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ORIGINAL RESEARCH

Allometric Scaling of Left Heart Structure and Function in Elite Cyclists: Development of Sport-Specific Prediction Equations

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BACKGROUND: Elite athletes frequently exceed conventional left ventricular (LV) and left atrial thresholds when guideline-recommended linear scaling for body size is applied, prompting unnecessary investigation. Few athlete-specific allometric equations yield percentage predicted values or *Z* scores. We aimed to develop allometric equations for LV and left atrial structure and function in elite cyclists, accounting for body size, sex, discipline, and heart rate, and to compare these with body surface area (BSA) indexing.

METHODS: We evaluated 181 elite cyclists (105 male, 76 female; age 22.7±5.5 years; 128 endurance, 53 sprint) with normal preparticipation cardiac screening. Weighted least squares allometric regression determined optimal scaling exponents for height, weight, and BSA, with models advancing in complexity only when prediction accuracy significantly improved. Equations were externally validated in 62 independent elite male endurance cyclists.

RESULTS: Men had larger BSA-scaled LV and left atrial size than women (both $P<0.001$). Many cyclists exceeded conventional thresholds (American Society of Echocardiography 2015: LV end-diastolic volume indexed to BSA 69.6%, LV end-systolic volume indexed to BSA 62.9%; British Society of Echocardiography 2020: LV end-diastolic volume indexed to BSA 50.8%, left atrial volume indexed to BSA 28.7%). Height provided superior allometric fit versus weight or BSA. Height, sex, discipline, and RR interval were key determinants. On external validation, only 6.5% exceeded the *Z* score threshold for LV end-diastolic volume indexed to BSA, compared with 90.3% classified abnormal by ASE guidelines.

CONCLUSIONS: Height-based allometric scaling outperformed weight or BSA for cardiac dimensions and function in elite cyclists. These sport-specific equations, validated in an independent cohort, provide clinically usable percentage predicted values and *Z* scores that permit quantitative assessment rather than binary thresholds and may reduce misclassification of physiological adaptation as disease in preparticipation cardiac screening programs.

Key Words: allometric scaling ■ athlete's heart ■ echocardiography ■ preparticipation cardiac screening ■ *Z* score

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Elite athletes undergo profound cardiac remodeling characterized by increases in left ventricular (LV) chamber dimensions, wall thickness, and mass that support enhanced cardiovascular performance.[1–5] The magnitude and pattern of this remodeling vary across sporting discipline, with endurance athletes demonstrating greater chamber dilation than their strength trained counterparts.[6–10] These physiological

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CLINICAL PERSPECTIVE

What Is New?

- A substantial proportion of healthy elite cyclists exceeded American Society of Echocardiography and British Society of Echocardiography guideline thresholds for left ventricular and left atrial dimensions under conventional body surface area indexing, and this study developed and externally validated sport-specific allometric prediction equations incorporating height, sex, cycling discipline, and RR interval to generate percentage-predicted values and *Z* scores for left heart structure and function in elite cyclists.

What Are the Clinical Implications?

- Cyclist-specific *Z* score equations markedly reduced abnormal classifications compared with conventional thresholds, improving differentiation between physiological remodeling and pathological cardiac enlargement, and may reduce unnecessary investigations, athlete anxiety, and health care costs.
- The methodological framework used in this study may provide a scalable approach for developing sport-specific and population-specific echocardiographic reference values across broader athletic cohorts.

Nonstandard Abbreviations and Acronyms

ASE	American Society of Echocardiography
BSE	British Society of Echocardiography
LAV	left atrial volume
LVEDVi	left ventricular end-diastolic volume indexed to body surface area
LVESV	left ventricular end-systolic volume
LVESVi	left ventricular end-systolic volume indexed to body surface area
LVM	left ventricular mass
PPCS	preparticipation cardiac screening
SEAMLSS	systematic evaluation and allometric modeling using least squares scaling

adaptations, termed the "athlete's heart," present a diagnostic challenge during preparticipation cardiac screening (PPCS), hence differentiating physiological remodeling from pathological conditions such as hypertrophic or dilated cardiomyopathy is especially difficult when relying on standard nonathletic reference values.[11,12]

Elite cycling exemplifies these challenges. The sport demands substantial cardiovascular exertion during both training and competition, resulting in high cardiorespiratory fitness and pronounced LV/left atrial (LA) remodeling. Cycling also comprises distinct subdisciplines broadly classified as either endurance (prolonged, moderate-intensity efforts) or sprint (brief, high-intensity bouts maximizing power output). These divergent physiological demands create a unique potential for discipline-specific cardiac remodeling within the same sport. Given that the Union Cycliste Internationale mandates annual PPCS including echocardiography, for all licensed professional cyclists, establishing accurate discipline-specific characterization of LV structural and functional (and LA structural) indices is essential.

