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# Influence of genetic polymorphism on sports talent performance versus non-athletes: a systematic review and meta-analysis

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## Abstract

**Background** Talented athletes exhibit remarkable skills and performance in their respective sports, setting them apart from their peers. It has been observed that genetic polymorphisms can influence variations in sports performance, leading to numerous studies aimed at validating genetic markers for identifying sports talents. This study aims to evaluate the potential contribution of genetic factors associated with athletic performance predisposition in identifying sports talents.

**Methods** A systematic review was conducted following the PRISMA framework, utilizing the PICO methodology to develop the research question. The search was limited to case-control studies published between 2003 and June 2024, and databases such as Medline, LILACS, WPRIM, IBECs, CUMED, VETINDEX, Web of Science, Science Direct, Scopus and Scielo were utilized. The STREGA tool was employed to assess the quality of the selected studies.

**Results** A total of 1,132 articles were initially identified, of which 119 studies were included in the review. Within these studies, 50 genes and 94 polymorphisms were identified, showing associations with sports talent characteristics such as endurance, strength, power, and speed. The most frequently mentioned genes were ACTN3 (27.0%) and ACE (11.3%).

**Conclusion** The ACE I/D and ACTN3 R577X polymorphisms are frequently discussed in the literature. Although athletic performance may be influenced by different genetic polymorphisms, limitations exist in associating them with athletic performance across certain genotypes and phenotypes. Future research is suggested to investigate the influence of polymorphisms in elite athletes from diverse backgrounds and sports disciplines.

**Keywords** Athletic performance, Elite athletes, Genetic polymorphisms, sports talents

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## Introduction

The term sports talent has been used to describe individuals who express aptitude for excellence in physical performance in certain sports [1]. Being a talent requires not only dedication, determination, specialized training, nutrition and favorable environmental factors from the athlete, but also is affected by maturational [2], psychological [3], and genetics [4] factors. In fact, genetics has been pointed out as partially responsible for the physical, anthropometric or physiological characteristics necessary for athletic excellence [5, 6].

The influence of genetics and its mechanisms on sports performance have been extensively researched worldwide, in an attempt to use genetic information as predictors of elite status [7]. Genetic polymorphisms are well known for affecting protein expression, thereby potentially influencing an individual's physical abilities, athletic performance, and response to exercise [8]. Among the polymorphisms associated with the performance of elite athletes, we can mention the  $\alpha$ -actinin-3 (ACTN3) R577X and angiotensin converting enzyme (ACE) I/D (endurance and power) [9], bradykinin receptor B2 (BDKRB2) (endurance) [10], angiotensinogen (AGT) M235T (rs699) (strength and power) [11, 12], nuclear respiratory factor 2 (NRF-2) intron 3 A/G (endurance) [13, 14], as well as nitric oxide synthase 3 (NOS3) Glu298Asp (rs1799983) and adenosine monophosphate deaminase 1 (AMPD1) Gln45Ter (rs17602729) (resistance) [15].

Studies indicate that genetic factors account for 44–68% of the phenotypic variability [7, 16]. Genetic elements have great influence on athletic performance components such as endurance, strength, power and other important characteristics in sport [12, 17]. However, despite the existence of studies supporting these findings, numerous genetic variants and the underlying mechanisms of their effects remain unknown [18]. Due to this lack of knowledge, it is worrying to know the existence of an emerging market of direct-to-consumer genetic tests that aim to identify athletic talents in children [19], focusing mainly on ACTN3 and ECA genes, due to the greater volume of research on these polymorphisms since 2015 [20]. Thus, the objective of the present meta-analysis was to assess whether the potential genetic factors identified as predictors of athletic performance can aid in identifying sports talents.

## Methods

### Search strategy

This systematic review was conducted in accordance with the framework provided by PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis statement) [21] and was registered with PROSPERO (CRD42022311044) on March 18, 2022. A literature

search was conducted by two independent researchers using Scielo, BVS (Medline, LILACS, WPRIM, IBECs, CUMED, VETINDEX), Web of Science, Science Direct, and Scopus databases, covering the period from 2003 to June 2024. The review used a research question developed with the PICO methodology [22], in which the population was elite athletes or sport talents, the intervention was genetic polymorphisms, the comparator was control or non-athlete, and the outcome was athletic or sports performance. The guiding question used in this study was: Can genetic polymorphisms influence athletic performance of sports talents compared to controls or non-athletes?

Keywords used for the search included the following: “elite athletes”, “professional athletes”, “sports performance”, “genetic fitness” and “polymorphism”. Descriptors were obtained from the Health Sciences Descriptors (DeCS) and Medical Subject Headings (MeSH) and related keywords, combined with the Boolean operators “AND” and “OR”.

### Inclusion and exclusion criteria

Articles were included if they met the following five criteria: (one) case control design, (two) with athletes of any age or sex, (three) associated with athletic performance (strength, speed, endurance and power), (four) written in English language and (five) be published in the last 20 years. Studies that did not meet the inclusion criteria, involving animals, repeated studies, placebo-controlled studies, cell studies, thesis, dissertations, abstracts, not available in full and that did not answer the guiding question were excluded from this review.

Case-control articles, including polymorphisms associated with sports performance (strength, endurance, speed and power) of elite athletes were included in the study. On the other hand, studies that contained unclear data did not include a control group, and those whose full text could not be available were excluded from this meta-analysis.

### Data extraction

The search of the articles was performed by two reviewers (C.P.F. and V.O.S.). Independently, each author analyzed the title and abstract of the studies found in the databases. The files resulting from the search were sent to the Rayyan Systematic Review Online Data Management Platform, for exclusion of duplicate and screening of the articles. Then, the articles included after the screening were analyzed in full, in accordance with the eligibility criteria. Data from published studies were extracted according to the following characteristics and numbers: first author, year of publication, gene (full name), polymorphism, objective of the study, results, study design, groups, number of subjects (sex), age (years), and

nationality of the athletes. In case of conflict of decision during the selection of articles, a third reviewer was consulted (M.A.P.S.).

### Quality assessment

The methodological quality of the studies was determined by two independent reviewers (C.P.F. and R.C.M.), according to the Strengthening the Reporting of the Genetic Association (STREGA) guidelines for case-control studies [23]. The STREGA statement represents an extension of Strengthening the Reporting of Observational Studies in Epidemiology (STROBE). 40 items from the STROBE checklist were analyzed following the guidelines by the STREGA declaration. After the evaluation of the items, a total score of 0 to 40 was reported for each article. The studies were rated as: A - High quality (30 to 40 points), B - Moderate quality (20 to 29 points) and C - Low quality (0 to 19 points). For each item, there are 2 scores: “yes” (score 1) or “no” (score 0). Discrepancies between reviewers were resolved by consensus and, in case of persistent disagreement, the evaluation was performed by a third reviewer (M.A.P.S.). The STROBE quality scoring system proposed by Liu et al. [24] was modified and used in this study.

### Statistical analysis

The statistical analysis involved the grouping of data from the included studies. The publication bias was evaluated by funnel graphs. The effect size was calculated as the risk ratio, followed by 95% confidence intervals. In this study, using a case-control design, we examined the polymorphism distributions of ACE I/D and ACTN3 R577X or rs1815739 among elite athletes and healthy control subjects. Statistical analysis of the frequencies of polymorphism between groups (athletes and controls) was performed using R Studio 4.2.3 (RStudio, PBC, Boston, MA), supported by R version 4.0.0 (The R Foundation, Vienna, Austria). The evaluation of frequencies by polymorphism between groups was determined via meta-cont function, considering ID+DD and II for ACE and RR+RX and XX for ACTN3.

### Results

The systematic search yielded a total of 180 articles, which were then subjected to full reading. Among them, 119 articles were included for the purpose of conducting a systematic review, while 53 articles were included in the meta-analysis. The publication dates of the selected studies spanned from 2003 to 2024. The selection process of this study is depicted in Fig. 1.

The characteristics of the 119 studies included in this review are summarized in Table 1. A total of 50 genes and 94 different polymorphisms were investigated. The most frequent genes were ACTN3 and ACE, representing

