

Unraveling the Roles of ACTN3, ACE, and PPARGC1A Genes in Power Performance: A Systematic Review and Meta-Analysis

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ABSTRACT

Background:

Power performance is a crucial component of athletic success, particularly in sports requiring explosive movements. Genetic polymorphisms such as *ACTN3*, *ACE*, and *PPARGC1A* have been implicated in influencing muscle strength, metabolism, and efficiency. The *ACTN3* RR genotype supports fast-twitch muscle fiber function, *ACE* DD enhances muscle efficiency, and *PPARGC1A* SerSer improves energy metabolism. This study aimed to compare the impact of these genotypes on power performance to address existing research gaps and support the development of personalized athletic training and rehabilitation strategies.

Methods:

A systematic search was conducted in PubMed, Scopus, and Web of Science for studies published between 2015 and 2025 investigating the association of *ACTN3*, *ACE*, and *PPARGC1A* polymorphisms with power athletic status. Ten *ACTN3*, four *ACE*, and four *PPARGC1A* studies were included, comprising 2,530 power athletes and 6,652 controls. Data were analyzed using Review Manager to calculate pooled odds ratios (ORs) with 95% confidence intervals (CIs) under a random-effects model. Study quality and heterogeneity were assessed by three independent reviewers.

Results:

The pooled ORs [95% CI] for athletes versus controls were 1.32 [1.15–1.53] for *ACTN3* RR, 1.08 [0.69–1.67] for *ACE* DD, and 1.20 [0.79–1.81] for *PPARGC1A* CC. The *ACTN3* RR genotype showed a significant association with power performance, supported by low heterogeneity and narrower confidence intervals.

Conclusions:

The *ACTN3* RR (*rs1815739*) variant plays the most significant role in enhancing muscle strength and speed, suggesting its importance in identifying genetic potential for power-based athletic excellence.

Keywords: *ACTN3*, *ACE*, *PPARGC1A*, power, genetic polymorphisms, athletic performance.

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INTRODUCTION

Power performance, defined as the capacity to produce maximal force within a brief time frame, is a key determinant of success in explosive disciplines such as sprinting, weightlifting, and throwing events. Beyond training and environmental factors, genetic variation has a substantial influence on athletic traits, including muscle strength, speed, and physiological adaptations. Among the most studied genes related to athletic performance, *ACTN3*, *ACE*, and *PPARGC1A* have demonstrated strong associations with muscular function and energy metabolism. The *ACTN3* R577X (*rs1815739*)

polymorphism encodes α -actinin-3, a structural protein expressed predominantly in fast-twitch muscle fibers. Individuals with the *ACTN3* RR genotype retain functional α -actinin-3 and exhibit superior sprint and power abilities compared to those with the XX genotype, who lack the protein and show enhanced oxidative metabolism instead.^{1,2}

Similarly, the *ACE* I/D polymorphism has been linked to muscle efficiency and cardiovascular adaptation. The *ACE* DD genotype is associated with higher angiotensin-converting enzyme activity and enhanced power-oriented performance, while the II genotype is often linked to endurance traits.^{3,4} The *PPARGC1A* Gly482Ser (rs8192678) variant regulates mitochondrial biogenesis and energy homeostasis. Its SerSer genotype has been associated with increased oxidative capacity and improved energy metabolism, potentially influencing both power and endurance outcomes.^{5,6}

Despite these insights, existing studies remain inconsistent due to small sample sizes, heterogeneous athletic definitions, and limited comparative analyses among these genes. Furthermore, to date, no comprehensive systematic review and meta-analysis has simultaneously evaluated the relative impact of *ACTN3*, *ACE*, and *PPARGC1A* polymorphisms on power performance.

METHODS

Study Design

This systematic review and meta-analysis was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) and Cochrane Library guidelines. The study aimed to identify and synthesize available evidence on the association between *ACTN3* (R577X), *ACE* (I/D), and *PPARGC1A* (rs8192678) polymorphisms and power performance among athletes.

Search Strategy

Electronic databases including PubMed, Scopus, and Web of Science were systematically searched for articles published between 2014 and 2024. The search strategy combined the terms “*ACTN3*,” “*ACE*,” “*PPARGC1A*,” “power,” “gene polymorphism,” and “athletic performance.” Three independent reviewers screened, extracted, and verified the data to minimize selection bias and ensure accuracy.

