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The frequency of the *ACTN3* polymorphism in Brazil: a systematic review and meta-analysis

Valmir Oliveira Silvino[1,2*], Cirley Pinheiro Ferreira[1,2], Helen Matias Apaza[3], Valtemir Silvino de Souza-Junior[4], Sérgio Luís Galan Ribeiro[1], Sandro Soares Almeida[3,5,6] and Marcos Antonio Pereira dos Santos[1,2]

Abstract

Background The *ACTN3* gene encodes the protein alpha-actinin-3, which is crucial for fast-twitch muscle fibers, contributing to rapid and forceful contractions. The distribution of these genotypes and their impact on sports performance in Brazilian populations are not well-documented. This study aimed to determine the allelic and genotypic frequency of the *ACTN3* R/X polymorphism in Brazil and its association with sports performance.

Methods A systematic review was conducted, including studies sourced from PubMed, Scielo, LILACS, LIPECS, Coleciona SUS, CUMED, BINACIS, IBECS, and MEDLINE databases, resulting in 42 studies included. The quality of these studies was assessed using the Strengthening the Reporting of Genetic Association (STREGA) guidelines.

Results Among all the 8,746 participants, 35.2% had the RR genotype, 46.2% had the RX genotype, and 18.6% had the XX genotype. Regarding allelic frequency, 58.3% were R allele carriers, while 41.7% were X allele carriers. Meta-analysis showed that there was no consistent association between the *ACTN3* genotypes and sports performance, although some data suggested potential benefits in athletic performance.

Conclusion This study revealed that the RX genotype of the *ACTN3* R577X polymorphism is the most prevalent in Brazil, followed by the RR and XX genotypes. While the R allele was more frequent, the meta-analysis did not confirm a consistent association between *ACTN3* genotypes and sports performance, suggesting that other genetic and environmental factors contribute to athletic success.

Keywords Alpha-actinin-3, Genetics, Brazilian, Strength, Endurance, Sports

Background

The sarcomeric protein α-actinin-3 is a key component of the Z-line in muscles, anchoring the actin filament in fast-twitch fibers. These fibers are responsible for generating rapid and forceful contractions, making them essential for high-intensity, power-based activities such as sprinting and weightlifting [1]. The α-actinin-3 gene (*ACTN3*) encodes this protein, and a common null polymorphism in the gene results in the substitution of an arginine (R) residue with a premature stop codon (X) at amino acid position 577 [2]. Indeed, α-actinin-3 deficiency is believed to affect the muscle's ability to generate rapid, forceful contractions and thus might

*Correspondence:
Valmir Oliveira Silvino
valmirsilvino@live.com
[1] Department of Biophysics and Physiology, Nucleus of Study in Physiology Applied to Performance and Health (NEFADS), Federal University of Piaui, Teresina, Brazil
[2] Rede Nordeste de Biotecnologia (RENORBIO) Post-Graduation Program, Teresina, Brazil
[3] Department of Obstetrician, Escola Paulista de Medicina, Universidade Federal de São Paulo (UNIFESP), São Paulo, SP, Brazil
[4] Department of Physical Education, State University of Piauí, Teresina, Brazil
[5] Hospital Israelita Albert Einstein, São Paulo, SP, Brazil
[6] Faculdade Anhanguera de Guarulhos, Guarulhos, SP, Brazil

be detrimental for the production of fast and explosive movements [3]. Individuals with at least one R allele (*ACTN3*-RR or *ACTN3*-RX) produce α-actinin-3, while those with two X alleles (*ACTN3*-XX) lack this protein in their skeletal muscles, which is linked to a quicker decline in muscle strength and function [4].

The *ACTN3* R577X polymorphism has been studied in athletes from power-oriented sports, revealing that the RR and RX genotypes are more frequent among elite sprint/power athletes compared to elite endurance athletes and controls [5, 6]. This indicates that α-actinin-3 positively influences skeletal muscle function by enhancing forceful contractions at high speeds, offering an evolutionary edge due to improved sprint performance [7]. Although the RR and RX genotypes are associated with enhanced performance in sprint/power sports, the association between the XX genotype and endurance athletes remains inconclusive [8]. Furthermore, while the *ACTN3* gene might be linked to better performance in European endurance athletes, this has not been consistently demonstrated in studies involving Japanese athletes [9]. In this sense, it has been suggested that the inconsistencies in the current literature might be attributed to ethnic differences, as the distribution of the *ACTN3* R/X gene polymorphism has been reported to vary among different ethnic groups in populations around the world [10].

