Received: 29 May 2023 | Revised: 25 November 2023 | Accepted: 23 January 2024

DOI: 10.1002/pmrj.13173

ORIGINAL ARTICLE

PM&R

Years of running, chronic diseases, and allergies are associated with gradual onset Achilles tendon injuries in 61,252 running race entrants: SAFER XXXIX study

Jonah Young[1,2] | **Paola Wood**[1,2] | **Martin Schwellnus**[2,3,4] | **Esmè Jordaan**[5,6] | **Sonja Swanevelder**[5]

[1]Biokinetics and Sports Science Division, Department of Physiology, Faculty of Health Sciences, University of Pretoria, Pretoria, South Africa

[2]Sport, Exercise Medicine and Lifestyle Institute (SEMLI), Faculty of Health Sciences, University of Pretoria, Pretoria, South Africa

[3]International Olympic Committee (IOC) Research Centre, Pretoria, South Africa

[4]Emeritus Professor, Faculty of Health Sciences, University of Cape Town, Cape Town, South Africa

[5]Biostatistics Unit, South African Medical Research Council, Cape Town, South Africa

[6]Statistics and Population Studies Department, University of the Western Cape, Cape Town, South Africa

Correspondence
Martin Schwellnus, Sport, Exercise Medicine and Lifestyle Institute (SEMLI), Faculty of Health Sciences, University of Pretoria, South Africa, Sports Campus, Burnett Street, Hatfield, Pretoria 0020, South Africa.
Email: mschwell@iafrica.com

Funding information
South African Medical Research Council; IOC Research Center (South Africa)

Abstract

Background: Gradual-onset Achilles tendon injuries (GoATIs) in runners are common. Data show that chronic diseases are associated with GoATI.

Objective: To determine risk factors associated with a history of GoATIs among long-distance runners (21.1 and 56 km) entering a mass community-based running event.

Methods: Online pre-race medical screening questionnaire data from 76,654 consenting Two Ocean Marathon race entrants (71.8% entrants) were collected prospectively over 4 years (2012–2015); this cross-sectional study is a retrospective analysis of these data. A total of 617 entrants (0.8%) reported a GoATI in the last 12 months; 60,635 entrants reported no history of any running injury (controls). Categories of factors associated with GoATI were explored (univariate and multiple regression analyses): demographics (age group, sex, race, distance), training/racing history, and history of allergy, history of chronic disease, and Composite Chronic Disease Score. Prevalence and prevalence ratios (PRs; 95% CI) are reported.

Results: Factors associated with a higher prevalence of a history of GoATI (univariate analysis vs. controls) were older age (>31 years) ($p < .001$), male sex (PR = 1.76; $p < .001$), and longer race distance (56 km vs. 21.1 km) (PR = 2.06; $p < .001$). Independent factors associated with a history of GoATI (multiple regression) were increased years of recreational running (PR = 1.17 for every 5-year increase, $p < .001$), higher Composite Chronic Disease Score (PR = 2.07 for every 2-unit increase, $p < .001$), and allergy history (PR = 1.98 $p < .001$).

Conclusion: Novel independent factors associated with a history of GoATI in distance runners were increased years of recreational running, chronic disease history, and allergy history. Runners at risk for GoATI could be targeted for injury prevention interventions. Future studies should focus on establishing a causal relationship.

INTRODUCTION

Regular physical activity is associated with multiple health benefits and reduces the risk of non-communicable disease (NCDs).[1,2] A "dose" of >150 minutes of moderate intensity endurance activity per week is recommended for the prevention and treatment of NCDs.[1–3] Distance running is an easy, low-cost, and easily accessible endurance activity that can be performed at the "prescribed" dose.[4–7] The ease of accessibility and simplicity of running has led to an increase in the popularity of running events in many countries.[5,8]

A potential negative side effect of running is the development of a gradual-onset running-related musculoskeletal injury (RRMI).[5] An RRMI can be described as musculoskeletal pain within the lower extremities, attributable to running-related activities such as training or competitive engagement, resulting in an impingement upon or cessation of running endeavors (inclusive of aspects such as distance, velocity, duration, or training regimens) for a minimum duration of 7 days or over the course of three successive scheduled training sessions, or necessitating the runner's recourse to medical consultation with a physician or other qualified health care practitioner.[8–10] The most common anatomic region for RRMI is the lower limb, particularly below the knee.[11] The majority of RRMIs are as a result of repetitive cycles of tissue loading with insufficient repair, resulting in accumulated tissue damage. These injuries typically present with progressive symptoms over time, have a complex multifactorial etiology, and are classified as gradual-onset injuries.[9,12]

Gradual-onset Achilles tendon injury (GoATI) is reported as the second most prevalent RRMI, and results in significant time off from training and racing.[13] GoATIs are often caused by repetitive microtrauma to the tendon without sufficient time to recover.[6,9] GoATI can be succinctly characterized as a compromised reparative process marked by the erratic expansion of tenocytes, irregularities in tenocyte behavior leading to the disturbance of collagen fiber integrity, and the subsequent augmentation of non-collagenous matrix constituents.[14] GoATIs typically present with progressive pain that develops over days or weeks, and can be persistent and even result in cessation of activity if pain is severe.[15,16] Several risk factors associated with GoATIs have been identified, and GoATIs are generally the result of a combination of both internal and external risk factors.[16] Identified internal risk factors for GoATIs are age, sex, body weight, compromised capacity to regulate tissue temperature, systemic disease, muscle strength, flexibility, previous injury, anatomic variants, blood supply to the tendon, and certain genetic traits.[16,17] Identified external risk factors are training errors, equipment, and running surfaces, with more recent reports of increased risk of injury when athletes use certain medications, such as fluoroquinolone antibiotics.[6,16,18] Recent studies report that chronic disease and allergies are associated with a history of gradual-onset injuries in runners and cyclists,[19–22] but this has not been reported for GoATIs. There are some reports in the non-athletic population linking GoATIs to chronic diseases such as diabetes, hyperuricemia, and obesity.[16,23,24] The clinical importance of determining associated risk factors is to develop injury-mitigation strategies for individuals where physical activity prescription is particularly important for the prevention and treatment of chronic diseases.