Eligibility Criteria

Studies were included if they met the following criteria: (1) observational design; (2) comparison between power athletes and non-athlete controls; (3) evaluation of at least one of the targeted genetic polymorphisms; (4) published in English; and (5) peer-reviewed. Exclusion criteria comprised non-observational studies, non-English publications, and articles without peer review.

Data Extraction and Variables

Data extraction focused on the genotypic distribution of *ACTN3* RR, *ACE* DD, and *PPARGC1A* CC (SerSer) variants among athletes and controls. Extracted information included author, publication year, population characteristics, genotyping methods, and allele frequencies.

Statistical Analysis

All statistical analyses were performed using Review Manager (RevMan) version 5.4. Pooled odds ratios (ORs) and 95% confidence intervals (CIs) were calculated to assess the strength of association between each genotype and power performance. Heterogeneity was evaluated using Chi-square (Q test) and I^2 statistics, applying a random-effects model when appropriate. Effect sizes and confidence intervals were prioritized over p-values to interpret findings with greater precision. All statistical terms, abbreviations, and symbols are defined upon first mention.

RESULTS

Study Selection

The study selection process followed the PRISMA guidelines (Figure 1). A total of 910 articles were initially identified from PubMed, Scopus, and Web of Science databases, including 442 *ACTN3*, 142 *PPARGC1A*, and 326 *ACE* studies. After the removal of 383 duplicate records, 527 studies were

screened by title and abstract. Of these, 403 articles were excluded because they were review papers, guidelines, or irrelevant to the research question.

A total of 124 full-text articles were assessed for eligibility, and 106 studies were excluded due to an unsuitable study design, non-athlete populations, or absence of allele-specific data. Finally, 18 studies were included in the systematic review and meta-analysis, consisting of 10 ACTN3, 4 ACE, and 4 PPARGC1A studies.

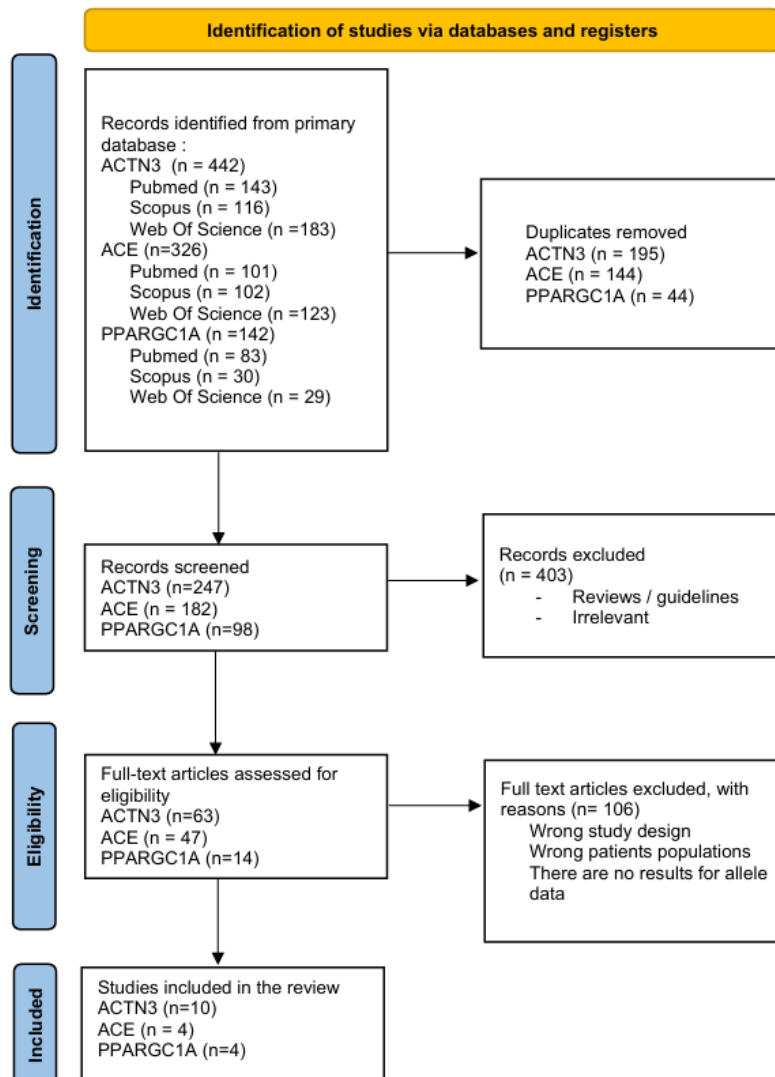


Figure 1. PRISMA Flow Diagram

Study Design and Participants

All included studies used observational case–control designs, comparing power athletes (e.g., sprinters, jumpers, weightlifters) with non-athlete control groups. The total sample comprised 2,530 power athletes and 6,652 controls, with participants originating from various ethnic backgrounds, including European, Asian, and mixed populations.