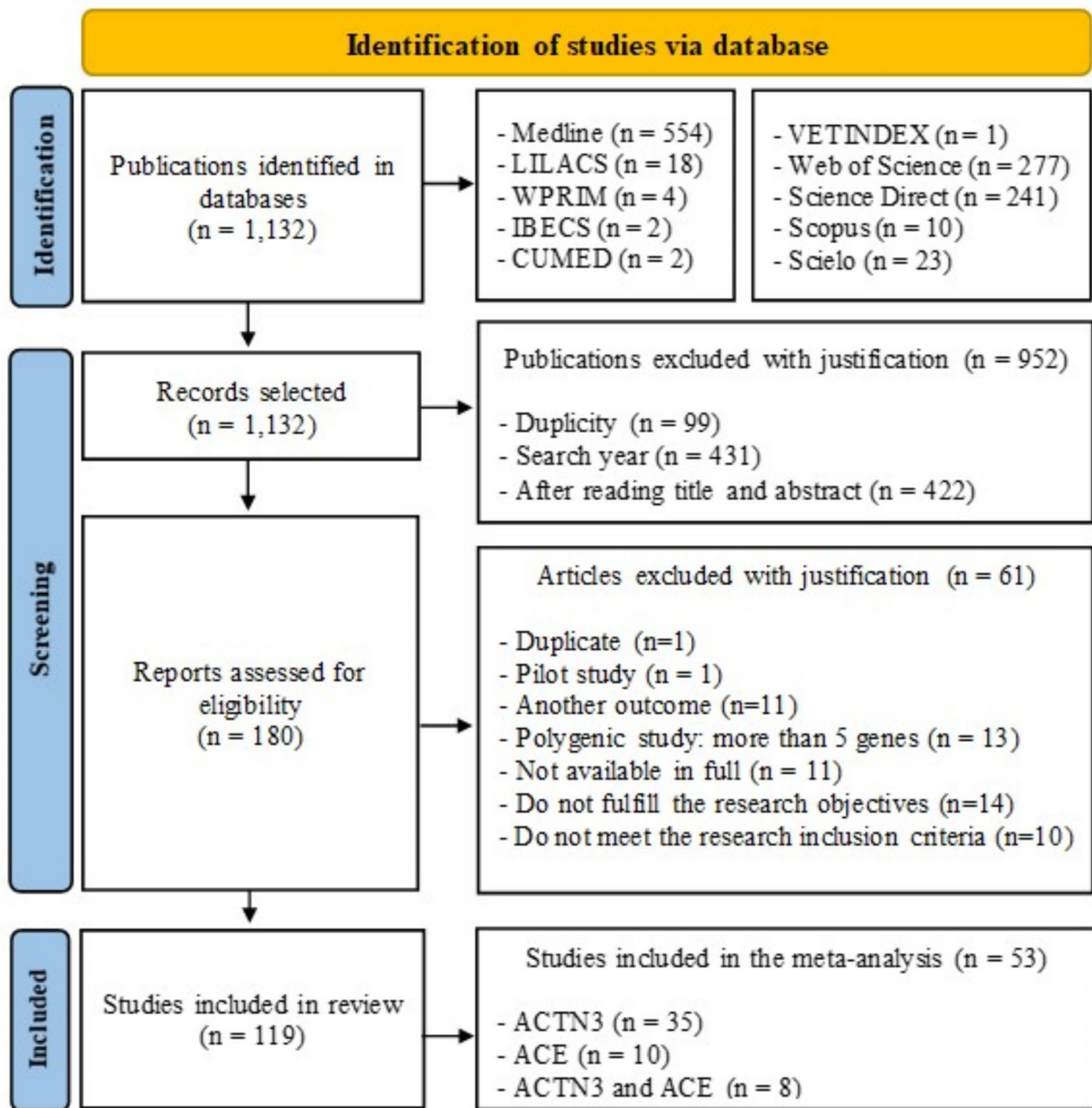
27.0% ( $n=43$ ) and 11.3% ( $n=18$ ) of the sample, respectively. Among the 94 polymorphisms cited, ACTN3 R577X=rs1815739 and ACE I/D were the most frequent with 22.4% ( $n=43$ ) and 9.4% ( $n=18$ ), respectively.

All studies presented in this review are case-control. 77,690 participants were analyzed, of which 32,198 were athletes and 45,492 were non-athlete controls. As for the description of sex, 107 articles showed that 75.2% ( $n=20,998$ ) of the athletes were men and 24.8% ( $n=6,933$ ) were women, 5 articles did not mention the number of athletes and controls by sex and 7 articles described only partially. The studies included participants expert in strength, power, speed and endurance sport disciplines. Considering the nationality of the participants (athletes and controls), the majority were Polish (20.0%), followed by Israeli (16.6%), Russian (11.7%) and Spanish (10.3%), as shown in Table 2.

The quality evaluation showed that 89.1% ( $n=106$ ) of the studies had grade A (high quality) and 10.9% ( $n=13$ ) grade B (medium quality), according to the STREGA [23] as shown in Table 3. Therefore, the studies are adequate for this review as they met the quality expected for the investigation.

However, it is important to highlight that all the studies analyzed had methodological limitations, specifically concerning sample size calculation. The absence of sample size calculation in the original studies can bias the true effect of the investigated associations. Studies indicate that when sample size calculation is not performed, the results regarding power, effect size, and reproducibility are directly affected [25, 26] (Andrade, 2020; Serdar et al., 2020). Therefore, despite the quality of the studies included in the sample, it is important to assess this limitation, considering that even well-executed studies may fail to adequately address the research question. The results of Tables 1 and 2, and 3 can be found in the supplementary material 1 (S1).

Regarding the meta-analysis, we evaluated the data regarding the genotypic frequency and total number of participants available in the original articles. We aimed to determine whether there was a predominance of any genetic profile between athletes and non-athletes, based on the frequency of ACE (DD+ID vs. II) and ACTN3 (RR+RX vs. XX) genotypes. Polymorphisms were selected due to their presence in a larger number of studies included in this review. The frequencies of the DD and ID genotypes for the ACE and the RR and RX genotypes for the ACTN3 were combined in order to improve the graphical visualization of the analysis in the forest plot, which mainly took into consideration the frequency of genotypes among the groups of cases and controls. This approach was adopted in accordance with a previous investigation [58].

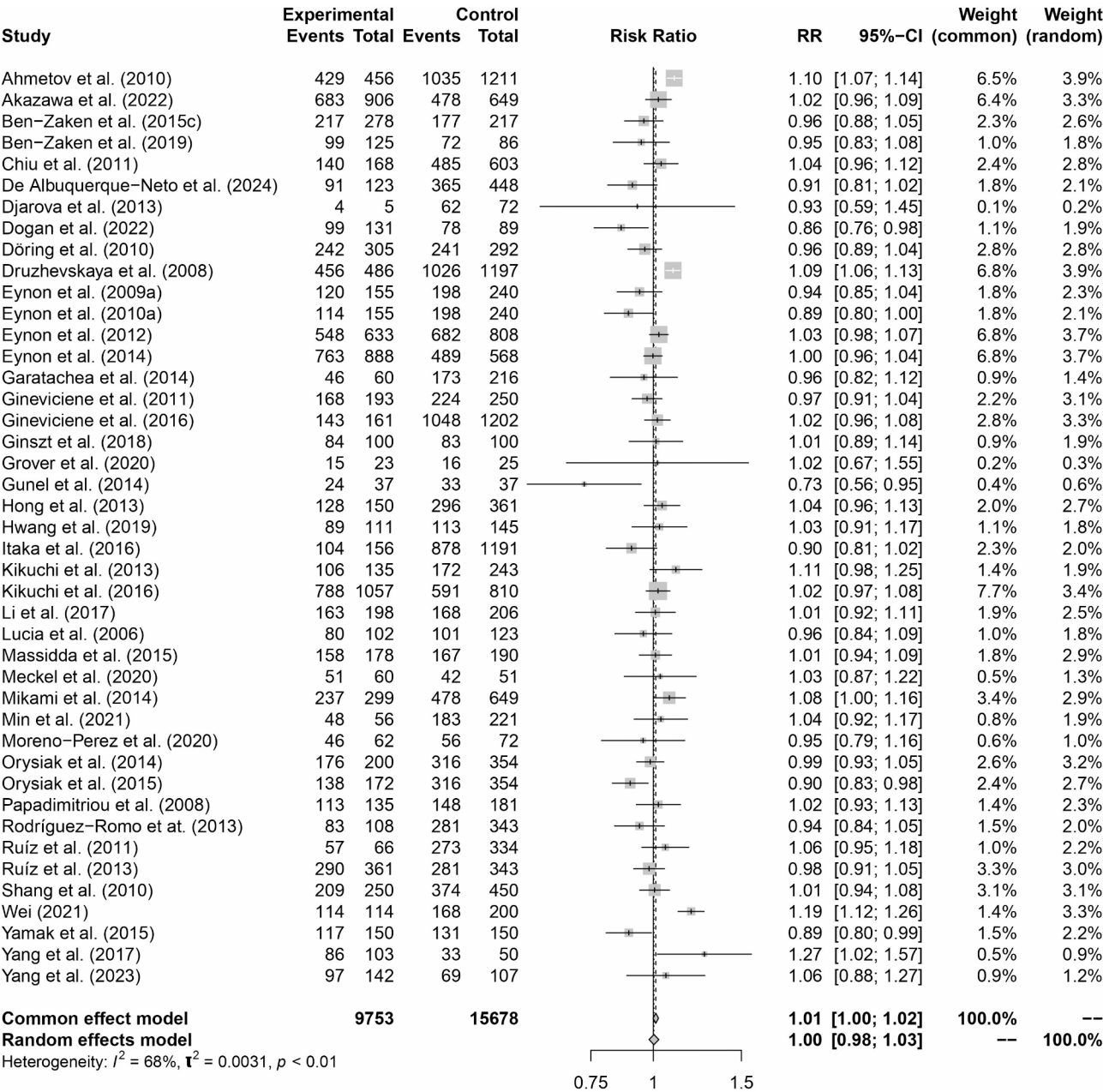


**Fig. 1** Study selection PRISMA flow diagram

Source: Developed by the authors

The meta-analysis found no significant difference comparing athletes and controls regarding the RR+RX (Fig. 2) and XX (Fig. 3) polymorphisms of the ACTN3. Similarly, there was no significant difference between athletes and controls regarding the II and the DD+ID polymorphisms of the ACE gene (Fig. 4). The Egger's test was performed to provide statistical evidence of funnel plot asymmetry. The results indicated publication bias for the performed analysis ( $p < 0.10$ ) regarding the ACTN3

RR (Fig. 5, Panel A), ACTN3 RR+RX (Fig. 5, Panel B), ACE II (Fig. 5, Panel C), and ACE DD+ID (Fig. 5, Panel D), polymorphisms. It is worth mentioning that the asymmetry of the ACE gene (Fig. 5, Panels C and D) is more evident.



