance in the last 12 months, and average training speed), history of chronic disease (risk factors for cardiovascular disease (CVD), history of CVD, symptoms of CVD, endocrine disease, respiratory disease, gastrointestinal disease (GIT), nervous system/psychiatric disease, kidney/bladder disease, hematological/immune disease, and cancer), history of any allergies, and history of prescription medication use [24].

Defining the study groups

Defining the control group

If a runner responded "no" to the question related to a running injury in the past 12 months, they were in our non-injured (Control) group. Runners reporting other specific injuries and non-verified MTSS injuries were excluded from the analyses, resulting in a sample of 61,193. Of the 61,193 entrants, 60,635 responded "no" to the question related to a running injury in the past 12 months, and this was our control group.

Defining the MTSS group

If a runner responded "yes" to the question related to a running injury in the past 12 months, they were directed to a further dropdown list of common running-related injuries and asked to select the specific injury/ies from the following list: "*patellofemoral pain, iliotibial band (ITB), plantar fasciitis, Achilles tendon injury, lower back pain, hip muscle injury (including gluteus/buttock muscles), hamstring injury, quadriceps muscle injury, calf muscle injury, shin splints (bone), shin splints (muscle/tendon), lower leg compartment syndrome, foot pain, heel pain, or other*" injury. A total of 650 entrants selected "*shin splints (muscle/tendon)*," and these entrants were considered for possible inclusion in the history of MTSS group.

To reduce the risk of over-reporting and to improve the self-reported diagnosis of the injury, we also used data obtained from a question on treatment to control the over-reporting of MTSS injuries. Runners were asked to select treatment modalities for the injury from a list. Most of the treatment modalities were treatment modalities that could only be administered by a health professional for example surgery, cortisone injection, other injection, physiotherapy and orthotics. If a runner selected one or more treatment modalities that could only be administered by a health professional, we considered the self-reported diagnosis of the specific injury to be "treated" by a health professional. Of the 650 entrants that selected "*shin splints (muscle/tendon)*," 558 (81%) entrants were in the category where the diagnosis of MTSS was "treated" by a health care professional. These entrants were selected as the MTSS group.

Main outcome variables

The primary outcome for this study was a history of MTSS in the past 12 months among race entrants. The following main categories of variables of interest as factors predicting MTSS were explored in a multivariate model: (1) *runner demographics* (sex, race distance, age), (2) *running training/racing history* (years of recreational running, average weekly training/running distance in the last 12 months, and average training speed, (3) *history of chronic disease*, and (4) *history of any allergies*.

A chronic disease composite score was calculated by combining 10 chronic disease variables (CVD risk factors, CVD symptoms, CVD history, metabolic/endocrine, respiratory, GIT, nervous system/psychiatric, kidney/bladder, hematological/immune, and cancer) to present a single score based on multiple chronic diseases [24].

Statistical data analysis

All questionnaire data were entered into an Excel spreadsheet (Microsoft 2010) and analyzed using the SAS v9.4 statistical program. Only data for consented runners race entries was used for analysis.

Prevalence ratios (PR) were calculated as the measure of association. Univariate unadjusted prevalence's (% and 95% CIs) and PR were reported for age and gender, running training/racing history, history of chronic disease, and history of medication use. The total sample (n = 76,654) was used to estimate the overall prevalence and for the assessment of risk factors in the regression models. Runners reporting other specific injuries and MTSS injuries that were not treated using modalities that a health care provider administered were excluded from the analyses, resulting in a sample of 61,193. A multiple regression model was performed to determine independent risk factors associated with a history of MTSS. The demographic, chronic disease, history of medication variables were entered into the model as categorical variables. The chronic disease composite score was entered into the multiple regression model rather than the individual's chronic diseases to provide a more parsimonious and robust model without the confounding effect of multi-collinearity. The training and race pace variables were entered into the model as continuous variables and the prevalence of a history of MTSS (% and 95% CIs) were reported at the first quartile, median and third quartile for these variables. Initially, the multiple regression model included all the significant univariate risk factors. The results for the final model only included the retained significant risk factors. The statistical significance level was 5%, unless otherwise specified.

Results

All race entrants and study participants

Of the 106,743 race entrants, 76,654 (71.8%) gave consent that their data may be used for research purposes. Of these, there were 61,193 participating race entrants. This group of entrants included the entrants with a history of MTSS (n = 558) and the non-injured entrants that were the control group (n = 60,635). The profile (race distance, sex, and age groups) of all race entrants in both the 21.1 km & 56 km Two Oceans Marathon were compared with all consenting race entrants and the study participants in this study (Table 1).