In addition to impacting exercise performance, *ACTN3* genotypes may also affect exercise-induced muscle damage, especially after endurance events like marathon running [11]. The X allele has been linked to higher levels of several muscle damage markers following exercise in amateur athletes [12]. Whereas, individuals with the XX genotype have shown greater muscle flexibility and a superior range of motion compared to their RR counterparts [13]. Additionally, the *ACTN3* XX genotype has been associated with lower body mass and lower fat-free mass in physically active subjects [14]. However, the influence of *ACTN3* genotypes on fat mass and body composition in sedentary and clinical populations remains unclear.

In this context, it is essential to determine the allele and genotype frequency of the *ACTN3* R/X polymorphism in the diverse This study is relevant and necessary because it provides the first systematic review and meta-analysis investigating the frequency of the *ACTN3* R/X polymorphism in Brazil. The Brazilian population alone comprises three main ethnic groups: Caucasian, Mestizo, and Black, resulting from the intermixing of Europeans, Amerindians, and Africans [15]. Given this diversity, notable variations in conditions and characteristics among participants can be expected. Therefore, understanding the genotypic frequency and its phenotypic impacts in the Brazilian population can aid researchers in future studies and improve clinical practice. To our knowledge, no systematic review has been conducted to examine the frequency of *ACTN3* polymorphism genotypes and their associations within the Brazilian population. Additionally, this research fills a critical gap by consolidating data on the prevalence of *ACTN3* polymorphisms in Brazil, facilitating comparisons with global data and contributing to a more comprehensive understanding of the genetic factors that influence sports performance and muscle physiology. The findings may also have practical implications for sports science, talent identification, and personalized training strategies, making this study highly relevant for researchers, athletes, and health professionals alike. Therefore, this review aims to determine the allele and genotype frequency of the *ACTN3* polymorphism in Brazil. Secondarily, we aimed to identify the relationship between this polymorphism and athletic status.

Methods

This systematic review was carried out following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [16]. The review protocol is registered with the International Prospective Register of Systematic Reviews (PROSPERO) under protocol number CRD42024569927.

Data collection

We conducted the search using Boolean operators "AND" and "OR," along with parentheses and quotation marks. The term "AND" was used to combine at least one word from each block, while "OR" was used to connect at least one word from each block. Parentheses were used to group search terms by outcome category, technique used, and population of interest, and quotation marks were used for exact terms or phrases. The search covered the period from inception until July 6, 2024, and was performed in the PubMed, Scielo, LILACS, LIPECS, Coleciona SUS, CUMED, BINACIS, IBECS, and MEDLINE databases. We combined the terms *ACTN3*, alpha-actinin-3, Brazilian or Brazil to find relevant publications regardless of their date. Additionally, we manually reviewed the references of the included studies and performed a Google Scholar search using grouped descriptors to identify any potentially relevant articles that were not previously included.

Eligibility criteria

Inclusion criteria encompassed publications that specified the frequency of the studied *ACTN3* polymorphism genotypes, written in Portuguese, English, or Spanish, and conducted with samples from Brazil. These criteria were applied regardless of sex, age, pathological

condition or sports discipline. Reviews and meta-analyses, dissertations, theses, course completion papers, E-books, in vitro or animal research, studies focusing on different polymorphisms, and research on unrelated subjects were excluded.

Data extraction

Data from the articles were manually extracted and organized into Microsoft Excel spreadsheets. The key data from the articles, such as the title, authors, date, and database, were extracted and organized in a Microsoft Excel spreadsheet (Microsoft Excel, Microsoft, Redmond, WA, USA). After removing duplicate records, two authors (VOS and CPF) independently and blindly screened the search results based on the inclusion/exclusion criteria established via the Rayyan website. Any disagreements between the reviewers were resolved either by consensus or with the involvement of a third reviewer (MAPS). References that could not be excluded based on the title or abstract alone were retrieved for further evaluation. Excluded publications were cataloged by numbering, reference (author and year of publication), title, and reasons for exclusion. The selected publications were organized by numbering, country, author, year of publication, title, total participants (N), total genotypes (RR, RX and XX), total men, total women, mean age, age range, main condition or sports studied, and significant results.

Quality evaluation

We assessed the quality of the studies included in this review using the Strengthening the Reporting of Genetic Association Studies Report (STREGA), which extends the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) initiative by adding 12 new criteria to the 22 items in the STROBE checklist. These additional criteria focus on five main areas: genotyping errors, population stratification, modeling of haplotype variation, Hardy–Weinberg equilibrium, and whether the report is a replication [17]. Two reviewers independently (VOS and CPF) applied the STREGA checklist, and inter-reviewer agreement was deemed satisfactory. In cases of disagreement, a third reviewer was involved in the evaluation (MAPS) and resolved the issue by consensus. Each item could be scored as "yes" (score 1) or "no" (score 0), resulting in a total score ranging from 0 to 22 points. Studies were classified into three quality ranks: rank 1 (scores 15 to 22, high quality), rank 2 (scores 8 to 14, medium quality), or rank 3 (scores 0 to 7, poor quality).