**Fig. 2** Forest plot of the meta-analysis comparing the frequency of RR+RX (ACTN3 polymorphism) genotypes in athletes (experimental) and non-athletes (controls)

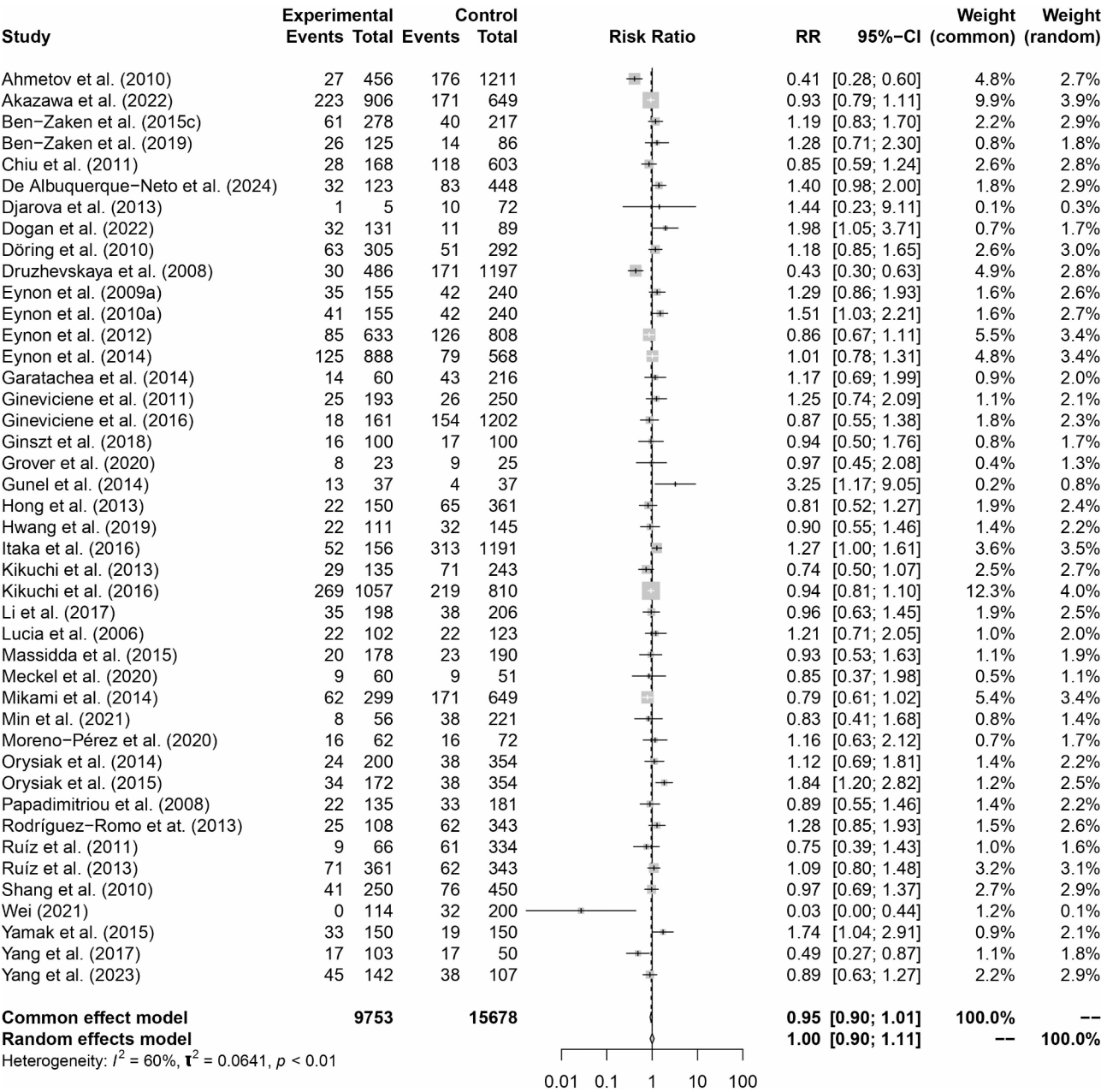
**Discussion**

The objective of this systematic review was to evaluate the potential contribution of genetic factors, which are commonly associated with athletic performance, in identifying sports talents. The comprehension of genetic variations linked to sports performance can offer valuable insights for the detection, selection, and development of individuals with exceptional athletic abilities. Moreover, by gaining a better understanding of the impact of specific polymorphisms and their underlying mechanisms, it becomes possible to optimize individual training

programs. This optimization aims to positively influence physical performance and potentially compensate for any unfavorable environmental or genetic factors.

In this review, we have compiled a list of genetic markers that have the potential to influence the physical performance of athletes in various categories, including endurance, power, speed, and strength. During the meta-analysis, we specifically investigated the variations in frequencies of ACE and ACTN3 polymorphisms among athletes and control groups. We considered different sports categories, sexes, ages, and ethnicities to provide a



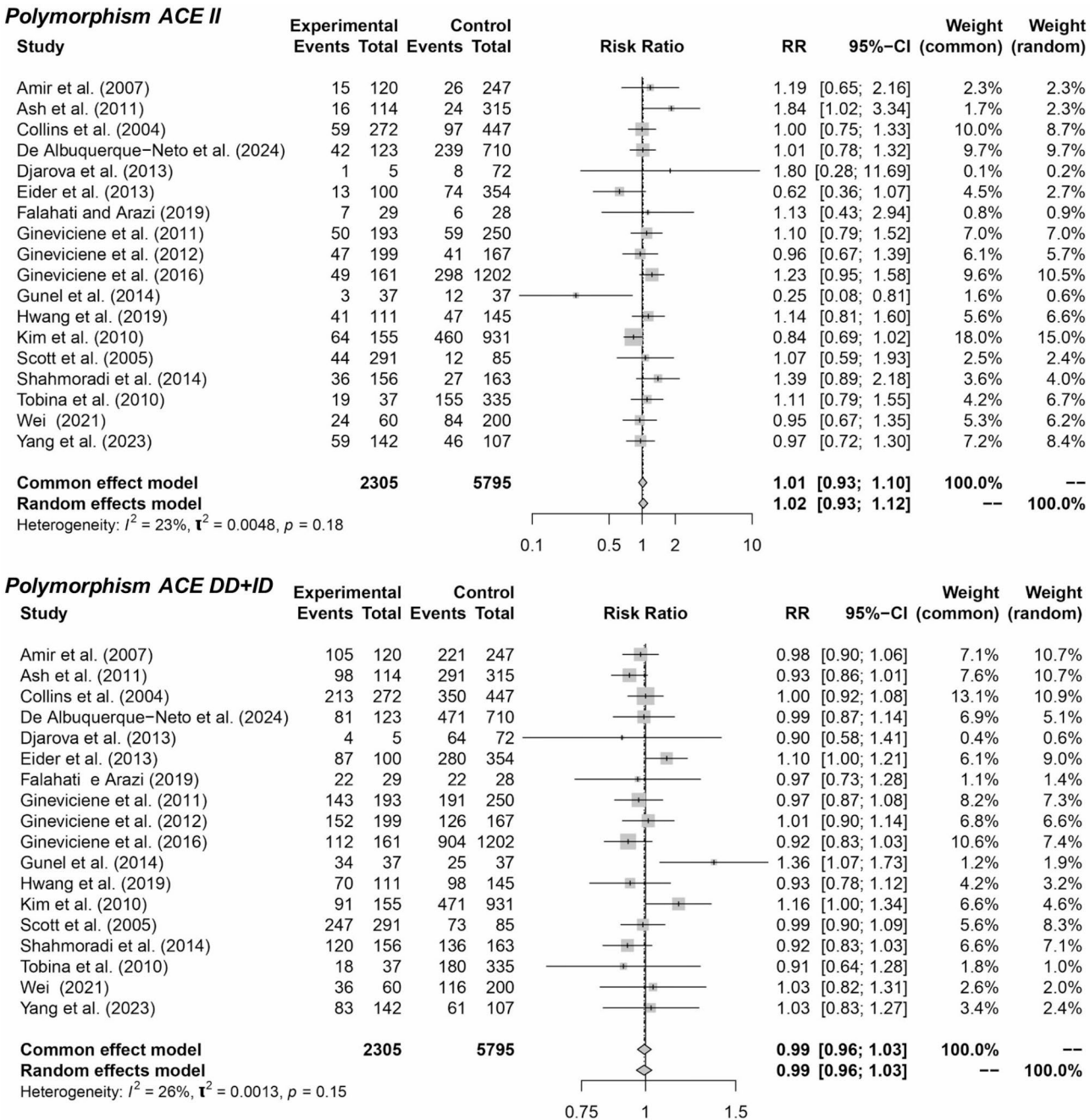


**Fig. 3** Forest plot of the meta-analysis comparing the frequency of the XX genotype of ACTN3 polymorphism in athletes (experimental) and non-athletes (controls)

comprehensive analysis. The selection of these two polymorphisms was based on the abundance of data available from the articles included in this review, ensuring a robust analysis of their potential impact on athletic performance. Our aim was to conduct a comprehensive and rigorous analysis of the association between these polymorphisms and athletic performance. However, due to the heterogeneity in the data available from the included studies, we were unable to evaluate specific factors such as BMI, strength, and respiratory capacity parameters. Additionally, when analyzing the frequencies of ACE

polymorphisms (ID+DD vs. II) and ACTN3 (RR+RX vs. XX), we did not find statistically significant differences between the groups of athletes and controls, as illustrated in Figs. 2 and 3, and 4.