The athletes were classified according to national or international competition levels, ensuring that performance-based inclusion was standardized across studies. Each study used genotyping methods (PCR or real-time PCR) to identify allelic variations of ACTN3 R577X (rs1815739), ACE I/D (rs4646994), and PPARGC1A Gly482Ser (rs8192678).

Table 1. Study Characteristics ACTN3 for Athlete and Non-athlete

No	Author (Year)	Population Athletes	Population Control	Sample Size (Athletes/Control)	Study Design	Genotype
1.	Akkoc et al. (2020)	Asian; male; female; Turkish, athletes	Asian; male; female; Turkish	26/140	Cross-sectional study	RR, RX, XX
2.	Balberova et al. (2023)	European; male; female; athletes	European; male; female	40/50	Cross-sectional study	RR, RX, XX
3.	Ben-Zaken et al. (2019)	Asian; male; female; Israel; athletes	Asian; male; female; Israel	125/86	Cross-sectional study	RR, RX, XX
4.	Ginevicene et al. (2016)	European; male; female; Caucasians; athletes	European; male; female; Caucasians	51/250	Case-control	RR, RX, XX
5.	Grover et al. (2020)	Asian; male; female; Indian; athletes	Asian; male; female; Indian	23/25	Case-control	RR, RX, XX
6.	Guilherme et al. (2017)	America; male; female; Brazilian; athletes	America; male; female; Brazilian	328/966	Case-control	RR, RX, XX
7.	Kikuchi et al. (2015)	Asian; male; female; Japanese; athletes	Asian; male; female; Japanese	627/810	Case-control	RR, RX, XX
8.	Massidda et al. (2015)	European; male; Caucasians; athletes	European; male; Caucasians;	64/190	Cross-sectional study	RR, RX, XX
9.	Peplonska et al. (2016)	European; male; female; Caucasians (Polish); athletes	European; male; female; Caucasians (Polish)	188/451	Case-control	RR, RX, XX
10.	Yang et al. (2017)	Asian; male; female; Chinese (Han); athletes	Asian; male; female; Chinese (Han)	59/50	Case control study	RR, RX, XX

Table 2. Study Characteristics ACE for Athlete and Non-athlete

No.	Author (Year)	Population Athletes	Population Control	Sample Size (Athletes/Control)	Study Design	Genotype
1.	Akkoc et al. (2020)	Asian; male; female; Turkish, athletes	Asian; male; female; Turkish	26/140	Cross-sectional study	DD, ID, II

2.	Fluek et al. (2019)	European; male; female; Caucasians; athletes	European; male; female; Caucasians	17/63	Cross-sectional study	DD, ID, II
3.	Gineviciene et al. (2016)	European; male; female; Caucasians; athletes	European; male; female; Caucasians	51/250	Case-control	DD, ID, II
4.	Peplonska et al. (2016)	European; male; female; Caucasians (Polish); athletes	European; male; female; Caucasians (Polish)	188/451	Case-control	DD, ID, II

Table 3. Study Characteristics PPARGC1A for Athlete and Non-athlete

No.	Author (Year)	Population Athletes	Population Control	Sample Size (Athletes/Control)	Study Design	Genotype
1.	Gineviciene et al. (2016)	European; male; female; Caucasians; athletes	European; male; female; Caucasians	51/250	Case-control	Gly/Gly, Gly/Ser, Ser/ser
2.	Guilherme et al. (2017)	America; male; female; Brazilian; athletes	America; male; female; Brazilian	328/966	Case-control	Gly/Gly, Gly/Ser, Ser/ser
3.	Jin et al. (2015)	Asian; male; female; Korean; athletes	Asian; male; female; Korean; athletes	111/145	Cross-sectional study	Gly/Gly, Gly/Ser, Ser/ser
4.	Peplonska et al. (2016)	European; male; female; Caucasians (Polish); athletes	European; male; female; Caucasians (Polish)	188/451	Case-control	Gly/Gly, Gly/Ser, Ser/ser

Meta-Analysis of ACTN3 R577X (rs1815739)

Ten studies, encompassing 1,570 athletes and 3,936 controls, were included in the ACTN3 meta-analysis. The pooled odds ratio (OR) demonstrated a significant association between the ACTN3 RR genotype and power performance (OR = 1.33; 95% CI: 1.10–1.62; $p = 0.003$). Heterogeneity analysis showed moderate variability ($I^2 = 36\%$), indicating good consistency among studies. These findings suggest that the RR genotype enhances fast-twitch muscle fiber performance, favoring explosive power-related athletic ability.