The 21.1 km race distance entrants were significantly over-represented compared to all the race entrants (p = 0.0011). There were no significant differences when comparing sex or age groups between all race entrants and consenting race entrants.

Risk factors predicting a history of MTSS (Univariate analysis)

Demographics

490 race individual runners reported a total of 558 verified MTSS injuries. The period prevalence of a history of MTSS among race entrants in the past 12 months was 0.67% (95% CI: 0.61–0.74).

The number (n), prevalence (%; with 95% CI) and prevalence ratio (PR; with 95% CI) of race entrants with a history of MTSS by race distance, sex and age group are depicted in Table 2.

There was a significantly higher prevalence of a history of MTSS in the 56 km compared to the 21.1 km entrants (PR = 1.6; p < 0.0001). There was no significant difference in prevalence of a history of MTSS between males and females (PR = 1.2; p = 0.1215). There was a higher prevalence of a history of MTSS in the 31–40 year old age group compared to the >50-year age group (PR = 1.4; p = 0.0305).

Table 1. The profile of all race entrants and consenting participants by race distance, sex, and age groups.

		All race entrants (n = 106,743)		Consenting race entrants (n = 76,654)		p-value*
		n	%	n	%	p
Race distance	21.1 km	64,740	60.7	47,069	61.4	p = 0.0011
	56 km	42,003	39.4	29,585	38.6	
Sex	Males	61,815	57.9	44,042	57.5	p = 0.0520
	Females	44,928	42.1	32,612	42.5	
Age groups	≤30 years	27,710	26.0	20,168	26.3	p = 0.3643
	31–40 years	35,049	32.8	25,045	32.7	
	41–50 years	26,964	25.3	19,340	25.2	
	˃50 years	17,020	15.9	12,101	15.8	

p: p value
*: All race entrants vs consenting race entrants;

Table 2. The number (n), prevalence (%; 95% CI) and prevalence ratio (PR; 95% CI) of participating race entrants (n = 61,193) and entrants with MTSS (MTSS group = 558) by race distance, sex, and age group.

Characteristics		Participating race entrants (n = 61,193)	MTSS group (n = 558)			
		n	n	Prevalence % (95% CI)	PR (95% CI)	p-value
Race distance						
	21.1 km	39,142	261	0.77 (0.68–0.87)	1.6 (1.3–1.9)	p < 0.0001
	56 km	22,051	297	1.21 (1.06–1.39)		
Runner demographics						
Sex	Males	34,799	293	0.87 (0.76–0.98)	1.2 (1.0. – 1.4)[$]	p = 0.1215
	Females	26,394	265	1.00 (0.88–1.14)		
Age groups	≤30 years	16,978	168	0.97 (0.82–1.15)	1.3 (1.0–1.8)[a]	p = 0.0664
	31–40 years	20,086	198	1.01 (0.87–1.18)	1.4 (1.0–1.9)[b]	p = 0.0305
	41–50 years	15,064	129	0.87 (0.72–1.05)	1.2 (0.9–1.7)[c]	p = 0.2581
	˃50 years	9 065	63	0.73 (0.56–0.94)	1.0	

n: number
%: % out of total
PR: Prevalence Ratio
p: p-value
95% CI: 95% Confidence Intervals
$: Female to Male
a: ≤30 vs. >50
b: 31 to 40 vs. >50
c: 41–50 vs. >50

Running, training /racing history

The prevalence (%; with 95% CI) and crude unadjusted prevalence ratio (PR; with 95% CI) of MTSS group, by running, training/racing history is depicted in Table 3.

The prevalence a history of MTSS was not related to years of recreational running (p = 0.0875) or average weekly running distance (p = 0.3133). However, for average running speed, the prevalence of a history of MTSS was observed to be significantly lower for every 1 km/hr increase in running speed (p = 0.0381).

The interaction of race type and the training variables were explored further in the model. There was a significant interaction between race type (21.1 km and 56 km) and average weekly running distance (p < 0.01). In the 56 km race entrants the prevalence of MTSS was significantly lower with increased average weekly distance (PR = 0.85;0.78–0.91 for a 15 km increase; p < 0.001). In the 21 km race entrants, the prevalence of a history of MTSS was significantly higher with increasing weekly training distance (PR = 1.09; 95%CI:1.00–1.18 for a 15 km increase; p = 0.0413).