The purpose of this study is to determine risk factors associated with GoATIs in endurance running race entrants, particularly the Two Oceans Marathon races. Specific risk factors are entrant demographics (sex, age group, race distance), training-related variables (years of recreational running, weekly running distance, running speed), and history of chronic disease or allergies.

METHODS

Study design and ethical considerations

Data were collected prospectively over 4 years (2012–2015), and this cross-sectional study is a retrospective analysis of these data. This study forms part of a larger research program, known as the SAFER (Strategies to reduce Adverse medical events For the ExerciseR) studies.[25] The Research Ethics Committees of both the Faculty of Health Sciences at the University of Cape Town (REC number 431/2015) and the Faculty of Health Sciences of the University of Pretoria (REC number 513/2018) approved the study.

Participants (selection and description)

The Two Oceans Marathon (ultra-marathon of 56 km and half-marathon of 21.1 km) are popular races in South Africa that take place annually in the late summer and attract many race entrants.

Study participants

In the 4-year period of this study (2012–2015), 106,743 entrants entered for one of two race distances (21.1 or 56 km) and 76,654 entrants who were recreational runners gave consent for their data to be analyzed (21.1 km [$n = 64{,}740$] and 56 km [$n = 42{,}003$]) (overall response rate of 71.8% of all race entrants).The median training frequency of the included entrants in the study was 4 times per week and median weekly running volume was 40 km.

Data collection (pre-race medical screening questionnaire)

All participants completed a compulsory online pre-race medical screening questionnaire during the study period (2012–2015). The purpose and rationale for implementing the questionnaire has been described.[25,26] Briefly, the purpose of the screening questionnaire was to identify entrants who are at potential increased risk of acute medical complications. The questionnaire was designed using the guidelines for cardiovascular evaluation of middle-aged/senior individuals engaged in leisure-time sport

activities (Position stand from the European Association of Cardiovascular Prevention and Rehabilitation),[27] along with data from previous studies on distance runners.[26,28,29] Recommended in these guidelines is the inclusion of a pre-screening question on musculoskeletal symptoms. We elaborated on this question to include information about specific running-related injuries in the previous 12 months. The final screening questions included the following: running training/racing history, medical history (history of chronic cardiovascular disease [CVD]), risk factors for CVD, symptoms of CVD, respiratory disease, metabolic or hormonal disease, gastrointestinal tract disease, nervous system disease, renal or bladder disease, hematological or immune system disease, cancer, allergies (respiratory allergies or allergies to certain medications, animal or plant materials), or general medication use for chronic disease and injury history (in the previous 12 months).

Defining the study groups (injured and control)

The pre-race screening questionnaire included a specific question on injury history in the past 12 months, as follows: "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? Note: Only if an injury is/was severe enough to interfere with running or require treatment e.g., use medication or require you to seek medical advice from a health professional." If an entrant 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 739 entrants selected "Achilles tendon injury," and these entrants were considered for possible inclusion in the history of GoATI 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 GoATIs. Entrants were asked to select treatment modalities for the injury from a list. Most of the treatment modalities listed could be administered only by a health professional, for example, surgery, cortisone injection, other injection, physiotherapy, and orthotics. If an entrant selected one or more treatment modalities that could be administered only by a health professional, we considered the self-reported diagnosis of the specific injury to be "verified" by a health care professional. Of the 739 entrants who selected "Achilles tendon injury," 617 (83.5%) were in the category where the diagnosis of GoATI was "verified" by a health care professional. These entrants were selected as the GoATI study group ($n = 617$). Of the 76,654 entrants, 60,635 have never been injured; this was our control group. Entrants reporting other specific injuries and non-verified GoATIs were excluded from the analyses, resulting in an entrant sample of 61,252.

Measures of outcome

The primary outcome was a history of GoATI in the past 12 months among long-distance running race entrants. The following four categories of independent variables of interest as factors associated with a history of GoATI were explored. (1) Demographics (age groups, sex, race distance). (2) Running training/racing history variables (years of recreational running, years of participation in distance running events, average number of training sessions per week in the last 12 months, average weekly distance in the last 12 months, and increased average running speed). (3) History of chronic disease (history of existing CVD, risk factors for CVD, symptoms of CVD, respiratory disease, endocrine disease, gastrointestinal tract disease, nervous system or psychiatric disease, kidney or bladder disease, hematological system disease or immune system disease, cancer, and allergies). (4) We calculated a further variable, a Composite Chronic Disease Score (CCDS), which is a score out of 10 and represents a continuous variable of the sum of an individual's answers to 10 questions pertaining to a history of chronic diseases (any risk factors for CVD, history of existing CVD, symptoms of CVD, endocrine disease, respiratory disease, gastrointestinal tract disease, nervous system/psychiatric disease, kidney/bladder disease, hematological/immune system disease, and cancer).