The role of genetic polymorphism in determining athletic performance is widely recognized [27]. Innate factors play a key role in sports performance and related phenotypes such as power, strength, aerobic capacity, flexibility and coordination [28]. However, the search for genetic variants that may confer a greater predisposition to athletic success, taking into account the diversity of



**Fig. 4** Forest plot of the meta-analysis comparing the frequency of the II and DD + ID ACE polymorphisms in athletes (experimental) and non-athletes (controls)

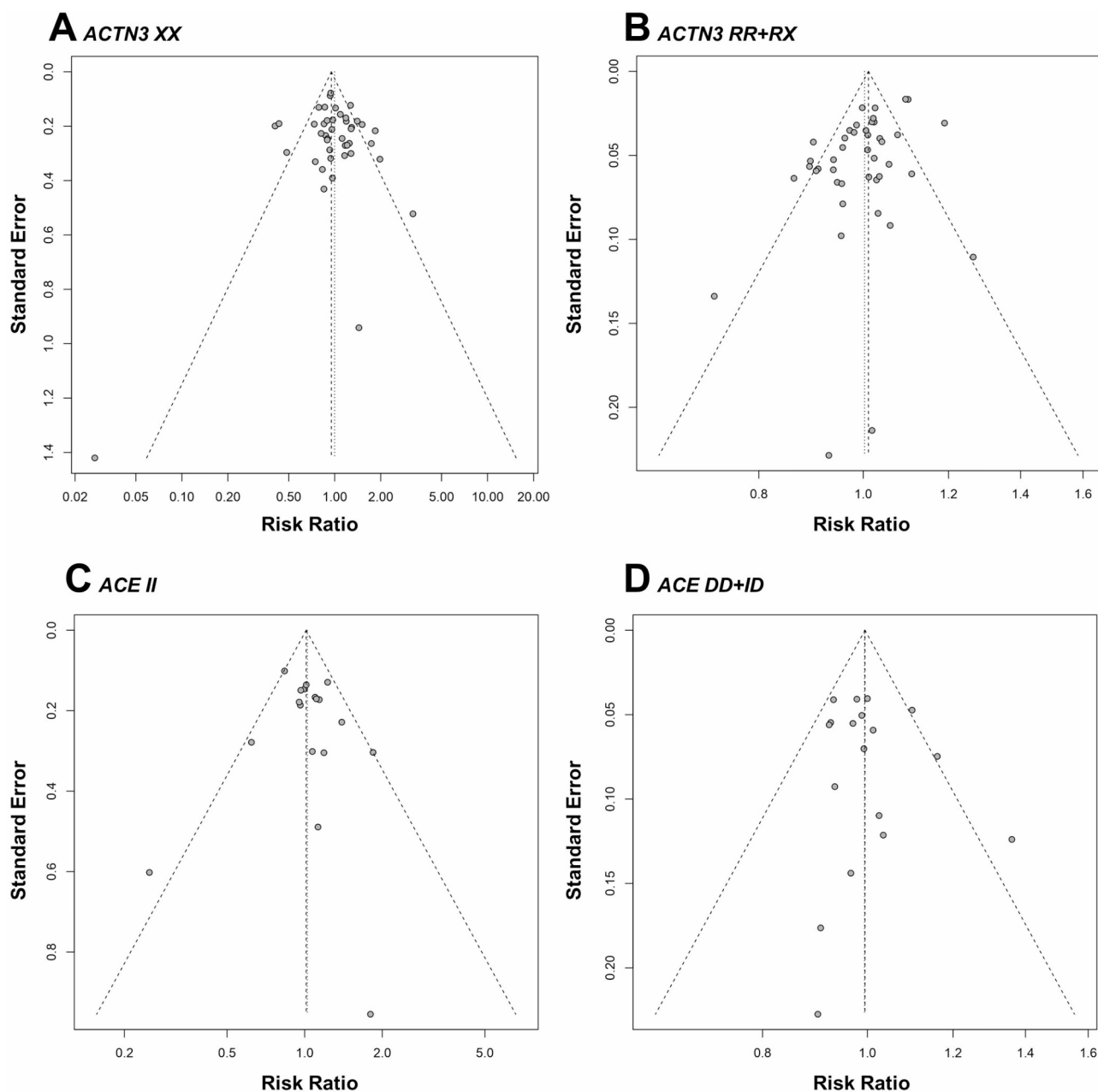
sports modalities, has not yet been adequately replicated [7, 12].

Athletic status, regardless of the type of sport, is influenced by several factors, including heredity [29]. Height, which plays a crucial role in the success of some sports, is estimated to account for approximately 80% of the variation attributed to genetic factors [4]. Likewise, the body type (mesomorphic or ectomorphic) is highly influenced by heritability [30]. However, there is still a gap in

knowledge about the specific genetic variants that contribute to physical performance. Further studies to elucidate this scenario and provide a more comprehensive understanding of the genetic factors involved in athletic performance are suggested.

**ACTN3 and ACE polymorphisms and athlete performance**

In our review, we observed that, of the 50 genes mentioned, 27.0% ( $n=43$ ) referred to ACTN3 and 11.3%



**Fig. 5** Funnel plot of risk ratio versus standard error for the ACTN3 XX (Panel **A**), ACTN3 RR+RX (Panel **B**), ACE II (Panel **C**), ACE DD+ID (Panel **D**), polymorphisms

( $n=18$ ) mentioned ACE. Regarding these genes, several studies have been conducted their influence on physical performance [31–34], as they affect phenotypic characteristics related to athletic performance [32–35]. In humans, the ACTN3 gene is expressed primarily in type II skeletal muscle fibers, which are associated with explosive muscle contractions and strength [36]. ACE, on the other hand, is involved in the regulation of circulatory homeostasis, in growth of skeletal muscles, and cardiovascular functions [37].

The R577X polymorphism of ACTN3 presents three genotypes. The RR and RX, which express the  $\alpha$ -actinin-3 protein, and the XX, which is deficient of that protein [38]. The XX genotype has been frequently associated with resistance phenotype [39, 40], while RR has been more frequent in speed, power and strength athletes [41]. The ACE I/D gene polymorphism has two alleles, namely I (insertion) and D (deletion), which compose the genotypes II, ID and DD. In general, the I allele seems to be associated with endurance sports and the D with power-oriented sports [3, 42].



Several studies have been conducted to examine the influence of the ACTN3 XX genotype on athletic performance in endurance sports [43, 44]. Polish canoe athletes in endurance events (1000 m) were reported to be 2.95 times more likely to have the XX genotype than non-athletic controls [45]. Brazilian swimmers are 1.79 times more likely to belong to the athlete group compared to the control group ( $p=0.04$ ) [46]. Israeli long-distance runners had a higher prevalence of the XX genotype when compared to control groups, short-distance runners, and short- and long-distance swimmers [47].

When analyzing the frequency of ACTN3 R577X polymorphisms in an Israeli population, it was found that the XX genotype is significantly more prevalent in endurance athletes compared to controls ( $p=0.02$ ) and sprinters ( $p=0.002$ ), indicating that the XX genotype and the X allele may not be critical but rather additive for endurance performance [48]. The chances of an endurance athlete harboring the XX genotype are 1.88 times higher (95% CI: 1.07–3.31;  $p=0.028$ ) compared to power athletes with the RR genotype [49].

According to Lucia et al. [50], the literature indicates that the ACTN3 XX polymorphism may confer some advantage in endurance events. Their study with professional Spanish endurance cyclists showed a trend toward a higher frequency of the XX genotype compared to controls, although this difference did not reach statistical significance. The study highlighted a limitation in the small sample size, suggesting the need for future studies with larger samples to increase the statistical power of comparisons between groups.

Yamak et al. [51] also observed a higher frequency of the XX genotype in athletes from nine sports (soccer, basketball, athletics, volleyball, handball, judo, wrestling, taekwondo, rugby) living in the Black Sea region, although no significant difference was found in the distribution when compared to the control group. Similarly, Döring et al. [52] did not find a significant association with endurance performance.

When associating the ACTN3 R577X polymorphism with power status in various sports among Russian athletes, the frequencies of the XX genotype ( $P<0.0001$ ) and the X allele ( $P=0.004$ ) were significantly lower in power-oriented athletes compared to controls [53].

Results from a study involving a rowing competition (endurance-oriented athletes) showed that the frequencies of the ACTN3 577XX genotype and the 577X allele were significantly lower in endurance-oriented athletes compared to controls [54]. The presence of this genotype appears to be detrimental to the speed and power performance of athletes [55]. Additionally, according to Hong and Jin [56], the effect of the XX genotype in Korean endurance/power athletes may be influenced by sex.