History of underlying chronic disease and allergies

The number (n), prevalence (%; 95% CI), and prevalence ratio (PR; 95% CI) of race entrants with a history of MTSS by main categories of chronic disease and allergies are reported in Table 4. The association between the number of chronic diseases and a history of MTSS is reported in a supplementary table (Appendix Table A1).

In the MTSS group, the following chronic diseases were more prevalent (PR > 2): any symptoms of CVD (PR = 4.2; 95%CI:2.6–6.7; p < 0.0001); any GIT disease (PR = 3.3; 95% CI:2.3–4.9; p < 0.0001); any kidney/bladder disease (PR = 3.3; 95%CI:2.1–5.2; p < 0.0001); any nervous system/psychiatric disease (PR = 3.2; 95%CI:2.1–4.9; p < 0.0001); any respiratory disease (PR = 2.9; 95%CI:2.3–3.7; p < 0.0001) a history of any

Table 3. The prevalence (%; with 95% CI) and unadjusted prevalence ratio (PR; with 95%CI) of MTSS group by running, training/racing history.

Running, training /racing history	Points in the continuous variable#	MTSS group prevalence (%) (95% CI)	PR (95% CI)	p value
Number of years as a recreational runner (years)	3 years	0.98 (0.88–1.10)	0.95 (0.89–1.01)*	p = 0.0875
	6 years	0.95 (0.87–1.05)		
	13 years	0.89 (0.79–0.99)		
Average weekly running distance in the last 12 months (km/week)	20 km	0.91 (0.82–1.01)	1.01 (0.99–1.02)**	p = 0.3113
	35 km	0.93 (0.85–1.02)		
	50 km	0.95 (0.86–1.05)		
Average running speed (km/hour)	9 km/h	0.97 (0.88–1.07)	0.97 (0.94–1.00)***	p = 0.0381
	10 km/h	0.94 (0.86–1.03)		
	11 km/h	0.91 (0.83–1.00)		

#points on the continuous variables are the 1st quartile, median and 3rd quartile for each training variable
PR: Prevalence Ratio
p: p-value
*average increase in risk for every 5 years
**average increase in risk for every 5 km distance training per week
***average decrease in risk for every 1 km/hr increase in average running speed

CVD (PR = 2.9; 95%CI:1.9–4.4; $p < 0.0001$); and any risk factors of CVD (PR = 2.4; 95%CI:2.0–3.0; $p < 0.0001$). A history of any allergies (PR = 2.6; 95%CI: 2.0–3.2; $p < 0.0001$) was also associated with a higher prevalence of a history of MTSS.

The relationship between prevalence of a history of MTSS and the number of chronic diseases (chronic disease composite score) is shown in Figure 1. For every two additional chronic diseases, the prevalence of a history of MTSS increased 3.1 times ($p < 0.0001$).

Independent risk factors associated with a history of MTSS (Multiple regression analysis)

The multiple regression analyses included all the significant risk factors identified by the univariate analysis ($p < 0.01$). The model was adjusted for three possible confounding variables (sex, age group, and race distance [21.1 km or 56 km]). Significant independent risk factors associated with a history of MTSS are depicted in Table 5.

Independent risk factors associated with a higher prevalence of a history of MTSS in race entrants were a higher chronic disease composite score (PR = 3.1 for every two additional chronic diseases; $p < 0.0001$) and a history of allergies (PR = 1.9; $p < 0.0001$).

Discussion

Our most important novel findings are that multiple chronic diseases, and a history of allergies were significant independent risk factors predictive of a history of MTSS in distance runners. Other findings were that the risk of a history of MTSS was higher in 56 km race entrants and 31–40 year old race entrants and that average running speed is associated with an increased risk of MTSS. Years of running and weekly running distance were not associated with an increased risk of a history of MTSS.