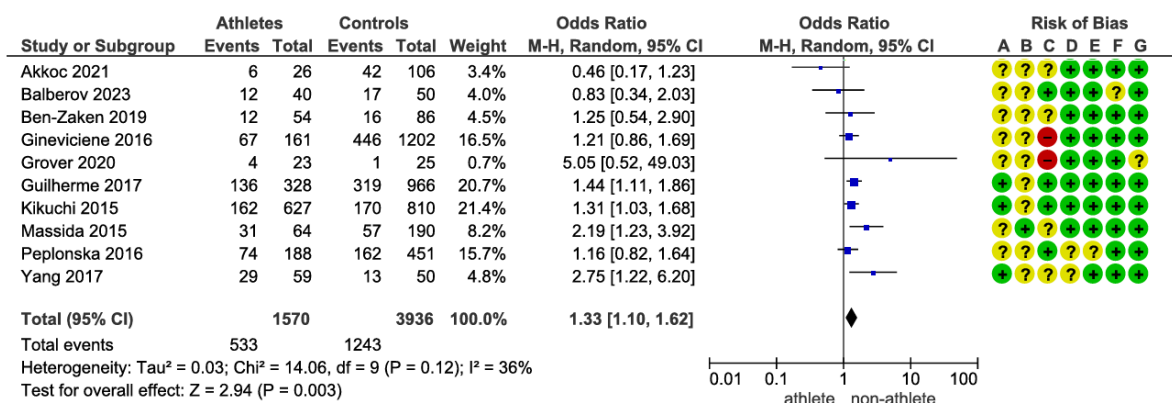


Figure 2. Forest Plot of ACTN3

Meta-Analysis of ACE I/D (rs4646994)

Four studies involving 282 athletes and 904 controls assessed the association between the ACE DD genotype and power performance. The pooled estimate showed no significant relationship (OR = 0.98; 95% CI: 0.58–1.63; p = 0.93) with moderate heterogeneity (I² = 52%). This indicates that the ACE polymorphism may not play a major independent role in determining power-based athletic status.

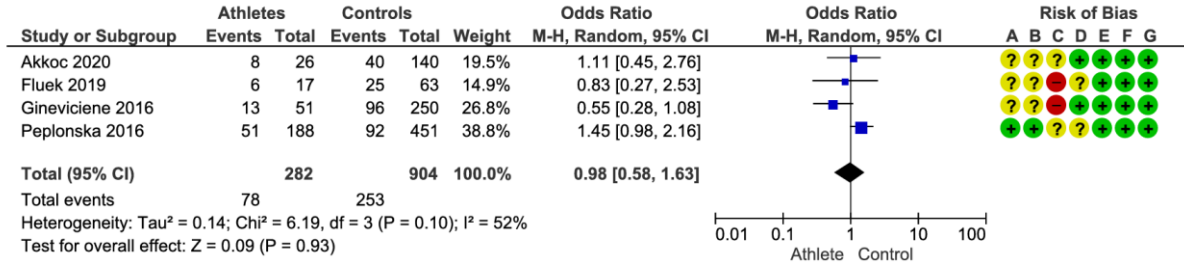


Figure 3. Forest Plot of ACE

Meta-Analysis of PPARGC1A Gly482Ser (rs8192678)

Four studies including 678 athletes and 1,812 controls evaluated the impact of the PPARGC1A SerSer (CC) genotype. The pooled OR revealed no statistically significant association (OR = 1.20; 95% CI: 0.79–1.81; p = 0.39) and moderate heterogeneity (I² = 45%). Although not significant, the trend toward increased OR suggests a potential influence of PPARGC1A on energy metabolism and mitochondrial biogenesis related to power performance.