The ACTN3 X allele in Chinese runners appears to provide an advantage in endurance performance for female athletes but not for male athletes [57]. Additionally, a significant association was found between the X allele and endurance performance levels in Polish athletes across various sports including 3,000 m to marathon running, cross-country skiing, speed skating (3,000–10,000 m), swimming (400–1,500 m), modern pentathlon, orienteering, biathlon, mountain biking, road cycling, triathlon, and rowing (Olympic, world-class, or national level) [3].

Murtagh et al. [58] investigated different genes, including ACTN3, to determine the maturity status of soccer players by comparing their genetic profile, associated with power and speed performance, according to the predicted age at peak-height-velocity (PHV). They revealed that the frequency of the ACTN3 XX genotype was higher in athletes in the predicted pre-PHV compared to controls. This is due to the fact that the XX homozygote does not produce the structural alpha-actinin-3 protein.

In elite athletes from Lithuania, the ACTN3 X allele has been shown to influence speed and power performance, with those carrying the XX and RX genotypes having greater potential to achieve better results in power-demanding sports [59]. Contrary to these findings, a study involving two Bulgarian mountaineers who reached the summit of Mount Everest revealed that the frequency of the X allele is more predominant in endurance athletes [60].

Considering power performance among elite athletes, the RR genotype of ACTN3 has been overrepresented in European power/sprint athletes (Polish, Russian, and Spanish) [61], more frequent in Israeli sprinters and jumpers [32], and in Greek track and field athletes [62].

Studies examining the relationship between the R577X (rs1815739) polymorphism of ACTN3 and strength performance have indicated associations with lower limb explosive strength in young male Polish athletes [63], long jump and vertical jump performance in Chinese sprint/power athletes [55], middle to long-distance swimming performance ( $\geq 400$  m,  $\leq 1,500$  m) in Chinese athletes, particularly among female swimmers [64], climbing in European athletes (Poland, Russia, Austria) [31], running and jumping in Israeli athletes [32], and hand grip strength in Korean male combat athletes [34].

Dogan et al. [65] indicated that the RR genotype of the ACTN3 gene was more prevalent in both sprinters and long-distance athletes, suggesting that this genotype could serve as a potential biomarker for personalized training programs. On the other hand, Eynon et al. [66] showed that the interaction between the RR genotype of ACTN3+HIF1A Pro/Pro in Israeli individuals is more frequent in sprint athletes compared to endurance athletes and the control group.

The ACTN3 R577X polymorphism appears to have no influence on explosive power performance in elite volleyball players from Spain [67]. According to Moreno-Perez et al. [68], it was not possible to support the hypothesis that the ACTN3 RR genotype would be more frequent in professional players. The authors found that the distribution of the RR, RX, and XX genotypes were statistically similar between professional and non-professional Spanish tennis players. Similarly, regarding national-level Israeli soccer players, no association was found in the frequency of the RR genotype when compared to national-level long-distance runners or sprinters/jumpers [69].

The R allele, responsible for the expression of the ACTN3 protein in fast glycolytic muscle fibers, has shown higher frequencies in Indian power/speed athletes [30], associated with sprint performance in Israeli international-level track and field athletes [48], speed performance in international Taiwanese swimmers [70], strength and power events in Chinese soccer players [71], sports requiring greater muscular strength [72], and power performance in Brazilian athletes [73] compared to controls. Additionally, it was significantly overrepresented in elite Chinese female soccer players compared to controls [37].

When evaluating Japanese track and field athletes, the frequency of the RR+RX genotype of the ACTN3 R577X polymorphism was significantly associated with 100 m sprint ( $p=0.025$ ) [74] and 100–200 m ( $p=0.003$ ) [75] performances when compared to the control groups. Additionally, the R allele has been associated with hand grip strength (left hand) in male athletes [34] and positively correlated with the athletic status of elite Japanese wrestlers [76].

Of the 43 studies mentioning ACTN3, eight showed no significant association with performance parameters, including explosive lower limb muscle strength in basketball players [77] and Spanish volleyball players [67], strength/power in Russian and Lithuanian athletes [78], athletic performance in Japanese [79] and Spanish athletes [80], athletic performance in Italian football and hockey players [81], athletic performance in Korean athletes across 28 different sports [82], and endurance performance in Caucasian athletes (North American, Finnish, and German) [52].

A study that assessed the polygenic profile to determine sprint and power performance in Japanese track and field athletes found no association between the ACE (rs4340) and ACTN3 (rs1815739) polymorphisms and sprint and power performance [83].

Several studies have been conducted to investigate the relationship between ACE allele frequency and performance in elite athletes. In one study, the ACE D allele was more prevalent in strength performance in Polish athletes [84] as well as endurance performance in Iranian

long-distance cycling athletes [85]. Additionally, the ACE I allele has been suggested to be favorable for endurance sport [86]. However, studies carried out with Brazilian athletes did not find an association between the I allele and endurance performance [73]. Furthermore, the ACE polymorphism did not demonstrate an association with sport performance in a study involving Korean athletes [82].

A study that evaluated genetic profiles associated with cardiorespiratory fitness in Spanish male athletes showed that the frequency of the II genotype or the I allele was lower in elite endurance athletes compared to non-athlete controls [87].

These findings indicate the complexity of the relationship between ACE polymorphism and athletic performance, highlighting the influence of genetic, environmental and ethnic factors in this context.

The ACE I/D polymorphism has been consistently associated with the performance of sprint athletes [43]. Moreover, it was found that the high frequency of the I/D genotype and the I allele was related to the success of Bulgarian climbers in high altitude [60]. However, the same genotype was not associated with cardiovascular determinants such as maximal oxygen consumption ( $VO_2$  max), and resting heart rate, systolic and diastolic blood pressure in Iranian soccer players. Importantly, that study was limited by the lack of measurement of serum ACE activity and the small sample size [88].

According to Ash et al. [89], no significant differences were observed in the frequency of the ACE genotype ID between endurance athletes and control groups, indicating that this genotype is not a crucial determinant for elite Ethiopian endurance runners. Similarly, Scott et al. [90] concluded that the ACE I/D and A22982G polymorphisms are not strongly associated with elite endurance athlete status among Kenyans.

In Lithuanian athletes, the ID genotype is more frequent compared to controls and is associated with better results in strength and power tests [59]. In another study, Gineviciene et al. [78] concluded that the II genotype of ACE is more favorable for Russian strength/power athletes (OR=1.71; 95% CI: 1.01–2.92;  $p=0.04$ ), while the ID genotype is preferred among Lithuanian athletes (OR=2.35; 95% CI: 1.10–5.06;  $p=0.028$ ) [78].

The D allele of the ACE I/D polymorphism is associated with better performance in endurance running among elite Japanese runners [91]. Similarly, the I allele has been associated with endurance performance among top finishers in triathlons in South Africa [92]. Additionally, the D allele of the ACE rs4341 polymorphism has been linked as a positive predictor of athletic performance in high-level Polish athletes [3]. These studies demonstrate that ACE gene polymorphisms influence athletic

performance, although this influence may vary depending on the type of sport and the population studied.

The D allele and DD genotype of the ACE I/D polymorphism were overrepresented among elite Israeli marathon athletes, suggesting a possible association between increased ACE activity and the likelihood of being an elite endurance athlete in certain ethnic groups [93]. In contrast, these results were less frequent among high-level Korean power athletes, with individuals carrying the DD genotype having 3.83 times less success in power-oriented sports compared to those with II+ID genotypes [94].

In a study with Brazilian swimmers, the DD genotype of the ACE gene was more frequent among elite athletes compared to sub-elite athletes, showing a higher likelihood of belonging to the elite group with strength phenotypes [46].

Wei [37] investigated the association between ACE I/D and ACTN3 R577X polymorphisms and performance in Chinese female soccer players. The results revealed that there was no difference in the frequency of ACE I/D genotypes between the athletes vs. control (II 40%, ID 46.7%, DD 13.3% vs. II 42%, ID 48%, DD 10%). However, they found that the combination of ACE and ACTN3 genotypes (II/ID/DD+RR /RX) was a synergistic determinant in their athletic performance, as it was associated with higher  $\text{VO}_2$  max values.

Studies that associate ACE I/D and ACTN3 R577X polymorphisms are important because they can guide coaches in selecting the most appropriate exercises and facilitate personalized training based on individuals' genetic characteristics. A study evaluating the effectiveness of different muscular exercises to improve explosive strength, considering ACE and ACTN3 polymorphisms, revealed that individuals with the DD genotype of ACE showed improvements in explosive lower limb strength (measured by the Sargent Test) and sprint speed. On the other hand, individuals with the RR genotype of ACTN3 showed improvements in long jump, the Sargent Test, and power jump. These results indicate that genetics can significantly influence the response to muscle training and improvement in explosive strength variables, highlighting the importance of considering genetic polymorphisms when planning physical training programs [95].