Statistical analysis

The Hardy–Weinberg equilibrium of the genotypic frequencies of the *ACTN3* polymorphism for each country were assessed using the Chi-square test. Statistical significance was tested with the χ^2 test ($p < 0.05$). The statistical analysis involved aggregating data from the included studies. Publication bias was assessed using funnel plots. The effect size was determined by calculating the risk ratio, along with 95% confidence intervals. This study investigated the distributions of the *ACTN3* R577X polymorphisms among athletes and healthy control subjects employing a case–control design. The frequencies between the groups (athletes and controls) were statistically analyzed using R Studio 4.2.3 (RStudio, Boston, USA), with support from R version 4.0.0 (The R Foundation, Vienna, Austria). The analysis of polymorphism frequencies between groups was carried out considering RR + RX and XX for *ACTN3*.

Results

The database search resulted in a total of 1963 articles. After removing 776 duplicates, the remaining 1160 articles were screened for relevance based on titles and abstracts, which led to the exclusion of 1094 studies. Additionally, one study obtained through other sources was included. Consequently, 67 articles were selected for in-depth review and analysis. Upon further examination of the full texts, 18 studies were excluded for not meeting the eligibility criteria. Finally, 42 studies were included in the qualitative synthesis (Fig. 1). Moreover, five studies were included in the meta-analysis as they provided genotype frequency data for the *ACTN3* polymorphism in both athletes and control groups, allowing for a comparative analysis of its potential association with sports performance.

The quality assessment revealed that 45.1% ($n = 19$) of the studies were rated as grade A (high quality), while 52.5% ($n = 22$) were rated as grade B (moderate quality) based on the STREGA guidelines. One study was rated as low quality (2.4%). Details regarding the quality assessment can be found in Supplementary Table 1.

The characteristics of the studies are displayed in Table 1. The studies presented report data from individuals across various age groups. One study evaluated the frequency of the *ACTN3* polymorphism in populations from Brazil, Chile and Japan [18]. Naturally, the Japanese and Chilean sample were not included in our results. Similarly, one study included subjects from the United States and Argentina in its sample [19]. To address this, we contacted the corresponding author of the study to accurately quantify the genotypic and allelic frequencies. Finally, two studies in the meta-analysis examined both strength and endurance athletes [20, 21]. However, for the purposes of this study, only the strength-oriented athletes were considered in the meta-analysis count.