By reporting these outcomes, we acknowledge that we cannot make any causal inference to guide injury prevention interventions specifically.[30] In reporting on the outcomes in this article, we use the terminology "prediction" instead of "association," based on recently published guidelines regarding clear goal setting in sports injury research.[30]

Statistical analysis

All questionnaire data were entered into an Excel spreadsheet (Microsoft 2010) and analyzed using the SAS v9.4 statistical program. Only data for consenting running race entries were used for analysis. All race entrants' data were entered into Excel and then transferred to the SAS (V.9.4) statistical analysis system.

The binary-scaled dependent variable in the model was the response to the question related to GoATI, and entrants were coded as having a GoATI if they reported (1) a GoATI in the past 12 months or (2) a current GoATI ($n = 617$). The control group of entrants have never been injured ($n = 60{,}635$). Entrants who reported any other running injuries or GoATIs that were not treated by a professional health care provider were excluded from all analyses, resulting in a final sample of 61,252. The denominator for the overall prevalence included all entrants who reported never being injured as well as all entrants who reported injuries that were not confirmed GoATIs. Prevalence ratios (PRs) were calculated as the measure of association. Univariate unadjusted prevalences (% and 95% CIs) and PRs were reported for age group, sex, race distance, running training/racing history, history of chronic diseases, and history of allergies using a Poisson regression model with a log link function. Using only highly significant risk factors ($p < .01$, due to the small sample size) from the individual univariate models, a multiple regression model was performed to determine independent risk factors associated with a history of GoATI. Consequently, for the final multiple regression model, only years being a recreational runner and the CCDS as well as an interaction term for allergy history and race distance were entered, adjusting for age group and sex. The reported level of significance is 5%.

RESULTS

Study participants

We conducted a retrospective analysis to determine if the participants in this study were representative of all race entrants (2012–2015). The demographics (race distance, sex, and age group) of the participants in this study were compared against all race entrants in the TOM (2012–2015) (Table 1).

Our study entrants differed from all race entrants. There was an over-representation of female entrants, younger age group, and 21.1 km race entrants in our study entrants compared to all race entrants (Table 1).

Risk factors associated with a history of GoATIs in distance runners (univariate analysis)

Demographics (sex, age group) and race distance (univariate analysis)

A total of 617 verified GoATIs were reported. The period prevalence of a history of GoATIs among race entrants in the past 12 months was 0.76% (95% CI: 0.70–0.83).

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

The main observation is that there is a higher PR of a history of GoATIs among the following subgroups of entrants: male sex (PR = 1.55, $p < .001$), older age (PR = 3.67, $p < .001$), and longer race distance (56 vs. 21.1 km) (PR = 2.07, $p < .001$).

Running training/racing history (univariate analysis)

The number (n), prevalence (%; 95% CI), and prevalence ratio (PR; 95% CI) of running race entrants with a history of GoATIs by running training/racing history is presented in Table 3.

The unadjusted univariate results show that several training variables are associated with a history of GoATIs. The highest PR of a history of GoATIs was associated with increased years of being a recreational runner (PR = 1.28 for every 5-year increase in years of recreational running; $p < .001$) and increased average weekly training/running distance in the last 12 months (PR = 1.07 for every 10 km increase in weekly training distance; $p < .001$).

History of chronic disease and allergies (univariate analysis)

The number (n), prevalence (%; 95% CI), and prevalence ratio (PR; 95% CI) of entrants with a history of GoATIs by CCDS and any allergies is presented in Table 4. Table S1 shows these adjusted for age group and sex.

The main observation from Table 4 is that a history of several chronic diseases is associated with a history of GoATIs. Specifically, the crude unadjusted analysis showed that the highest PR of a history of GoATIs is associated with a history of chronic diseases in the following organ systems: gastrointestinal tract (PR = 4.37; $p < .001$), any nervous system/psychiatric disease (PR = 3.30; $p < .001$), any kidney/bladder disease (PR = 2.93; $p = .002$) and any risk factor for CVD (PR = 2.92; $p < .001$), any respiratory disease (PR = 2.48; $p < .001$), any history of CVD (PR = 2.19; $p = .014$), any symptoms of CVD (PR = 1.99; $p = .079$), and any cancer (PR = 1.80; $p = .112$). In addition, a history of any allergies was associated with a higher PR of GoATIs (PR = 2.73; $p < .001$).

A higher CCDS (sum of all chronic diseases as a score out of 10), is associated with a higher prevalence

TABLE 1 Characteristics of all running race entrants, consenting race entrants (study participants), and not included race entrants by sex, age group, and race distance.

Characteristics		All race entrants ($n = 106,743$)		Consenting race entrants ($n = 76,654$)		Consenting study entrants ($n = 61,252$)		Not included race entrants ($N = 45,491$)		*p* value*	*p* value**	*p* value***
		n	%	*n*	%	*n*	%	*n*	%			
Sex	Male	61,815	57.9	44,042	57.5	34,921	57.0	26,894	59.1	.052	<.001	<.001
	Female	44,928	42.1	32,612	42.5	26,331	43.0	18,597	40.9			
Age group (years)	≤30	27,710	26.0	20,168	26.3	16,880	27.6	10,830	0.364	.364	<.001	<.001
	31–40	35,049	32.8	25,045	32.7	20,060	32.8	14,989	33.0			
	41–50	26,964	25.3	19,340	25.2	15,165	24.8	11,799	25.9			
	≥50	17,020	15.9	12,101	15.8	9147	14.9	7873	17.3			
Race distance	21.1 km	64,740	60.7	47,069	61.4	39,133	63.9	25,607	0.001	.001	<.001	<.001
	56 km	42,003	39.4	29,585	38.6	22,119	36.1	19,884	43.7			

*p value: All race entrants versus consenting race entrants.
**p value: All race entrants versus consenting study entrants.
***p value: All race entrants versus not included entrants.