### Genetic polymorphisms and resistance performance

In this review, the majority of the studies associated genetic polymorphisms with endurance performance, which can be determined by several factors, including cardiovascular and pulmonary function, muscle metabolism, and musculoskeletal adaptations [93], food intake,  $\text{VO}_2$  max, cardiac output [96], body mass or composition [97] or blood lactate levels [98], for instance NRF-2 A/C (rs12594956) [99], ACSL1 (rs6552828) in Chinese [100],

ADRB2 (Arg16Gly) [93, 97], ADRB3 (Trp64Arg) [101] and monocarboxylate transporter 1 (MCT1) A1470T (rs1049434) [102]. In a study with Russian rowers, a higher frequency of the MCT1 A1470T (rs1049434) A allele and AA genotype was observed in athletes when compared to controls. Furthermore, an association of the MCT1 A1470T polymorphism (rs1049434) with endurance status and blood lactate level after intensive exercise has been shown [98]. On the other hand, the T allele of the MCT1 T1470A polymorphism (rs1049343) was overrepresented in Polish climbers, when compared to the controls [103]. These results indicate the relevance of these genetic polymorphisms in determining endurance performance in different sport disciplines.

The myostatin gene (MSTN), which is expressed in skeletal muscle cells, play a negative role in the regulation of cell growth [18], being considered promising for the treatment of loss of muscle mass [104], bone mineral density and sarcopenia [105], as well as physical performance parameters [106]. Interestingly, the genetic predisposition to gain muscle mass comes from lower MSTN expressions, which benefits the increasing of strength [107]. Thus, this gene has been associated with phenotypic characteristics of not only muscle strength [108, 109] but also endurance performance [110].

Ben-Zaken et al. [106] investigated the MSTN polymorphism (rs1805086) in Israeli runners and swimmers and found a greater frequency of the MSTN 153R allele in elite long and short distance runners of national level. Furthermore, Ben-Zaken et al. [111] showed that the combined frequency of the mutations of MSTN 153Arg(R) and IGF 1245T (rs35767) was significantly greater in endurance runners compared to sprint runners, short- and long-distance swimmers, and controls. However, the authors stated that athletes with the combined IGF-1-MSTN are not guaranteed to have greater benefits in track and field than in swimming. Likewise, Ginevičienė et al. [18] found an association between the MSNT polymorphism (rs11333758) and endurance performance in a cohort of elite Lithuanian athletes. Results revealed that athletes involved in endurance sports, such as marathon, long-distance swimming and rowing, had a 2.1 times greater chance of having the MSTN deletion (-/-) genotype compared to non-athletic individuals (13.6% vs. 0.8%, OR (95% CI)=2.1 (1.2–3.8),  $p=0.001$ ).

The literature points to an interesting finding regarding the gene for the beta-3 subunit of the nicotinic cholinergic receptor (CHRNA3), which plays a role in regulating protein activity in the brain's emotional centers. It has been observed that the G variant of this gene (rs4950) is significantly more frequent in endurance athletes compared to power athletes ( $p=0.025$ ) [3].

Another polymorphism related to sports performance is BDKRB2 (-9/+9), which plays an important role as an

endothelium-dependent vasodilator [15]. The BDKRB2 -9 allele has been associated with reduced heart rate [10] and improved aerobic endurance in athletes [112]. In our analysis, the BDKRB2 (-9/-9) polymorphism was overrepresented in endurance athletes (Triathletes and Ironman triathletes) compared to male controls [113]. However, our analysis did not confirm these observations in five subsequent studies. Firstly, the allelic and genotypic frequencies of BDKRB2 (-9/+9) showed no significant differences between Polish and Russian athletes compared to controls [114]. In three other studies, variation in the BDKRB2 gene was not associated with swimming performance in well-trained Polish swimmers [115], elite and sub-elite Brazilian swimmers [46], nor with performance in short, medium, or long-distance swimming in Polish athletes of both sexes [116]. Finally, a fifth study found no significant differences among track and field athletes at different competitive levels (national and international) [117].

A study by Hall et al. [96] investigated the association between the PR/SET domain 1 (PRDM1) (rs10499043), glutamate ionotropic receptor NMDA type subunit 3 A (GRIN3A) (rs1535628), and potassium voltage-gated channel subfamily H member 8 (KCNH8) (rs4973706) polymorphisms with  $\text{VO}_2$  max in runners and rugby players. They observed that runners with the PRDM1 T allele had shorter marathon completion time, while rugby athletes were 1.57 times more likely to have the KCNH8 TT genotype, when compared to the control group. These results confirm the hypothesis that the aforementioned alleles and genotypes have an association with athletic performance and improvement of  $\text{VO}_2$  max. Furthermore, the GRIN3A (rs1535628) variant did not associate with running performance, rugby playing position or rugby performance.

Insulin-like growth factor-1 (IGF-1) is associated with the development of muscle mass and strength [118]. It has been observed that the IGF-1 TT genotype (rs35767) presented a significantly higher frequency among Caucasian Israeli athletes at international level when compared to those at national level ( $p < 0.02$ ). This suggests that the TT genotype may have a possible contribution to endurance performance and, in particular, to excellence in strength-related sports [119]. Additionally, IGF 1245T (rs35767) polymorphism may contribute to long-distance running success, although not necessarily to elite performance [111]. On the other hand, Ben-Zaken et al. [120] found no significant association between the IGF-1R 275,124 A>C (rs1464430) and strength or endurance compared when compared to the control group.

Interleukin-6 (IL-6) is a multifunctional cytokine, which, in high circulating concentrations after exercise, is related to training duration and intensity, muscle mass recruitment and resistance capacity [16, 121, 122].

The analysis of the IL-6 polymorphism by Ben-Zaken et al. [121] demonstrated that the CC genotype and the frequency of the C allele were significantly higher in long-distance swimmers compared to long- and medium-distance runners. The authors also suggested that the use of genetic polymorphisms could be an additional tool for identifying and selecting talents in sports, as well as helping to build effective training programs. In another study conducted by Ben-Zaken et al. [123], it was observed that the prevalence of the IL-6 C and IGFBP3C mutations was significantly higher among long-distance swimmers (44%) compared to long-distance runners (21%).

It has been observed that NOS3 is related to the aerobic capacity of athletes [124], strength and endurance exercise performance [125]. Studies indicate that the NOS3 gene is considered a candidate for athlete status and physical performance. The NOS3 (rs1799983) polymorphism, in particular the G894 allele, may favor all types of sports, with a greater predisposition among power-oriented athletes [126]. Furthermore, another study suggested that the Glu allele of the NOS3 G894T polymorphic site (rs1799983) is disadvantageous in female short-distance swimmers, whereas the T allele of the 786T/C polymorphism (rs2070744) may be beneficial for long-distance swimmers [127].

Peroxisome proliferator-activated nuclear receptors (PPARs) have three different forms (PPAR $\alpha$ , PPAR $\beta/\delta$ , and PPAR $\gamma$ ), which are encoded by similar genes (PPARA, PPARG, and PPARG, respectively) [128]. Variants of the peroxisome proliferator activated receptor alpha (PPARA) (rs4253778) and peroxisome proliferator-activated receptor gamma coactivator-1 genes (PPARGC1A) Gly482Ser have been associated with endurance performance and aerobic capacity [129]. In soccer players, the frequency distributions for the PPARA alleles/genotypes (rs4253778) seem to favor resistance to fatigue [58]. In the cohort of endurance athletes, the odds ratio for those with the 'ideal genotype' (PPARD CC+PPARGC1A Gly/Gly+PPARGC1A Gly/Ser) to be elite-level athletes was 8.32 [130].

The PPARA polymorphism (rs4253778) was positively associated with endurance athlete status (GG genotype and G allele) in the elite group of Polish rowers [131]. In three cohorts of elite gymnasts (Polish, Italian and Lithuanian), the PPARA gene polymorphism (rs4253778) showed a higher frequency of the CC genotype when grouped and compared with a control group. However, when the cohorts were analyzed separately, no statistically significant differences were found in any of the analyses [132]. On the other hand, it is important to point out the limitations of the aforementioned study, including a small sample size of European artistic gymnasts, exclusively male and the limited number of polymorphisms analyzed.



Six groups of authors also focused on PPAR genes and their polymorphisms. Maciejewska-Karlowska et al. [133] pointed out that the rs2016529 and rs1053049 polymorphisms of the peroxisome proliferator-activated receptor delta gene (PPARD) were individually associated with elite athletic performance, whereas the PPARD A/C/C haplotype (rs2267668/rs2016520/rs1053049) were significantly underrepresented in athletes compared to controls, suggesting that A/C/C haplotypes may be unfavorable for achieving elite athletic performance. A low frequency of the 482Ser allele of the PPARGC1A gene was observed in Polish and Russian endurance athletes [134]. Ginevičienė et al. [135] suggested that PPARGC1A (rs8192678) and PPARGA (rs4253778) polymorphisms, separately or combined with ACE (I/D), are associated with the performance of male soccer players. Having the AG genotype of NRF2, along with the Gly/Gly+Gly/Ser genotypes of PPARGC1A, could be the “ideal genotype” for endurance athletes [13]. On the other hand, Jin et al. [136] did not find associations between PPARD T294C rs2016520 and PPARGC1A Gly482Ser (rs8192678) polymorphisms and elite athletic status. Likewise, Ben-Zaken et al. [32] found no significant difference in the PPARD polymorphism (rs2016520) when comparing sprinters, jumpers and weight lifters with controls.

A study by Proia et al. [137] demonstrated an association between the PPARGA polymorphism (rs4253778) and endurance performance. In that study, the G allele and the GG genotype were significantly more frequent in soccer players when compared to controls. However, Meckel et al. [69] found no significant difference in the PPARD 294CC polymorphism (rs2016520) when comparing soccer athletes with sprinters/jumpers and long-distance runners.