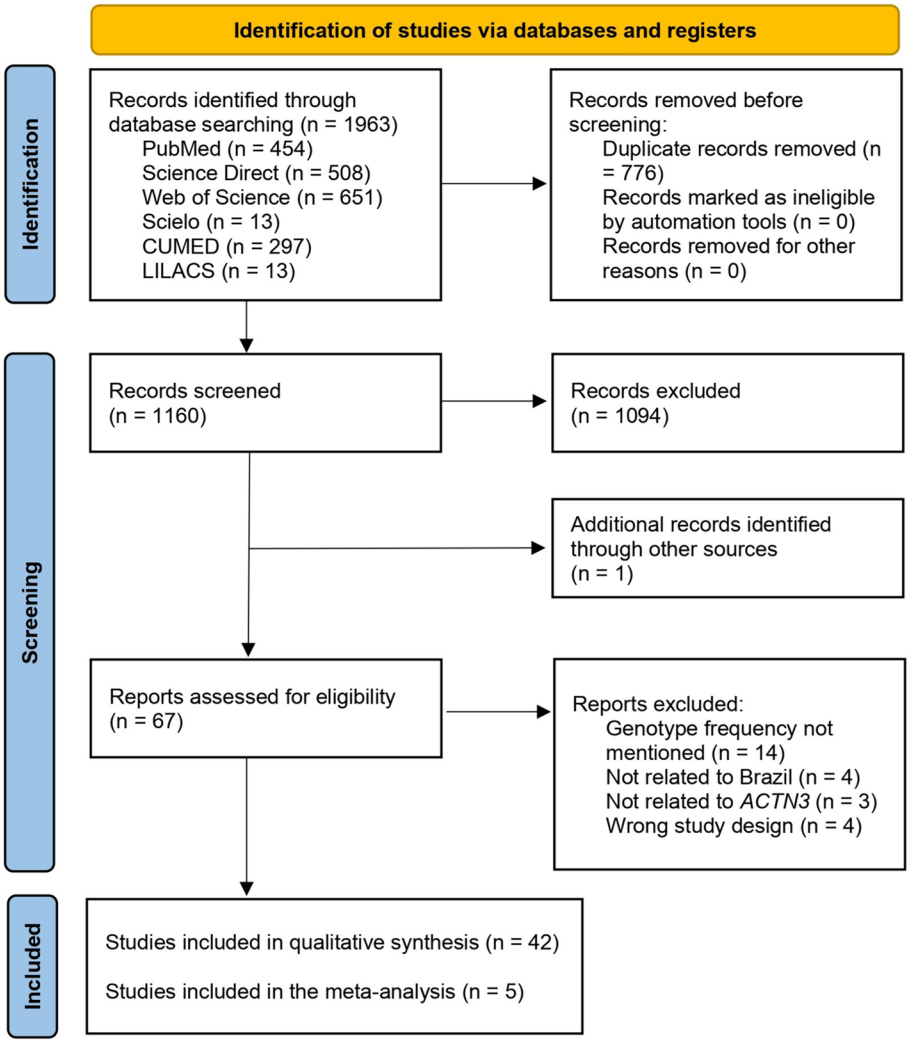

Fig. 1 PRISMA flow chart of the study selection [14]

The total number of participants was 8,746 subjects. Although some studies (14.3%) did not specify the sex of the participants, we observed that 60.4% of the subjects were men and 39.6% were women. Based on the studies that provided the average age of the participants, the sample included in this review was 36.9 ± 5.6 years old. Although some studies did not specify the average age, they disclosed the minimum and maximum age, ranging from 4 to 70 years old. Out of the total participants, 35.2% (3,077 people) had the RR genotype, 46.2% (4,038 people) had the RX genotype, and 18.6% (1,631 people) had the XX genotype for the *ACTN3* R/X polymorphism. Considering the allelic frequency, 58.3% were R carriers and 41.7% were X carriers. The genotypic frequency of the *ACTN3* gene in Brazil was not in Hardy–Weinberg Equilibrium ($\chi^2 = 22.4$, $p < 0.01$).

The forest plot depicted in Fig. 2 presents the risk ratios for the association between the *ACTN3* R/X polymorphism and sports performance across several studies. For this, we compared the frequency of athletes versus controls in each study using the metacont function. For the RR + RX genotypes, the combined effect model resulted in a risk ratio of 1.04 (95% CI: 1.00–1.08) under the common effects model and 1.04 (95% CI: 0.98–1.09) under the random effects model, indicating no significant association with improved sports performance. For the XX genotype, the combined effect model resulted in a risk ratio of 0.84 (95% CI: 0.70–1.01) under the common effects model and 0.87 (95% CI: 0.64–1.17) under the random effects model, also indicating no significant association. Finally, Table 2 presents the characteristics of the

Table 1 Characteristics of the studies included in the review. Age is presented as the mean and standard deviation or range (minimum to maximum). Genotype and allele frequencies are presented as counts and percentages