TABLE 2 The number (n), prevalence (%; 95% CI), and prevalence ratio (PR; 95% CI) of race entrants with a history of GoATIs by sex, age group, and race distance.

Characteristics		Consenting study entrants ($n = 61,252$)	GoATI ($n = 617$)			
		n	*n*	Prevalence (%) (95% CI)	PR (95% CI)	*p* value
Entrant demographics						
Sex	Female	26,331	202	0.79 (0.68–0.91)	1.55 (1.29–1.85)	<.001*
	Male	34,921	415	1.22 (1.10–1.36)		
Age groups (years)	≤30	16,880	70	0.44 (0.35–0.56)	1.99 (1.51–2.64)	<.001*
	31 to ≤40	20,060	172	0.88 (0.75–1.03)		
	41 to ≤50	15,165	230	1.56 (1.36–1.79)	3.52 (2.68–4.62)	
	≥51	9147	145	1.63 (1.37–1.94)	3.67 (2.74–4.93)	
Race distance						
	21.1 km	39,133	288	0.75 (0.66–0.85)	2.07 (1.75–2.44)	<.001*
	56 km	22,119	329	1.55 (1.38–1.74)		

Abbreviation: CI, Confidence Interval; GoATI, Gradual onset Achilles Tendon Injury; PR, prevalence ratio.
*Significant difference.

TABLE 3 The prevalence (%; 95% CI) and prevalence ratio (PR; 95% CI) of race entrants with a history of GoATI by running training/racing history (univariate analysis).

Running training/racing history	Points in the continuous variable[a]	GoATIs ($n = 617$) Prevalence (%, 95% CI)	PR (95% CI)	*p* value
Number of years as a recreational runner (years)	3	0.71 (0.63–0.79)	5-unit increase 1.28 (1.23–1.32)	<.001
	6	0.82 (0.74–0.91)		
	13	1.15 (1.06–1.26)		
Average weekly training/running distance in the last 12 months (km/week)	20	0.92 (0.83–1.01)	10-unit increase 1.07 (1.05–1.10)	<.001
	35	1.02 (0.93–1.11)		
	50	1.12 (1.03–1.23)		
Average training speed (km/h)	9	1.03 (0.94–1.13)	1-unit increase 1.00 (0.98–1.03)	.779
	10	1.04 (0.95–1.13)		
	11	1.04 (0.96–1.13)		

Abbreviation: CI, Confidence Interval; GoATI, Gradual onset Achilles Tendon Injury; PR, prevalence ratio.
[a]Points on the continuous variables are the first quartile, median, and third quartile for each training variable.

TABLE 4 The number (*n*), prevalence (%; 95% CI), and unadjusted prevalence ratio (PR; with 95% CI) of running entrants with a history of GoATI by history of chronic disease and allergies (unadjusted).

		Consenting race entrants (*n* = 61,252)	GoATI (*n* = 617)			
Characteristics		***n***	***n***	**Prevalence (%; 95% CI)**	**PR (95% CI)**	***p*value**
History of chronic disease						
CCDS (0–10)[a]	0	46,951	308	0.79 (0.77–0.86)	2-unit increase 3.08 (2.73–3.48)	<.001
	2	2727	86	2.42 (2.16–2.72)		
	4	131	4	7.48 (6.02–9.28)		
1. Any risk factor for CVD	Yes	6394	163	2.50 (2.13–2.93)	2.92 (2.44–3.50)	<.001
	No	54,241	454	0.86 (0.78–0.94)		
2. Any history of CVD	Yes	898	20	2.22 (1.43–3.45)	2.19 (1.40–3.42)	.014
	No	59,737	597	1.02 (0.93–1.11)		
3. Any symptoms of CVD	Yes	529	12	2.04 (1.14–3.66)	1.99 (1.10–3.59)	.079
	No	60,106	605	1.02 (0.94–1.12)		
4. Any endocrine disease	Yes	1504	22	1.45 (0.94–2.23)	1.42 (0.91–2.20)	.184
	No	59,131	595	1.02 (0.94–1.12)		
5. Any respiratory disease	Yes	4704	111	2.29 (1.89–2.77)	2.48 (2.09–3.05)	<.001
	No	55,931	506	0.92 (0.84–1.01)		
6. Any GIT disease	Yes	1192	55	4.21 (3.19–5.57)	4.37 (3.27–5.85)	<.001
	No	59,443	562	0.96 (0.88–1.05)		
7. Any nervous system/psychiatric disease	Yes	1145	42	3.25 (2.34–4.51)	3.30 (2.35–4.62)	<.001
	No	59,490	575	0.99 (0.90–1.08)		
8. Any kidney or bladder disease	Yes	691	22	2.96 (1.93–4.53)	2.93 (1.90–4.52)	.002
	No	59,944	595	1.01 (0.93–1.10)		
9. Any hematological or immune disease	Yes	393	5	1.39 (0.63–3.08)	1.35 (0.61–3.00)	.534
	No	60,242	612	1.03 (0.95–1.12)		
10. Any cancer	Yes	845	15	1.84 (1.07–3.15)	1.80 (1.04–3.09)	.112
	No	59,790	602	1.02 (0.94–1.11)		
History of allergies						
Any allergies	Yes	5058	130	2.44 (2.03–2.94)	2.73 (2.22–3.35)	<.001
	No	55,577	487	0.90 (0.82–0.98)		