We previously reported that a history of any gradual onset injury was associated with chronic diseases and history of allergies in three large cross sectional studies in endurance athletes: 21,824 recreational road cyclists [30], 2 824 trail runners [23] and 29,585 distance runners [24]. In this study, we show that a specific running injury, MTSS, is associated with a history of chronic diseases and allergies. For every two additional chronic diseases the risk of a history of MTSS increased by 3.1 ($p < 0.0001$) and with a history of allergies the risk increased by 1.9 ($p < 0.0001$). From our univariate analysis we show that particular chronic diseases are predictive of a history of MTSS: (1) any symptoms of CVD (PR = 4.2; $p < 0.0001$); (2) any GIT disease (PR = 3.3; $p < 0.0001$); (3) any kidney/bladder disease (PR = 3.3; $p < 0.0001$); (4) any nervous system/psychiatric disease (PR = 3.2; $p < 0.0001$); (5) any respiratory disease (PR = 2.9; $p < 0.0001$); (6) a history of any CVD (PR = 2.9; $p < 0.0001$); and (7) any risk factors of CVD (PR = 2.4; $p < 0.0001$).

In this descriptive cross sectional study, we cannot infer a cause-effect relationship between MTSS and chronic diseases or allergies but biological plausibility of this association is important to consider. The pathophysiology of MTSS is poorly understood, but the symptoms of MTSS are located at the interface of the crural fascia and bone [31], and there is evidence that MTSS is associated with specific changes at the muscle-tendon-bony interface (periosteal-fascial junction) [31–33]. Therefore, overload due to repetitive injury and inadequate healing responses in both bony and soft tissue structures can be implicated in MTSS. Data from several studies show that a variety of chronic diseases, which affect various organ systems, are associated with an increased risk for gradual onset soft tissue injuries such as tendinopathy (diabetes mellitus, hypercholesterolemia, and obesity) [34–37] and bone stress injuries (chronic obstructive pulmonary disease (COPD)) [38,39]. The medications that are used in the treatment of several chronic diseases may also be associated with an increased risk of tendinopathy (fluoroquinolones [40], statins

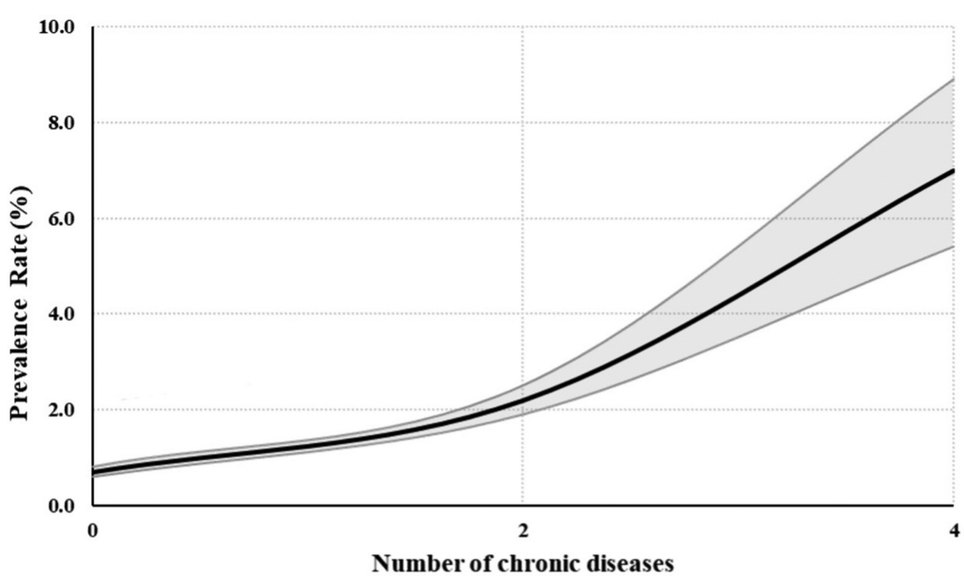

Figure 1. The relationship between prevalence of MTSS and the number of chronic diseases (chronic disease composite score) (shaded area is 95% CI).

Table 4. The number (n), prevalence (%; 95% CI) and prevalence ratio (PR; with 95% CI) of the MTSS group by chronic disease history and allergies