Studies with the polymorphism G protein subunit beta 3 (GNB3) C825T point out that there is a relationship between this polymorphism and the development of coronary artery disease [138], obesity [139] and heart rate and blood pressure response to resistance training [140]. Our results showed that Israeli athletes with the TT genotype of GNB3 have a 4.49 times higher chance of being endurance athletes [141]. However, its association with athletic status was not confirmed by Sawczuk et al. [142].

Guilherme et al. [73] evaluated 23 polymorphisms in 20 genes in a Brazilian cohort of 656 athletes and 966 non-athletes. They observed that only carriers of the A allele of the AGT M268T gene (rs699) were associated with endurance status. Another gene described in our review was the angiotensin II receptor type 2 (AGTR2), which is a component of the renin-angiotensin system (RAS), involved in the control of the circulatory system and blood pressure [143]. RAS acts on angiotensin II receptor, type 1 (AGTR1) and AGTR2. While AGTR2 can act as a vasodilator, antifibrotic, natriuretic

and anti-inflammatory, AGTR1 has the opposite effects [73]. Mustafina et al. [144] analyzed 15 polymorphisms, including the AGTR2 C allele (rs11091046) and concluded that it may be associated with endurance athlete status, increased slow-twitch muscle fibers, and aerobic performance.

The literature indicates that the vascular endothelial growth factor receptor 2 (VEGFR2) His472Gln polymorphism is associated with elite athlete status, endurance performance in female rowers, and muscle fiber type composition [145]. Eider et al. [84] suggested this polymorphism as a genetic marker in endurance athletes, although more experimental studies involving elite athletes are needed. However, Ercan et al. [146] found no association between the VEGFR2 (rs2305948) polymorphism and performance in Turkish endurance athletes.

Other examples of polymorphisms related to the status of endurance athletes, which make up our results, are the NRF-2 A/C (rs12594956) and solute carrier family 2 member 4 (SLC2A4) (rs5418) polymorphisms. Eynon et al. [66] noted that endurance athletes showed a higher frequency of the AA genotypes of NRF-2 (rs12594956) and CT genotypes of NRF-2 (rs8031031) compared to sprinters and control groups. In a subsequent study, Eynon et al. [99] found that the frequency of the AA genotype of the NRF-2 A/C polymorphism (rs12594956) was significantly higher in endurance athletes compared to strength athletes and controls. Concomitantly, the A allele of the SLC2A4 polymorphism (rs5418) was over-represented in Chinese athletes when compared to controls [147].

### Genetic polymorphisms and strength, power and speed performance

The ability of skeletal muscle to produce force is strongly influenced by genetics [148, 149]. Studies have investigated genetic markers related to strength status, such as the A allele of the leucine-rich pentatricopeptide repeat cassette (LRPPRC) (rs10186876), T allele of the methylmethanesulfonate-sensitivity protein 22-like (MMS22L) (rs9320823), C allele of the methylenetetrahydrofolate reductase (MTHFR) (rs1801131) [150], C allele of the phosphate and actin regulator 1 (PHACTR1) (rs6905419) in Russian weightlifters [16], T allele of the ciliary neurotrophic factor (CNTF) (rs41274853) in Japanese weightlifters [148], G allele of the carnosine Dipeptidase 2 (CNDP2) (rs3764509), C allele of the CNDP2-CNDP1 (rs2346061), A allele of the CNDP1 (rs2887) in Brazilian athletes [151], 12Ala allele of the PPARG (rs1801282) in Polish athletes [152], T allele of the GALNTL6 (rs558129) in Spanish and Russian athletes [153], and the C allele of the M235T polymorphism of AGT in Polish athletes [154]. In addition of these, the hypoxia inducible factor 1 subunit alpha (HIF1A) (rs11549465) [155] and AGTR2

(rs11091046) [156] polymorphisms have been linked to strength.

The fat mass and obesity associated polymorphism (FTO) (rs9939609) is widely recognized for its association with higher body mass indexes (BMI) and body fat content [157]. In a study carried out with elite athletes from two cohorts (Brazil and Russia), it was observed that the polymorphism FTO T>A (rs9939609) was overrepresented in heavier athletes [158]. Therefore, individuals carrying the TT genotype of the FTO polymorphism (rs9939609) may have advantage in succeeding in sports such as swimming. As a matter of fact, anthropometry and body composition, influenced by the FTO A/T polymorphism, play a crucial role in sports performance [159]. Furthermore, another study, carried out in the Russian population, showed a significant effect of the interaction between the FTO rs9939609 and physical activity, specifically aerobic sports activities, on BMI of young amateur and professional athletes [160]. However, in a study that compared European athletes from Spain, Poland and Russia, no association was found between FTO allele and genotype frequencies and elite athletic status [161].

According to Wojciechowicz et al. [162], the apolipoprotein E polymorphism (APOE) TC (rs429358) was overrepresented in power athletes. Furthermore, polymorphisms of the KIF6 (rs20455) and APOE (rs7412) genes were associated with power performance, but not with endurance performance, suggesting a possible relationship between KIF6 and APOE, or interactions at the molecular level, in modulating strength performance.

When analyzing the solute carrier family 6 member 2 polymorphism (SLC6A2) (rs1805065), Guilherme et al. [163] verified that the presence of the T allele may decrease the chance of the athlete being involved in explosive physical tasks. although there seems to be an association of this polymorphism with power status. For Ginevičienė et al. [164], the genotype and/or allele frequencies of the c.\*800A>G (rs8111989) in the muscle-specific creatine kinase (CKM) gene do not seem to influence the performance of weightlifters and powerlifters from Russia and Lithuania. The SNPs of CKM (rs344816, rs10410448, rs432979, rs1133190, rs7260359, rs7260463, rs4884) were not associated with the endurance performance of elite athletes [110]. Additionally, similar results were found in athletes whose anaerobic energy pathways are used to determine the success of elite athletes. Furthermore, the results indicate that G allele carriers of the CKM gene (rs8111989) are not predisposed to excel in power and strength sports.

A previous study demonstrated that the IGF-1 TT genotype (rs35767) is associated with endurance performance in Israeli track and field athletes [119]. However, regarding decathletes, Ben-Zaken et al. [165] suggested

that the IGF1 TT (rs35767) and IGF-2 GG (rs680) genotypes are associated with better speed performance. These findings indicate that the IGF-1 TT genotype may influence athletic performance in different aspects such as endurance and speed. When analyzing the polymorphism (rs1464430) of the insulin-like growth factor receptor (IGF-1R) in Israeli elite athletes, Ben-Zaken et al. [120] suggested that the IGF-1R genotype may be beneficial for endurance-related sport, but not for elite endurance performance.

In a study that evaluated the frequency of the IGF2 polymorphism (rs680) in Israeli athletes and controls, the authors found a significant difference in the frequency of the GG genotype among runners when compared to weightlifters, suggesting a beneficial association of this polymorphism with speed rather than strength-related sports. However, no significant differences were found in relation to carriers of the GG genotype when comparing distance runners, swimmers (short and long distance), weightlifters and controls [166]. On the other hand, the G allele of this polymorphism may be associated with strength status in judo athletes [79].

Catechol-O-methyltransferase (COMT) is a gene involved in the metabolism of catecholamines, including dopamine, epinephrine, and norepinephrine [167]. A study carried out with mixed martial arts fighters suggested that these individuals have significantly higher frequency of the GG genotype of the COMT polymorphism (rs4680) than non-athletes [168]. However, Zmijewski et al. [169] showed no association between COMT with elite swimming status. The lack of association to establish the role of COMT polymorphism in athletes can be explained by the limitations of the previously mentioned study and solved with future replication studies.

The rs1799725 polymorphism, related to a variation in the SOD2 gene, is responsible for encoding the enzyme superoxide dismutase 2 (MnSOD). This polymorphism has been reported to be represented by the C (which codes for the amino acid alanine (Ala)) and the T allele (which codes for the amino acid valine (Val)) [170]. In a meta-analysis study, the MnSOD polymorphism (rs1799725) was identified as an influential factor in power phenotype [171]. Ben-Zaken et al. [172] evaluated Israeli endurance and power athletes and found that carriers of the MnSOD Ala/Ala genotype (rs1799725) had significantly higher results ( $p<0.05$ ) among elite athletes at international and Olympic levels compared to national level athletes. The Ala allele, on the other hand, presented a significantly higher frequency among endurance and power athletes compared to controls ( $p<0.001$ ). Interestingly, endurance and power athletes showed similar allelic distribution, suggesting that the beneficial effect of MnSOD is not mediated through aerobic pathways.

Instead, it may be related to reactive oxygen species, mitochondrial biosynthesis and muscle hypertrophy.

Genetic markers linked to antioxidant action have shown association with power athletes [170]. The ALDH2 rs671 polymorphism has been studied in relation to human diseases, particularly associated with cardio-metabolic risk factors [173]. Regarding physical performance, it has been associated with athletic status and muscular strength in a Japanese population [174]. However, our results did not confirm the relationship between the ALDH2 rs671 polymorphism and athletic status in power/strength athletes [175].