Abbreviations: CCDS, Composite chronic disease score; CI, Confidence Interval; CVD, cardiovascular disease; GIT, gastrointestinal disease; GoATI, Gradual onset Achilles Tendon Injury; PR: prevalence ratio

[a]Points on a continuous variable, therefore, no number of participants in the groups.

of a history of GoATIs in running race entrants, in a dose-dependent manner (Figure 1). Specifically, for every two additional chronic diseases, the prevalence of a history of GoATIs increased on average 3 times.

Independent factors associated with a history of GoATIs (multiple regression analysis)

The independent risk factors associated with a history of GoATIs in the past 12 months are reported in Table 5.

Independent risk factors associated with a history of GoATIs in running race entrants were increased years of being a recreational runner (PR = 1.18 for every

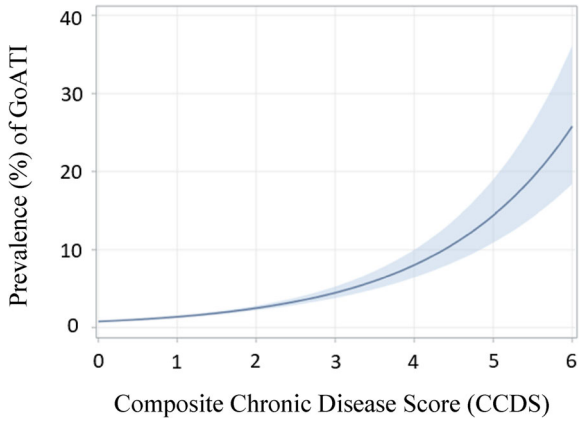

FIGURE 1 The relationship between prevalence (%) of a history of gradual-onset Achilles tendon injuries (GoATIs) and the Composite Chronic Disease Score (shaded area is 95% CI).

TABLE 5 Independent risk factors associated with a history of GoATIs in the past 12 months adjusting for sex, age group, and race distance (multiple regression analysis).

Risk factor		PR (95% CI)	*p* value
Running training/racing history			
Number of years as a recreational runner (y)	3 6 13	5-unit increase 1.18 (1.12–1.23)	<.001
History of chronic disease			
Composite chronic disease score (0–10)	0 2 4	2-unit increase 2.73 (2.38–3.14)	<.001
History of allergies			
Allergies	Yes (21.1 km)	1.78 (1.30–2.44)	<.001
	No (21.1 km)		
	Yes (56 km)	2.76 (2.06–3.71)	<.001
	No (56 km)		

Abbreviation: CI, Confidence Interval; PR, prevalence ratio.

5-year increase, $p < .001$), a higher CCDS (PR = 2.73, $p < .001$), and history of allergies for the 21.1 km entrants (PR = 1.78, $p < .001$) and for the 56 km entrants (PR = 2.76, $p < .001$).

DISCUSSION

Our study's first finding was that male sex, older age, and longer race distance were all associated with a history of GoATIs. Independent factors associated with a history of GoATIs were increased years of recreational running, a higher CCDS, and a history of allergies for the 21.1 and 56 km entrants.

Factors associated with a history of GoATIs in race entrants

Demographics (sex, age group) and race distance

We report that male sex, older age, and longer race distance (56 vs. 21.1 km) were all associated with a history of GoATIs ($p < .001$). These risk factors have been identified in prior studies.[13,31,32] In a recent large prospective cohort study, it was found that the incidence of Achilles tendinopathy increased with greater event distance, and it was noted that the incidence was highest in runners registered for a marathon (odds ratio 1.7, $p = .014$).[32]

Training and racing history

In our study we investigated multiple training and racing-related factors. We report that the following training variables are associated with a history of GoATIs: increased years of participation in distance running events, increase in years of recreational running, increased average weekly training/racing frequency in the last 12 months, and increased average weekly running distance in the last 12 months. These findings are similar to those that have been reported before.[5,6,31] Training errors such as increases in weekly volume and/or intensity and training sessions consisting of too much uphill or downhill running are associated with gradual-onset tendon injuries in runners.[31] Future research should continue to explore training variables/training errors, perhaps using larger sample sizes, and their cause–effect relationship to GoATIs.

History of chronic disease

Our univariate analysis shows that a history of several chronic diseases including gastrointestinal tract disease, any allergies, any risk factors for CVD, respiratory disease, and history of any nervous system or psychiatric disease are associated with a higher PR of a history of GoATIs: The inclusion of individual chronic diseases in the multivariate model was not possible due to the small sample size, but when a CCDS was included, we observed that for every two additional chronic diseases a running race entrant reported, the PR of a history of GoATIs increased 2.73 times. Prior studies have demonstrated that chronic disease is common among endurance athletes.[28] Recent research has found chronic disease is associated with a history of non-specific gradual-onset injury in both runners and cyclists.[19–22] Our data are novel and report this association with a specific injury: GoATI.