Characteristics		Consenting race entrants (n=61 193	MTSS group (n=558)			
		n	n	Prevalence (%) (95% CI)	PR (95% CI)	p-value
History of chronic disease						
Chronic Disease Composite Score (0-10)*	0 chronic diseases	N/A		0.70 (0.63 – 0.77)	3.16 (2.75 – 3.63)[a]	p<0.0001
	2 chronic diseases			2.20 (1.94 – 2.50)		
	4 chronic diseases			6.95 (5.44 – 8.88)		
(1) Any risk factor for CVD	yes	6 520	126	1.94 (1.61 – 2.34)	2.41 (1.95 – 2.98)	p<0.0001
	no	54 673	432	0.80 (0.73 – 0.89)		
(1) Any history of CVD	yes	921	23	2.56 (1.68 – 3.90)	2.85 (1.85 – 4.36)	p<0.0001
	no	60 272	535	0.90 (0.82 – 0.99)		
(1) Any symptoms of CVD	yes	551	22	3.78 (2.39 – 5.98)	4.21 (2.63 – 6.72)	p<0.0001
	no	60 642	536	0.90 (0.82 – 0.99)		
(1) Any endocrine disease	yes	1 524	20	1.41 (0.90 – 2.18)	1.53 (0.98 – 2.41)	p=0.0602
	no	59 669	538	0.91 (0.83 – 1.00)		
(1) Any respiratory disease	yes	4 826	122	2.34 (1.91 – 2.86)	2.93 (2.34 – 3.67)	p<0.0001
	no	56 367	436	0.80 (0.72 – 0.88)		
(1) Any GIT disease	yes	1 234	42	2.92 (2.01 – 4.22)	3.31 (2.26 – 4.85)	p<0.0001
	no	59 959	516	0.88 (0.80 – 0.97)		
(1) Any nervous system /psychiatric disease	yes	1 183	38	2.83 (1.89 – 4.24)	3.20 (2.11 – 4.86)	p<0.0001
	no	60 010	520	0.88 (0.80 – 0.97)		
(1) Any kidney /bladder disease	yes	715	24	2.95 (1.88 – 4.62)	3.28 (2.08 – 5.17)	p<0.0001
	no	60 478	534	0.90 (0.82 – 0.99)		
(1) Any haematological /immune disease	yes	401	8	1.77 (0.76 – 4.15)	1.93 (0.82 – 4.54)	p=0.1315
	no	60 792	550	0.92 (0.84 – 1.01)		
(1) Any cancer	yes	855	10	1.15 (0.55 – 2.43)	1.25 (0.59 – 2.66)	p=0.5613
	no	60 338	548	0.92 (0.84 – 1.01)		
History of Allergies						
Any allergies	yes	5 169	447	2.09 (1.71 – 2.57)	2.57 (2.04 – 3.22)	p<0.0001
	no	56 024	111	0.82 (0.74 – 0.90)		

n: number of race entrants
PR: Prevalence Ratio
*continuous variable, therefore, no number of participants in the groups
Chronic Disease Composite Score: the composite number of chronic diseases for an individual
CVD: Cardiovascular disease
GIT: Gastrointestinal disease
a: For every two additional chronic diseases

Table 5. The prevalence ratio (PR; 95% CI) of race entrants with MTSS (MTSS group) (multivariate analysis).

		MTSS group (n = 558)	
		PR (95% CI)	p-value
Chronic Disease Composite Score	0 chronic diseases	3.1 (2.6–3.5)*	$p < 0.0001$
	2 chronic diseases		
	4 chronic diseases		
Any allergies	yes	1.9 (1.5–2.4)	$p < 0.0001$
	no		

Adjusted for gender, race type and age groups
PR: Prevalence ratio
95% CI: 95% Confidence Interval
p: p-value
*average increase in prevalence of MTSS for every 2 more chronic diseases

[37,41], corticosteroids [42], aromatase-inhibitors [43], and isotretinoin [44], tendon ruptures [42], and osteoporosis [45] (corticosteroids)). Therefore, not only the presence of chronic disease, but also the choice of medication used in treatment, medication dosage, and medication interactions offer a biologically plausible explanation that chronic diseases can be predictive factors for MTSS and other gradual onset injuries.

The second main finding from our study was that a history of allergies was an independent risk factor predictive of a history of MTSS. This finding is similar to what we recently reported for any gradual onset injury in trail runners [23] and distance runners [24]. Again, we cannot show cause-effect, but there are also possible biological mechanisms linking chronic allergies to gradual onset soft tissue and bony injuries. Allergies are characterized by chronic inflammation, and there are epidemiological data in adults and children linking allergies to low bone mineral density and osteoporosis [46,47]. Common medications to treat allergies are corticosteroids and histamine receptor antagonists (antihistamines). Corticosteroids have been associated with the development of myopathy and osteopenia [38,48]. In a recent review, it was concluded that chronic blockade of histamine H1/H2 receptors can lead to impairment of microvascular and mitochondrial adaptations to interval training in humans [49]. Although speculative, this may affect tissue repair following injury. It is clear that the association between chronic diseases and/or allergies and gradual onset injuries such as a history of MTSS require further investigation. However, these associations may be very important for clinicians treating patients with MTSS because it may influence, for example, the rate at which healing may take place following repetitive injury in subgroups of higher risk individuals such as those with chronic diseases or allergies.