Study	Sample	Age (years)	RR	RX	XX	R	X
A. C. Silva et al. 2024 [22]	71	66.3 ± 6.2	25 (35.2)	37 (52.1)	9 (12.7)	87 (61.3)	55 (38.7)
Albuquerque-Neto et al. 2020 [23]	990	18 to 20	326 (32.9)	452 (45.7)	212 (21.4)	1104 (55.8)	876 (44.2)
Albuquerque-Neto et al. 2024 [20]	573	20 to 30	197 (34.4)	261 (45.5)	115 (20.1)	655 (57.2)	491 (42.8)
Almeida et al. 2022 [24]	83	25.9 ± 4.9	34 (41)	38 (45.8)	11 (13.3)	106 (63.9)	60 (36.1)
Aranalde et al. 2016 [25]	60	44.1 ± 11.3	24 (40)	31 (51.7)	5 (8.3)	79 (65.8)	41 (34.2)
Arejano et al. 2024 [26]	78	18 to 59	24 (30.8)	31 (39.7)	23 (29.5)	79 (50.6)	77 (49.4)
Belli et al. 2017 [27]	20	40.75	7 (35)	9 (45)	4 (20)	23 (57.5)	17 (42.5)
Bernardez-Pereira et al. 2014 [28]	463	58 ± 14	178 (38.4)	213 (46)	72 (15.6)	569 (61.4)	357 (38.6)
Bottura et al. 2019 [29]	61	29.2 ± 4.7	21 (34.4)	32 (52.5)	8 (13.1)	74 (60.7)	48 (39.3)
Coelho et al. 2018 [30]	453	17.6 ± 1	194 (42.8)	205 (45.3)	54 (11.9)	593 (65.5)	313 (34.5)
Corrêa et al. 2021 [31]	30	23 ± 5.2	11 (36.7)	13 (43.3)	6 (20)	35 (58.3)	25 (41.7)
Costa et al. 2020 [32]	400	4 to 13	155 (38.8)	161 (40.3)	84 (21)	471 (58.9)	329 (41.1)
Cunha-Montenegro et al. 2012 [33]	82	7 to 17	29 (35.4)	42 (51.2)	11 (13.4)	100 (61)	64 (39)
Dionísio et al. 2017 [34]	175	14 to 20	56 (32)	89 (50.9)	30 (17.1)	201 (57.4)	149 (42.6)
G. Lima et al. 2023 [19]	292	-	113 (38.7)	127 (43.5)	52 (17.8)	353 (60.4)	231 (39.6)
Gentil et al. 2011 [35]	141	22.2 ± 3.4	50 (35.5)	66 (46.8)	25 (17.7)	166 (58.9)	116 (41.1)
Guilherme et al. 2018 [21]	1616	27.6 ± 10.5	550 (34)	745 (46.1)	321 (19.9)	1845 (57.1)	1387 (42.9)
Guilherme et al. 2024 [36]	203	-	48 (23.6)	101 (49.8)	54 (26.6)	197 (48.5)	209 (51.5)
Henrique et al. 2022 [4]	347	71 ± 6.28	110 (31.7)	148 (42.7)	89 (25.6)	368 (53)	326 (47)
Hernández-Mosqueira et al. 2022 [18]	59	-	17 (28.8)	28 (47.5)	14 (23.7)	62 (52.5)	56 (47.5)
João et al. 2015 [37]	59	-	16 (27.1)	29 (49.2)	14 (23.7)	61 (51.7)	57 (48.3)
Luciano et al. 2016 [38]	215	10 to 35	73 (34)	105 (48.8)	37 (17.2)	251 (58.4)	179 (41.6)
M. S. M. Silva et al. 2015 [39]	205	25 ± 4	75 (36.6)	97 (47.3)	33 (16.1)	247 (60.2)	163 (39.8)
Machado et al. 2022 [40]	141	68.3 ± 6.2	65 (46.1)	63 (44.7)	13 (9.2)	193 (68.4)	89 (31.6)
Marques et al. 2024 [41]	344	23.9 ± 5.4	123 (35.8)	165 (48)	56 (16.3)	411 (59.7)	277 (40.3)
Moraes et al. 2018 [42]	87	60.6 ± 5.7	29 (33.3)	43 (49.4)	15 (17.2)	101 (58)	73 (42)
Oliveira et al. 2020 [43]	63	28 ± 5.8	18 (28.6)	34 (54)	11 (17.5)	70 (55.6)	56 (44.4)
Pasqua et al. 2015 [44]	150	25.2 ± 4	51 (34)	57 (38)	42 (28)	159 (53)	141 (47)
Pereira et al. 2013 [45]	139	65.5 ± 8.2	54 (38.8)	52 (37.4)	33 (23.7)	160 (57.6)	118 (42.4)
Pimenta et al. 2012 [46]	37	24.4 ± 3.5	15 (40.5)	13 (35.1)	9 (24.3)	43 (58.1)	31 (41.9)
Pimenta et al. 2013 [47]	200	24.4 ± 2	82 (41)	96 (48)	22 (11)	260 (65)	140 (35)
R. M. Lima et al. 2011 [48]	234	66.7 ± 5.5	78 (33.3)	119 (50.9)	37 (15.8)	275 (58.8)	193 (41.2)
Ribas et al. 2017 [49]	37	26.5 ± 5.7	17 (45.9)	14 (37.8)	6 (16.2)	48 (64.9)	26 (35.1)
Ribas et al. 2020 [50]	19	41.2 ± 6.1	3 (15.8)	11 (57.9)	5 (26.3)	17 (44.7)	21 (55.3)
Ribas et al. 2023 [51]	22	35.9 ± 6.5	5 (22.7)	12 (54.5)	5 (22.7)	22 (50)	22 (50)
Ribeiro et al. 2014 [52]	123	15 to 67	45 (36.6)	57 (46.3)	21 (17.1)	147 (59.8)	99 (40.2)
Rodrigues et al. 2022 [53]	70	50 to 70	22 (31.4)	38 (54.3)	10 (14.3)	82 (58.6)	58 (41.4)
Rosa et al. 2022 [54]	36	16.4 ± 1.2	14 (38.9)	19 (52.8)	3 (8.3)	47 (65.3)	25 (34.7)
Santos et al. 2024 [55]	97	27.2 ± 4.5	42 (43.3)	47 (48.5)	8 (8.2)	131 (67.5)	63 (32.5)
Sierra et al. 2019 [56]	81	38.3 ± 1.7	22 (27.2)	43 (53.1)	16 (19.8)	87 (53.7)	75 (46.3)
Silvino et al. 2025 [57]	165	16.4 ± 0.7	53 (32.1)	84 (50.9)	28 (17.0)	190 (57.6)	140 (42.4)
Wajchenberg et al. 2013 [58]	25	30.1 ± 13.5	6 (24)	11 (44)	8 (32)	23 (46)	27 (54)