A growing body of evidence links metabolic disorders (diabetes, hyperuricemia, and obesity) to tendon degeneration.[23,33–35] Achilles tendinopathy is one of the musculoskeletal manifestations in patients with inflammatory bowel disease.[36] There is also limited evidence showing that a reduced creatinine clearance capacity due to renal dysfunction is associated with Achilles tendinopathy.[37] In our study, we could not determine the biological plausibility or cause–effect relationship between chronic disease and GoATIs because this was a cross-sectional study. We encourage future research to explore possible causal relationships between specific chronic diseases and GoATIs.

Allergies

Finally, we report that a history of allergies is associated with a higher risk of a history of GoATIs. This

agrees with recent reports that also demonstrated that allergies are associated with a history of non-specific gradual-onset injuries in endurance athletes.[19–21,38] A high prevalence of allergies and asthma has been found in high-level athletes, particularly those involved in endurance sport.[39] However, we can only speculate the biological plausibility or cause–effect relationship between allergies and GoATIs. The higher PR reported for a history of allergies in the 56 km running race entrants could be due to a greater exposure to airborne allergens, as these entrants will have likely spent more time outdoors training.[42] The allergy itself and/or the treatment modality could be responsible for the increased injury risk. The treatment for allergic rhinitis and asthma can involve the use of topical and systemic corticosteroids,[40,41] which have been implicated in tendon damage.[34,42] Furthermore, antihistamines are used in the treatment of allergies, which could lead to drowsiness or fatigue during training and/or racing. This fatigue could lead to lower strength of the working musculature and poor postural control and proprioception, predisposing the athlete to injury.[43,44] The role of histamine during acute exercise and adaptation to exercise training has recently been highlighted.[45–47] Histamine receptor blockers are used to treat allergies and these drugs may influence recovery after exercise. This may be associated with increased risk of gradual-onset injury. Future studies should aim to determine predictions between allergies, treatment modalities of allergies, and GoATIs.

STUDY LIMITATIONS, STRENGTHS, AND FUTURE RESEARCH RECOMMENDATIONS

We acknowledge limitations to the study. Data were self-reported, and this may have introduced recall bias. There was an over-representation of female participants, younger age groups, and 21.1 km race entrants. This needs to be considered when generalizing results across all entrants. We also acknowledge that a trained clinician did not diagnose injuries. To improve the accuracy of the self-reported diagnosis of the injury, we used data obtained from a question on treatment to control the over-reporting of GoATIs. Entrants were asked to select treatment modalities for the injury from a list. Most of the treatment modalities listed could be administered only by a health care professional, for example, surgery, cortisone injection, other injection, physiotherapy, and orthotics. If an entrant selected one or more treatment modalities that could be administered only by a health care professional, we considered the self-reported diagnosis of the specific injury to be "verified" by a health care professional. For future studies, we recommend the use of a prospective cohort design and randomized clinical trials as the preferred study designs to determine the causal relationships between the risk factors and GoATIs in distance runners.

CONCLUSION

Independent factors that are associated with a history of GoATIs in distance runners are more years of being a recreational runner, a history of chronic diseases, and a history of allergies. Runners with these factors are more susceptible to GoATIs and could be targeted for future injury-prevention interventions. Future studies should focus on establishing a causal relationship between these factors and GoATIs in runners.

ACKNOWLEDGMENTS

The authors would like to thank the Two Oceans medical staff, the Two Oceans Marathon organizers, and all the race entrants participating in this study.

FUNDING INFORMATION

IOC Research Center (South Africa) (partial funding), South African Medical Research Council (partial funding, statistical analysis).

DISCLOSURES

The authors declare that there are no competing interests.

ORCID

Jonah Young https://orcid.org/0009-0005-6544-060X
Paola Wood https://orcid.org/0000-0002-1242-4842
Martin Schwellnus https://orcid.org/0000-0003-3647-0429
Esmè Jordaan https://orcid.org/0000-0002-0361-3473
Sonja Swanevelder https://orcid.org/0000-0003-0885-3190

REFERENCES

1. Pedersen BK, Saltin B. Exercise as medicine–evidence for prescribing exercise as therapy in 26 different chronic diseases. *Scand J Med Sci Sports*. 2015;25(Suppl 3):1-72. doi:10.1111/sms.12581
2. Booth FW, Roberts CK, Laye MJ. Lack of exercise is a major cause of chronic diseases. *Compr Physiol*. 2012;2(2):1143-1211. doi:10.1002/cphy.c110025
3. Haskell WL, Lee IM, Pate RR, et al. Physical activity and public health: updated recommendation for adults from the American College of Sports Medicine and the American Heart Association. *Med Sci Sports Exerc*. 2007;39(8):1423-1434. doi:10.1249/mss.0b013e3180616b27
4. Hulme A, Finch CF. The epistemic basis of distance running injury research: a historical perspective. *J Sport Health Sci*. 2016;5(2):172-175. doi:10.1016/j.jshs.2016.01.023
5. Nielsen RO, Buist I, Sørensen H, Lind M, Rasmussen S. Training errors and running related injuries: a systematic review. *Int J Sports Phys Ther*. 2012;7(1):58-75.