Unlike the results presented by several review studies, we found no statistically significant difference in the prevalence of a history of MTSS between male and female runners [13,14,16]. Some previous studies showed that physically active females engaging in various sports activities were at greater risk for a history of MTSS [13,14,16], but only one study was conducted on runners [13]. In the other studies, active individuals participating in a vast array of physical activities were included [14,16]. In line with our results, other review studies conducted on novice and recreational runners as well as physically active individuals did not report significant associations between MTSS and gender [15,21].

We show that 31–40 year old race entrants were at higher risk of a history of MTSS. This finding is consistent with one study reporting that below average age was a risk factor for MTSS in physical education teacher students [17]. The reason for this observation is not clear but may be related to less experience. However, this requires further investigation.

Finally, we show that several training variables, including years as a recreational runner and weekly running distance, were not associated with an increased risk of a history of MTSS. In one other study, years of running (0–3 years vs ≥4 years) was not associated with MTSS in cross country runners [50]. In contrast, fewer years of recreational running and fewer years participating in athletic activity were associated with a history of MTSS in other reports [13,51]. The discrepancy in results shown could possibly be attributed to the differences in the methodologies employed. In our study, and one other study [49], we included specific changes in training variables (e.g. 5 more years of running experience), whereas in the other review studies more general statements about training frequency (fewer years of recreational running or decreased running experience) are reported. In our study, increased average training or racing speed was associated with a history of MTSS, and this is a similar finding to that reported in one review [16].

The are several strengths to this descriptive cross-sectional study. To the best of our knowledge, this is the largest study to determine the risk factors predicting a history of MTSS for distance runners. Comprehensive data on all race entrants who registered for the race and started the race, over a 4-year period, were collected. We also report a high (71.8%) consent rate of all the race entrants. Several novel intrinsic risk factors were studied in a multivariate model and because of the large sample size results with narrow confidence limits are obtained. However, this study also has several limitations. Data were self-reported, and therefore are limited by recall bias. A specific potential limitation is that the selection of "*shin splints (muscle/tendon)*" (MTSS) was self-reported. However, we increased our confidence of this diagnosis by only including entrants that also consulted a health professional. Finally, we acknowledge that due to the cross-sectional nature of this study, a cause-effect relationship between any of the identified risk factors can not be determined.

Conclusion

Primary novel independent risk factors predictive of a history of MTSS in distance runners that entered for a mass community based 56 km and 21.1 km over a 4-year period were multiple chronic diseases and a history of allergies. A higher number of multiple chronic diseases and allergies was shown to be significant predictors of increased prevalence for a history of MTSS in distance runners.

What are the new findings

- Novel independent risk factors predictive of a history of MTSS (adjusted for gender, age group, and race type) are a higher chronic disease composite score and a history of allergies.
- Specific chronic diseases predictive of a history of MTSS (PR > 2) were: any symptoms of CVD, GIT disease, any kidney/bladder disease, any nervous system/psychiatric disease, any respiratory disease, a history of any CVD, and any risk factors of CVD.

How it might impact on clinical practice in the near future?

- Clinicians treating runners with MTSS should consider that chronic diseases, especially multiple chronic diseases, may be related to an increased risk of a history of MTSS.
- Clinicians treating runners with MTSS should consider that any history of allergies is predictive of an increased risk of a history of MTSS.
- These novel primary risk factors can potentially influence healing of soft tissue and bony injury and this information can guide healthcare professionals in their prevention and rehabilitation efforts.

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The authors report no conflict of interest pertaining to this manuscript.

Author contributorship

Pieter-Henk Boer (PB): manuscript (first draft), data analysis including statistical analysis, data interpretation, manuscript editing.
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Data sharing statement

No additional data are available.

Ethics (specific details removed to blind manuscript)

Ethics approval was obtained from both the Research Ethics Committees of the University of Cape Town (REC 009/2011) and the University of Pretoria (REC 433/2015 and 700/2019).

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