studies that tested the association of the polymorphism with athletic performance, which were included in the meta-analysis.

The publication biases of the studies included in the meta-analysis were assessed by visual inspection of the funnel plots. The shapes of funnel plots in the comparisons indicated no obvious asymmetry (Fig. 3).

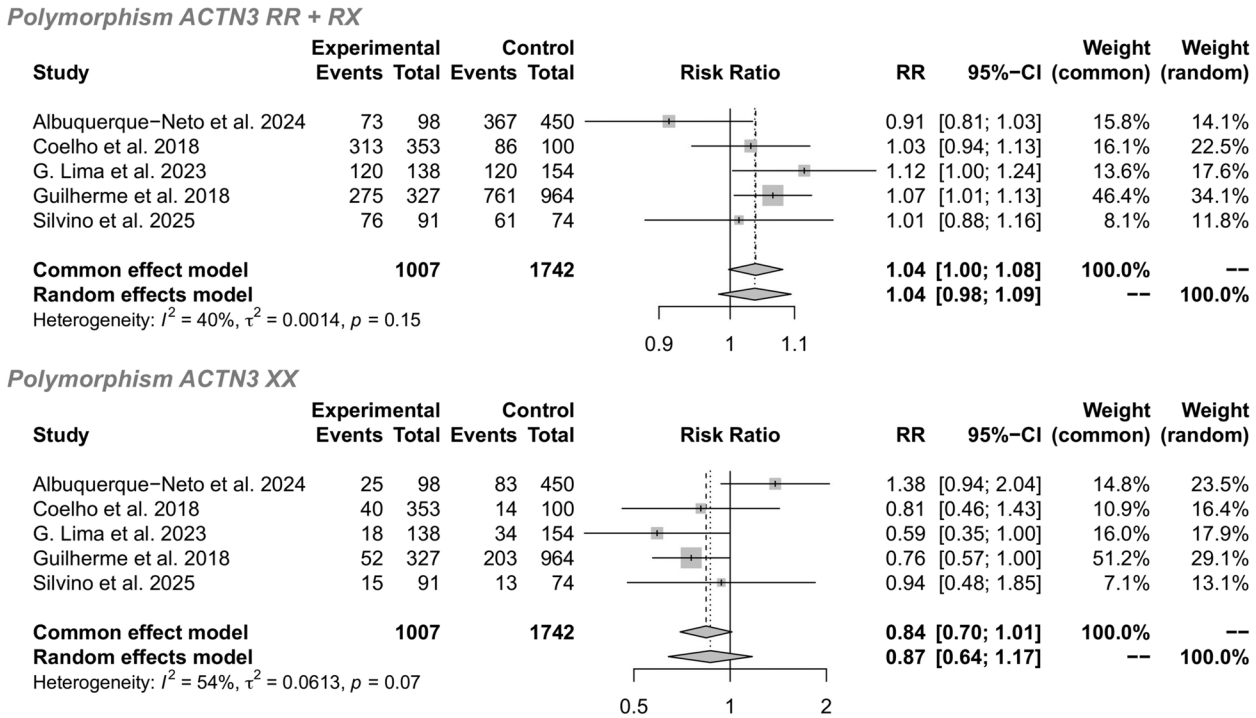

Fig. 2 Forest Plot between athletes and controls associated with the RR + RX and XX genotypes. Legends: RR, risk ratio; CI, confidence interval

Table 2 Description of the studies included in the meta-analysis

Study	Athletes (N)	Controls (N)	Sport
Albuquerque-Neto et al. 2024 [20]	98	450	Short distance swimming
Coelho et al. 2018 [30]	353	100	Soccer
G. Lima et al. 2023 [19]	138	154	Basketball
Guilherme et al. 2018 [21]	327	964	Strength sports
Silvino et al. 2025 [57]	91	74	Handball

Discussion

The present systematic review and meta-analysis aimed to elucidate the frequency of the *ACTN3* R/X polymorphism in Brazilian populations and explore its potential interactions with sports performance. A similar study has already been conducted on the frequency of the *ACE* polymorphism in South America [59]. However, to the best of our knowledge, this is the first investigation of the *ACTN3* gene. Our findings revealed a substantial variation in the distribution of the *ACTN3* genotypes across Brazil, which can be attributed to the diverse ethnic backgrounds and historical admixture present in this region.