6. Saragiotto BT, Yamato TP, Hespanhol Junior LC, Rainbow MJ, Davis IS, Lopes AD. What are the main risk factors for running-related injuries? *Sports Med*. 2014;44(8):1153-1163. doi:10.1007/s40279-014-0194-6
7. Hulme A, Salmon PM, Nielsen RO, Read GJM, Finch CF. From control to causation: validating a 'complex systems model' of running-related injury development and prevention. *Appl Ergon*. 2017;65:345-354. doi:10.1016/j.apergo.2017.07.005
8. Lopes AD, Hespanhol LC, Yeung SS, Pena Costa LO. What are the main running related musculoskeletal injuries. *Sports Med*. 2012;42(10):892-905. doi:10.2165/11631170-000000000-00000
9. Bertelsen ML, Hulme A, Petersen J, et al. A framework for the etiology of running-related injuries. *Scand J Med Sci Sports*. 2017;27(11):1170-1180. doi:10.1111/sms.12883
10. Almonroeder T, Willson JD, Kernozek TW. The effect of foot strike pattern on Achilles tendon load during running. *Ann Biomed Eng*. 2013;41(8):1758-1766. doi:10.1007/s10439-013-0819-1
11. Krabak BJ, Waite B, Lipman G. Evaluation and treatment of injury and illness in the ultramarathon athlete. *Phys Med Rehabil Clin N Am*. 2014;25(4):845-863. doi:10.1016/j.pmr.2014.06.006
12. Bahr R, Clarsen B, Derman W, Dvorak J, et al. International Olympic Committee Consensus Statement: methods for recording and reporting of epidemiological data on injury and illness in sports 2020 (including the STROBE extension for sports injury and illness surveillance (STROBE-SIIS)). *Orthop J Sports Med*. 2020;54:372-389. doi:10.1177/2325967120902908
13. Lorimer AV, Hume PA. Achilles tendon injury risk factors associated with running. *Sports Med*. 2014;44(10):1459-1472. doi:10.1007/s40279-014-0209-3
14. Maffulli N, Longo UG, Kadakia A, Spiezia F. Achilles tendinopathy. *Foot Ankle Surg*. 2020;26(3):240-249. doi:10.1016/j.fas.2019.03.009
15. Oestergaard Nielsen R, Aagaard Nohr E, Rasmussen S, Sirensen H. Classifying running-related injuries based upon etiology, with emphasis on volume and pace. *Int J Sports Phys Ther*. 2013;8(2):172-179.
16. Magnan B, Bondi M, Pierantoni S, Samaila E. The pathogenesis of Achilles tendinopathy: a systematic review. *Foot Ankle Surg*. 2014;20(3):154-159. doi:10.1016/j.fas.2014.02.010
17. Tenforde AS, Yin A, Hunt KJ. Foot and ankle injuries in runners. *Phys Med Rehabil Clin N Am*. 2016;27(1):121-137. doi:10.1016/j.pmr.2015.08.007
18. Hulme A, Nielsen RO, Timpka T, Verhagen E, Finch C. Risk and protective factors for middle- and long-distance running-related injury. *Sports Med*. 2017;47(5):869-886. doi:10.1007/s40279-016-0636-4
19. du Toit F, Schwellnus M, Wood P, Swanevelder S, Killops J, Jordaan E. Epidemiology, clinical characteristics and severity of gradual onset injuries in recreational road cyclists: a cross-sectional study in 21,824 cyclists - safer xiii. *Phys Ther Sport*. 2020;46:113-119. doi:10.1016/j.ptsp.2020.08.006
20. Swanevelder S, Sewry N, Schwellnus M, Jordaan E. Predictors of multiple injuries in individual distance runners: a retrospective study of 75,401 entrants in 4 annual races-safer xx. *J Sport Health Sci*. 2022;11(3):339-346. doi:10.1016/j.jshs.2021.11.002
21. Mokwena PL, Schwellnus MP, Van Rensburg AJ, Ramagole DA, Boer P, Jordaan E. Chronic disease, allergies, and increased years of running are risk factors predicting gradual onset running-related injuries in ultramarathon runners-safer xix study in 29 585 race entrants. *Clin J Sport Med*. 2022;32(4):e422-e429. doi:10.1097/JSM.0000000000000949
22. Artal R, Clapp J, Vigil D. ACSM current comment: exercise during pregnancy. *Exp Dermatol*. 2016.
23. Abate M, Schiavone C, Salini V, Andia I. Occurrence of tendon pathologies in metabolic disorders. *Rheumatology (Oxford)*. 2013;52(4):599-608. doi:10.1093/rheumatology/kes395
24. Batista F, Nery C, Pinzur M, et al. Achilles tendinopathy in diabetes mellitus. *Foot Ankle Int*. 2008;29(5):498-501. doi:10.3113/FAI.2008.0498
25. Schwellnus M, Derman W. The quest to reduce the risk of adverse medical events in exercising individuals: introducing the safer (strategies to reduce adverse medical events for the exerciser) studies. *Br J Sports Med*. 2014;48(11):869-870. doi:10.1136/bjsports-2014-093606
26. Schwellnus M, Swanevelder S, Derman W, Borjesson M, Schwabe K, Jordaan E. Pre-race medical screening and educational intervention reduces medical complications: a safer study in 153 208 runners. *Med Sc Sports Exerc*. 2017; (in press);49:186.
27. Borjesson M, Serratosa L, Carre F, et al. Consensus document regarding cardiovascular safety at sports arenas position stand from the European Association Of Cardiovascular Prevention And Rehabilitation (EACPR), section of sports cardiology. *Eur Heart J*. 2011;32(17):2119-2124. doi:10.1093/eurheartj/ehr178
28. Schwabe K, Schwellnus M, Swanevelder S, Jordaan E, Derman W, Bosch A. Leisure athletes at risk of medical complications: outcomes of pre-participation screening among 15,778 endurance runners–SAFER VII. *Phys Sportsmed*. 2018;46:405-413. doi:10.1080/00913847.2018.1505569
29. Rotunno A, Schwellnus MP, Swanevelder S, Jordaan E, Janse Van Rensburg DC, Derman W. Novel factors associated with analgesic and anti-inflammatory medication use in distance runners: pre-race screening among 76 654 race entrants-SAFER study VI. *Clin J Sport Med*. 2018;28(5):427-434. doi:10.1097/JSM.0000000000000619
30. Nielsen RO, Simonsen NS, Casals M, Stamatakis E, Mansournia MA. Methods matter and the 'too much, too soon' theory (part 2): what is the goal of your sports injury research? Are you describing, predicting or drawing a causal inference? *Br J Sports Med*. 2020;54:1307-1309. doi:10.1136/bjsports-2020-102144
31. Paavola M, Kannus P, Järvinen TA, Khan K, Józsa L, Järvinen M. Achilles tendinopathy. *J Bone Joint Surg Am*. 2002;84(11):2062-2076.
32. Lagas IF, Fokkema T, Verhaar JAN, Bierma-Zeinstra SMA, van Middelkoop M, de Vos RJ. Incidence of Achilles tendinopathy and associated risk factors in recreational runners: a large prospective cohort study. *J Sci Med Sport*. 2020;23(5):448-452. doi:10.1016/j.jsams.2019.12.013
33. Lui PPY. Tendinopathy in diabetes mellitus patients-epidemiology, pathogenesis, and management. *Scand J Med Sci Sports*. 2017;27(8):776-787. doi:10.1111/sms.12824
34. Wise BL, Peloquin C, Choi H, Lane NE, Zhang Y. Impact of age, sex, obesity, and steroid use on quinolone-associated tendon disorders. *Am J Med*. 2012;125(12):1228.e23-1228.e28. doi:10.1016/j.amjmed.2012.05.027
35. Franceschi F, Papalia R, Paciotti M, et al. Obesity as a risk factor for tendinopathy: a systematic review. *Int J Endocrinol*. 2014;2014:670262. doi:10.1155/2014/670262
36. Fornaciari G, Salvarani C, Beltrami M, Macchioni P, Stockbrügger RW, Russel MG. Muscoloskeletal manifestations in inflammatory bowel disease. *Can J Gastroenterol Hepatol*. 2001;15(6):399-403.
37. Van der Vlist AC, Breda SJ, Oei EH, Verhaar JA, de Vos RJ. Clinical risk factors for Achilles tendinopathy: a systematic review. *Br J Sports Med*. 2019;53:1352-1361. doi:10.1136/bjsports-2018-099991
38. Viljoen CT, Sewry N, Schwellnus MP, Janse van Rensburg DC, Swanevelder S, Jordaan E. Independent risk factors predicting gradual onset injury in 2824 trail running race entrants: SAFER XVIII Study. *Wilderness Environ Med*. 2021;32(3):293-301. doi:10.1016/j.wem.2021.04.002
39. Thomas S, Wolfarth B, Wittmer C, Nowak D, Radon K. Self-reported asthma and allergies in top athletes compared to the