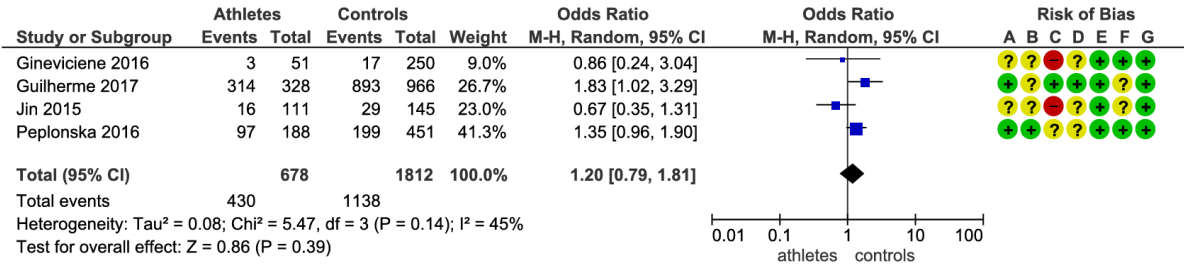


Figure 4. Forest Plot of PPARGC1A

Risk of Bias Assessment

The risk of bias evaluation, performed using the Cochrane tool, indicated an overall low to moderate risk of bias across the included studies. Most studies demonstrated adequate randomization, data completeness, and selective reporting control. However, some uncertainty remained in domains related to blinding and allocation concealment (Figure 2–4). No publication bias was detected upon visual inspection of the forest plots and funnel distributions.

DISCUSSION

The pooled analysis revealed a significant association between the ACTN3 R577X polymorphism and athletic performance, with an overall OR of 1.33 [95% CI: 1.10–1.62; $p = 0.003$]. The direction of the effect observed in most included studies^{7,8} consistently favored the RR genotype among power-oriented athletes. The current forest plot demonstrates that despite minor variations across studies, the cumulative evidence supports the biological role of ACTN3 in enhancing fast-twitch muscle fiber contractility through α -actinin-3 expression in type II fibers. This finding aligns with previous reports⁹ indicating that RR carriers exhibit superior sprint and explosive strength capacities compared to XX individuals. Moderate heterogeneity ($I^2 = 36\%$) suggests reasonable consistency between populations, although inter-study variability may be influenced by factors such as sample size, ethnic background, and athlete specialization. For instance, while certain studies³ demonstrated a stronger association in European cohorts, others^{10,11} reported weaker correlations among endurance-trained subjects. These discrepancies underline that the ACTN3 genotype may confer performance advantage predominantly in anaerobic, short-duration sports.

In contrast, the ACE I/D and PPARGC1A Gly482Ser polymorphisms did not exhibit significant associations (ACE OR = 0.98, PPARGC1A OR = 1.20). Studies included in the meta-analysis^{10,12,13} presented inconsistent effects across athletic disciplines. The lack of significance in the forest plot implies that these variants may influence performance only under specific physiological or environmental conditions, such as high-altitude exposure or endurance-dominant regimens. Likewise, the PPARGC1A polymorphism, which regulates mitochondrial biogenesis, may have greater relevance for endurance adaptation than for power performance, as supported by prior findings.^{13,14}

Taken together, these findings reaffirm that ACTN3 remains the most reliable genetic marker for power-oriented performance, while ACE and PPARGC1A show weaker or context-dependent effects. The forest plot patterns also highlight the polygenic and multifactorial nature of athletic traits, where gene–gene and gene–environment interactions jointly shape the expression of muscle strength, metabolism, and fatigue resistance. Future studies should employ genome-wide approaches and standardized phenotyping to clarify the combined influence of multiple variants on elite athletic status.

CONCLUSION

This meta-analysis provides strong evidence that the ACTN3 RR (rs1815739) genotype is significantly associated with enhanced athletic performance, particularly in strength- and speed-oriented disciplines (OR = 1.32 [1.15–1.53], $p < 0.01$), with low-to-moderate heterogeneity. These findings reinforce the crucial role of ACTN3 in regulating fast-twitch muscle fiber composition and contraction efficiency, offering molecular insights into power-oriented athletic potential. Conversely, the ACE I/D and PPARGC1A Gly482Ser polymorphisms showed no significant associations, suggesting that their influence may depend on specific physiological or environmental contexts such as endurance adaptation or oxygen availability. Collectively, these results indicate that athletic performance is polygenic and multifactorial, shaped by complex gene–environment interactions. The findings provide a valuable genetic framework for personalized athlete development and genotype-informed training strategies, while encouraging ethical integration of genomics in sports science. The study's strength lies in its robust meta-analytic design combining multiple polymorphisms, although heterogeneity among studies and moderate sample sizes may limit the generalizability of the conclusions.

Conflict of Interest

The authors declare no conflicts of interest related to this work.

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Declaration of Using AI

AI tools were used only for language refinement; all content and interpretations are the authors' own.

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