The deviation from Hardy–Weinberg Equilibrium in the Brazilian sample suggests potential selection pressures or population stratification, which may influence the distribution of *ACTN3* genotypes. These differences could be attributed to the distinct ethnic compositions and historical admixtures in this country. In this sense, Moura et al. [60] conducted a systematic review with a meta-analysis comparing genetic admixture in the Brazilian population with other Latin American countries. They found that the Brazilian population has an average genetic ancestry composition of 62% European, 21% African, and 17% Native American. This highlights the importance of considering population-specific genetic backgrounds in sports performance research and highlights the need for tailored athletic training programs that account for these genetic differences.

Out of the 42 studies included in our review, 27 investigated the interaction between the *ACTN3* polymorphism and physical performance. The studied sports disciplines included soccer [24, 30, 33, 34, 43, 46, 47], running [27,

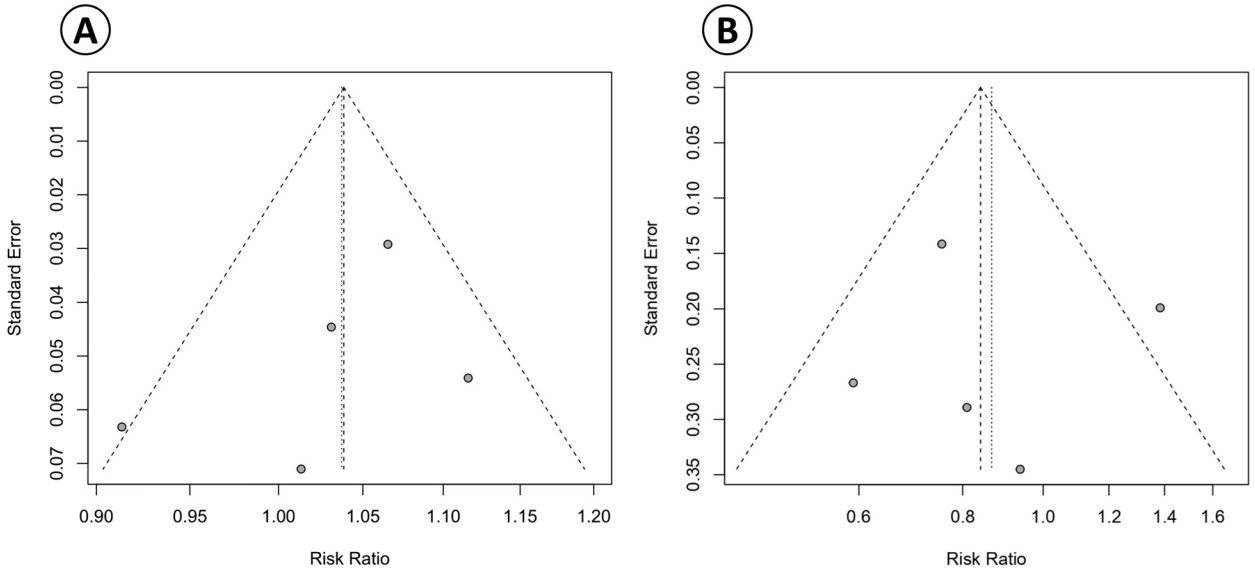

Fig. 3 Publication bias test for the *ACTN3* genotypes. Panel **A** *ACTN3* RR + RX. Panel **B** = *ACTN3* XX

50–52, 56], gymnastics [18, 37], swimming [20, 23], handball [57], volleyball [55], weightlifting [35], wrestling [49], and basketball [19]. Other studies focused on athletes from multiple sports [21, 36, 41, 54]. Six studies examined the role of *ACTN3* in various diseases, including sarcopenia [22, 45], diabetes and hypertension [26], heart failure [28], acute motion sickness [29], and scoliosis [38, 61]. Other topics investigated regarding the role of *ACTN3* in a non-athletic young population include aerobic fitness [31, 39, 44], lipid profile [25], and nutritional status [32]. Finally, five studies explored the frequency of the *ACTN3* polymorphism in older adults and its relationship with their functional performance [4, 40, 42, 48, 53].