general population–results of the German part of the ga2len-olympic study 2008. *Allergy Asthma Immunol Res*. 2010;6:31.
40. Selroos O, Pietinalho A, Lofroos AB, Riska H. Effect of early vs late intervention with inhaled corticosteroids in asthma. *Chest*. 1995;108(5):1228-1234. doi:10.1378/chest.108.5.1228
41. Taramarcaz P, Gibson PG. Intranasal corticosteroids for asthma control in people with coexisting asthma and rhinitis. *Cochrane Database Syst Rev*. 2003;4:CD003570. doi:10.1002/14651858.CD003570
42. Kirchgesner T, Larbi A, Omoumi P, et al. Drug-induced tendinopathy: from physiology to clinical applications. *Joint Bone Spine*. 2014;81(6):485-492. doi:10.1016/j.jbspin.2014.03.022
43. Robson-Ansley P, Howatson G, Tallent J, et al. Prevalence of allergy and upper respiratory tract symptoms in runners of the London marathon. *Med Sci Sports Exerc*. 2012;44(6):999-1004. doi:10.1249/MSS.0b013e318243253d
44. Verschueren J, Tassignon B, De Pauw K, et al. Does acute fatigue negatively affect intrinsic risk factors of the lower extremity injury risk profile? a systematic and critical review. *Sports Med*. 2019;50:767-784.
45. Ely MR, Sieck DC, Mangum JE, et al. Histamine-receptor antagonists slow 10-km cycling performance in competitive cyclists. *Med Sci Sports Exerc*. 2019;51(7):1487-1497. doi:10.1249/MSS.0000000000001911
46. Luttrell MJ, Halliwill JR. The intriguing role of histamine in exercise responses. *Exerc Sport Sci Rev*. 2017;45(1):16-23. doi:10.1249/JES.0000000000000093
47. Van der Stede T, Blancquaert L, Stassen F, et al. Histamine H1 and H2 receptors are essential transducers of the integrative exercise training response in humans. *Sci Adv*. 2021;7:eabf2856.

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Young J, Wood P, Schwellnus M, Jordaan E, Swanevelder S. Years of running, chronic diseases, and allergies are associated with gradual onset Achilles tendon injuries in 61,252 running race entrants: SAFER XXXIX study. *PM&R*. 2024;16(11):1204-1213. doi:10.1002/pmrj.13173