Other studies associate genetic polymorphisms with power athletic status, such as: MCT1 D490E (T allele), AGT M268T (G allele), PPARG (C allele), PGC1A G482S (C allele), VEGFR2 Q472H (T allele), NOS3 C/T (T allele) and ACTN3 R577X (R allele) in Brazilian athletes [73], AGT M235T (CC genotype) in Spanish athletes [176], NOS3 rs2070744 (TT genotype and T allele) in Spanish athletes [125], and PPARGC1A (Ser/Ser genotype) in weightlifters from two European cohorts [78] and MCT1 T1470A (AA genotype) in Japanese athletes [177].

Rs1867785/rs11689011 polymorphisms of the endothelial PAS domain protein 1 (EPAS1) were found to be strong predictors of sprint/power athletic status. Additionally, the interaction between the rs1867785, rs11689011, and rs4035887 polymorphisms may contribute to success in sprint/power athletic performance [178]. Other polymorphisms associated with elite status in sprint/ power sports were mentioned in our review, including AMPD1 (C allele) [179], the ADRB2 alleles (Gly16 and Gly27 allele) [180], MCT1 A147T (TT genotype) [181], the genotype TT from CNTFR (rs41274853) [182] and the A allele from ACVR1B (rs2854464) [183], higher frequency of the C allele of AMPD1 [179] and lower frequency of the T allele of AMPD1 (C34T) [184].

The findings presented in this review provide evidence to support the hypothesis that athletic performance may be influenced by genetic factors in different sports. However, it should be noted that most studies state that their studies are limited by the sample size, quality of genotype/phenotype measurement and the number of polymorphisms analyzed.

The limitations of the study should be considered in the interpretation of the results, since the case-control studies included in the review present considerable variability in their findings. This heterogeneity complicates drawing definitive conclusions about the specific influence of genetic polymorphisms on performance parameters such as muscle strength, endurance, speed, and respiratory capacity. Differences in study design, participant characteristics, and measurement methods contribute to this variability. Additionally, many of the analyzed studies have small sample sizes, which limits statistical power

and generalizability, increasing the risk of Type II errors and potentially leading to overestimation or underestimation of genetic effects on athletic performance. There is also inconsistency in how performance parameters were measured and reported across studies, with frequently divergent definitions and evaluations for endurance, strength, speed, and power, which complicates direct comparisons and may obscure true associations between genetic polymorphisms and performance outcomes. Variability in sports modalities may also influence how genetic polymorphisms affect performance. The inclusion of a broad range of sports, from endurance-based to strength-based disciplines, complicates the generalization of findings. Lastly, most of the included studies were cross-sectional, assessing genetic polymorphisms and performance at a single point in time; longitudinal studies are needed to better understand how genetic factors influence the development and progression of performance throughout an athlete's career.

#### Future perspectives

Genetic factors have been proposed as potential determinants of sports talents or the traits associated with them. In our review, we examined studies that linked genetic polymorphisms with resistance, strength, power, and speed performance. These studies provided valuable insights that may assist athletes and coaches in understanding the factors that contribute to athletic performance, as some findings displayed promising data. A large number of articles describe athletic status but actually specify improvements in activities performed in sports. However, it is important to acknowledge that our study evaluated only a subset of the numerous polymorphisms associated with performance, and other factors such as environmental influences and unexplored genetic variants could have influenced the results. Therefore, our current understanding of this subject is limited, and further research is necessary to establish the utility of genetic polymorphisms in the identification of sports talents. Future studies should aim to establish more precise associations between genetic profiles and sports talents. This research can significantly facilitate the talent identification and development process by providing a more comprehensive understanding of the genetic factors influencing athletic performance.

#### Conclusion

This study aimed to investigate the influence of genetic polymorphisms on the performance of sports talents compared to non-athletes. Our results indicated that the ACE I/D and ACTN3 R577X polymorphisms are the most extensively studied in the literature. We found that the ACTN3 XX genotype is frequently associated with an endurance phenotype, while the RR genotype tends

to be more common among speed, power, and strength athletes. Regarding the ACE polymorphism, the I allele is associated with endurance sports, while the D allele is more related to power-oriented sports. Different genetic polymorphisms play crucial roles in influencing athletic performance across various disciplines, and conducting studies to identify and select sports talents is recommended to confirm associations in diverse populations and sports. However, we observed heterogeneity in the results of the analyzed studies, making it challenging to evaluate specific factors related to physical performance. Furthermore, many studies that associate polymorphisms with athletic status presented inconsistent data when considering performance parameters such as endurance, strength, speed, and power. These inconsistencies may be attributed to the unique characteristics of each sports discipline, as well as the use of small sample sizes. More research is needed to provide a more precise confirmation of the influence of genetic polymorphisms on elite athletes in various contexts and sports.

#### Abbreviations

ACE	Angiotensin converting enzyme
ACTN3	$\alpha$ -actinin-3
ACVR1B	Activin A receptor type 1B
ADRB2	$\beta$ -adrenergic receptors
AGT	Angiotensinogen
AGTR1	Angiotensin II receptor, type 1
AGTR2	Angiotensin II receptor, type 2
AMPD1	Adenosine monophosphate deaminase 1
APOE	Apolipoprotein E
BDKRB2	Bradykinin receptor B2
BMI	Body mass index
BVS	Virtual health library
CHRN3	Cholinergic receptor nicotinic beta 3 subunit
CKM	Muscle-specific creatine kinase
CNDP1	Carnosine dipeptidase 1
CNDP2	Carnosine dipeptidase 2
CNTF	Ciliary neurotrophic factor
CNTFR	Ciliary neurotrophic factor receptor
COMT	Catechol-O-methyltransferase
CUMED	National Information Center for Medical Sciences of Cuba
DeCS	Health sciences descriptors
EPSA1	Endothelial PAS domain protein 1
FTO	Fat mass and obesity associated
GALNTL6	N-acetylgalactosaminyltransferase-like 6 gene
GNB3	G protein subunit beta 3
GRIN3A	Glutamate ionotropic receptor NMDA type subunit 3 A
HIF1A	Hypoxia inducible factor 1 subunit alpha
IBECs	Spanish Bibliographic Index in Health Sciences
IGF-1R	Insulin-like growth factor 1 receptor
IGFBP3	Insulin like growth factor binding protein 3
IGFBP3C	Mutation of insulin like growth factor binding protein 3
IGF-1	Insulin-like growth factor 1
IGF-2	Insulin-like growth factor 2
IL-6	Interleukin-6
IL-6C	Mutation of interleukin-6
KCNH8	Potassium voltage-gated channel subfamily H member 8
KIF6	Kinesin family member 6
LILACS	Latin American and Caribbean Literature in Health Sciences
LRPPRC	Leucine-rich pentatricopeptide repeat cassette
MCT1	Monocarboxylate transporter 1

Medline	Medical Literature Analysis and Retrieval System Online
MeSH	Medical subject headings
MMS22L	Methyl methanesulfonate-sensitivity protein 22-like
MnSOD	Superoxide dismutase 2
MSTN	Myostatin
MTHFR	Methylenetetrahydrofolate reductase
NOS3	Nitric oxide synthase 3
NRF-2	Nuclear respiratory factor 2
OR	Odds ratio
PGC1A	Peroxisome proliferator-activated receptor $\gamma$ coactivator 1-alpha
PHACTR1	Phosphate and actin regulator 1
PPAR $\gamma$ or PPARG	Peroxisome proliferator-activated receptor gamma
PPARGC1A	Peroxisome proliferator-activated receptor gamma coactivator-1 alpha
PPARs	Peroxisome proliferator-activated nuclear receptors
PPAR $\alpha$ or PPARA	Peroxisome proliferator activated receptor alpha
PPAR $\beta/\delta$ or PPARD	Peroxisome proliferator-activated receptor delta
PRDM1	PR/SET Domain 1
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analysis statement
SCIELO	Scientific Electronic Library Online
SLC2A4	Solute carrier family 2 member 4
SLC6A2	Solute carrier family 6 member 2
STREGA	Strengthening the Reporting of the Genetic Association
STROBE	Reporting of observational studies in epidemiology
VEGFR2	Vascular endothelial growth factor receptor 2
VO <sub>2</sub> max	Maximal oxygen consumption
WPRIM	Western Pacific Region Index Medicus

#### Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s13102-024-01001-5>.

Supplementary Material 1 (S1): Includes a comprehensive overview of the study's key components: Table 1 categorizes the selected articles according to polymorphism type, sample size, main findings, authorship, and year of publication; Table 2 details the characteristics of the participants analyzed; and Table 3 provides a quality assessment of the studies based on the Strengthening the Reporting of Genetic Association Studies (STREGA) Statement

Supplementary Material 2 (S2): Outlines the search strategy, lists articles included and excluded from the study, presents the STREGA checklist, and identifies the articles incorporated into the meta-analysis focusing on ACTN3 and ACE polymorphisms

Supplementary Material 3 (S3): Encompasses the Modified STROBE quality score systems applied in the study

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#### Author contributions

Conceptualization, CPF, VOS, and MAPS; methodology, preparation of Figs. 1, 2, 3, 4 and 5, VOS and CPF; formal analysis, CPF, RGT, and RCM; investigation, CPF, SSA, and MAPS; writing – original draft preparation, CPF; writing – review and editing, CPF, VOS, and RGT; supervision, MAPS and SSA; project administration, MAPS. All authors have read and agreed to the published 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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