The studies included in this systematic review spanned a wide range of ages, with some focused on young adults, such as the sample aged 18 to 20 years [23], and others on older populations, such as the 71-year-olds in the study by Henrique et al. [4]. The distribution of *ACTN3* genotypes varied, with the RR genotype ranging from as few as 19 [50] to as many as 1616 in the study by Guilherme et al. [21]. The RX genotype was generally the most prevalent across the studies included in this systematic review.

The forest plot depicted in Fig. 2 presents the risk ratios for the association between the *ACTN3* R/X polymorphism and sports performance across several studies. Only one study reported a significant difference in the frequency of the RR + RX genotypes when comparing athletes and controls [19]. These findings suggest that while individual studies report varying degrees of association between *ACTN3* genotypes and sports performance, the aggregated data does not support a significant overall effect, highlighting the need for further research to account for study-specific factors and potential confounders.

The influence of the *ACTN3* R577X polymorphism on athletic performance is primarily linked to its role in muscle fiber composition and metabolism. The RR and RX genotypes produce α-actinin-3, a structural protein in type II (fast-twitch) fibers, enhancing forceful contractions, anaerobic capacity, and power-based performance. In contrast, XX individuals lack α-actinin-3, leading to a shift toward type I (slow-twitch) fibers, favoring endurance and oxidative metabolism [1]. Additionally, the absence of α-actinin-3 may impact muscle integrity, increasing susceptibility to exercise-induced muscle damage [62]. These mechanisms explain why RR and RX genotypes are more frequent among power athletes, while the XX genotype is not consistently associated with endurance performance, likely due to the influence of additional genetic and environmental factors.

Some limitations should be acknowledged. First, although we included studies from multiple databases, there may be unpublished or inaccessible data that could influence our findings, leading to potential publication bias. Second, the included studies varied in sample size, methodological approaches, and population characteristics, which may have introduced heterogeneity into the results. Finally, while the study explored the *ACTN3* polymorphism's frequency and its potential association with athletic performance, other genetic and environmental factors, such as training status, nutrition, and epigenetic modifications, were not accounted for and could

modulate these effects. Future research should aim to address these gaps by incorporating larger, more diverse cohorts and considering additional variables that influence performance and muscle function.

A key strength of this study is its inclusion of a large number of participants (8,746 individuals) from diverse regions of Brazil, allowing for a more representative understanding of genetic variability in this heterogeneous population. The findings from this review have significant implications for athletic training and talent identification programs in Brazil. Understanding the distribution of *ACTN3* genotypes can aid in developing specific training regimens that align with the genetic predispositions of athletes. For instance, individuals with the RR genotype may benefit from high-intensity, power-focused training, while those with the XX genotype might excel with endurance-based programs [6]. Moreover, genetic screening of polymorphisms, including *ACTN3*, could be integrated into talent identification processes to optimize athlete selection and development [63].

Conclusion

This systematic review and meta-analysis provide the first comprehensive synthesis of *ACTN3* R577X polymorphism frequencies in the Brazilian population, highlighting the genetic diversity shaped by Brazil's unique ethnic composition. While the RR and RX genotypes are often linked to power-oriented athletic performance, our findings indicate no consistent association between *ACTN3* and sports success in the Brazilian context, suggesting that other genetic, environmental, and training-related factors play a crucial role. These results challenge the simplistic view of *ACTN3* as a determinant of athletic ability and emphasize the need for a more integrative approach that considers multiple genetic markers, physiological adaptations, and individualized training strategies. By addressing a critical gap in sports genetics research in Brazil, this study lays the foundation for future investigations that can refine athlete selection models and optimize performance development through personalized interventions.

Abbreviations

ACTN3	α-actinin-3
HWE	Hardy-Weinberg Equilibrium
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PROSPERO	Prospective Register of Systematic Reviews
STREGA	Strengthening the Reporting of Genetic Association Studies
STROBE	Strengthening the Reporting of Observational Studies in Epidemiology
$\chi 2$	Chi-square test

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12920-025-02136-1.

Supplementary Material 1.

Consent to participate

Not applicable.

Clinical trial number

Not applicable.

Authors' contributions

VOS contributed with conceptualization, data curation, formal analysis, investigation, software, writing – original draft, and writing – review and editing. CPF contributed with data curation, formal analysis, investigation, and methodology. HMA contributed with data curation and methodology. SLGR contributed with validation, visualization, and writing – review and editing. VSSJ contributed with data curation. SSA contributed with formal analysis, investigation, and writing – review and editing. MAPS contributed with conceptualization, formal analysis, project administration, supervision, and writing – review and editing. All authors read and approved the final version of the manuscript.

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Data availability

The datasets analyzed in this manuscript are not publicly available but are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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