Current guidelines recommend linear scaling of cardiac parameters to body surface area (BSA).[1,2,11] However, body composition in athletes differs substantially from the general population, with typically higher fat-free mass and sport-specific variations in muscle mass distribution. These compositional differences may necessitate distinct allometric coefficients for accurate cardiac scaling in athletic populations. Previous studies in athletes have demonstrated that the relationship between body size and cardiac dimensions follows a power-law function, with optimal scaling exponents typically ranging between 1.5 and 2.5.[13] Conventional BSA-indexed values do not adequately account for these nonlinear allometric relationships, often leading to systematic over- or underestimation in individuals at the extremes of body habitus.[13,14] Furthermore, current reference ranges for physiological cardiac adaptation in athletes do not adequately incorporate sex-specific differences, variations in body composition, and sport-specific training effects.[15,16] As a result, guideline-based reference limits do not strictly apply to athletes,[17] with a substantial proportion of healthy athletes exceeding conventional thresholds and subsequently creating the potential for unnecessary onward investigations.[11,18]

Although reference limits in adults are typically presented as absolute thresholds with sex differentiation, there is an opportunity to adopt more sophisticated approaches, akin to those used in pediatric cardiology by developing percentage predicted values and *Z* scores tailored for athletic screening. Douglas Altman first proposed a systematic, stepwise framework for deriving reference values,[19] identifying 3 key principles to develop robust prediction equations: (1) an unbiased mean function across the full range of body size; (2) equal variance of residuals (homoscedasticity) to ensure consistent severity reporting; and (3) mapping to Gaussian *Z* scores to enable standardized communication where the same percentile applies universally (eg, Z=1.96 represents the 97.5th percentile regardless

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of the parameter measured). Optimal prediction equations should be unbiased across body sizes, address heteroscedasticity, and yield standardized residuals that facilitate clinical interpretation through *Z* scores and percentiles.[20–22] We have developed systematic evaluation and allometric modeling using least squares scaling (SEAMLSS), a methodology that automates this process and that is described in detail and applied for the first time, in the present report. This technique has the potential to be more widely applied to athletic cohorts and cyclist-specific reference values derived from robust allometric scaling equations and could address the key limitations in current practice.[17,23,24]

Consequently, the objectives of this study were 4-fold: (1) to determine the impact of current American Society of Echocardiography/British Society of Echocardiography (ASE/BSE) reference values for LV/LA indices when applied to elite cyclists, (2) to develop allometric scaling equations for LV structural and functional and LA structural parameters in elite cyclists; (3) to compare allometric scaling with conventional BSA indexing; and (4) to establish cycling discipline and sex-specific prediction equations to improve clinical interpretation during PPCS.

METHODS

Data Availability

The data, analytic methods, and study materials underlying this article will be made available to other researchers for purposes of reproducing the results or replicating the procedure, upon reasonable request to the corresponding author.

Study Design and Reporting

This was a cross-sectional observational study of a consecutively screened cohort. The study is reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology statement,[25] and a completed checklist is submitted as a supplemental file.

Study Population

One hundred and ninety-two elite international level cyclists were assessed as part of their national cycling team's PPCS program. Inclusion criteria comprised no history of cardiovascular disease, no cardiovascular medications, a normal PPCS (normal 12-lead ECG, no cardiac symptoms, and no echocardiographic evidence of cardiac disease). Subsequently, 181 cyclists consented to participate in the final analysis. The study was approved by an institutional review committee, the National Research Ethics Service at London – West London & GTAC Research Ethics Committee (IRAS 169429), was conducted in accordance with the Declaration of Helsinki, and all cyclists gave written informed consent before participation.

Cyclists were classified into 2 disciplines based on their primary competitive focus: endurance cyclists (n=128) including track and road racing, mountain bike cross-country racing, and tandem pilot racing, and sprint cyclists (n=53) including track sprint events (sprint, keirin, team sprint) and Bicycle Motocross racing. As part of a professional, national, Olympic cycling team, both endurance and sprint cyclists training volumes were not statistically different between groups (endurance 18±4 hours/week versus sprint 16±5 hours/week; $P>0.05$). The composition of training was as follows: endurance cyclists—strength training 11.1%, endurance training 67%, and cycling high-intensity training 22.2%; and sprint cyclists—strength training 30.4%, endurance training 26.1%, and cycling high-intensity training 43.5%.

Study Protocol

All assessments were performed at rest in a single session. Cyclists refrained from strenuous physical activity for at least 6 hours and avoided caffeine or alcohol consumption for 24 hours before examination. All participants completed a health questionnaire and underwent an assessment of systemic blood pressure, a 12-lead ECG, and a full transthoracic echocardiogram.

Echocardiography

Comprehensive transthoracic echocardiography was performed by a BSE-accredited sonographer adhering to BSE national guidelines.[2] Images were acquired using commercially available ultrasound systems (Vivid IQ or Vivid E95, GE Medical, Horten, Norway) with a 1.5 to 4 MHz phased array transducer. Data were stored in raw Digital Imaging and Communications in Medicine format and analyzed offline (EchoPAC, Version 204, GE Healthcare, Horten, Norway).

Two-dimensional linear LV dimensions in diastole and systole were obtained in the parasternal long-axis view. Septal and posterior wall thicknesses were measured in the parasternal short-axis view at the level of the mitral valve. LV mass (LVM) was calculated using theASE–recommended corrected formula. LV end-diastolic (LVEDV) and end-systolic (LVESV) volumes were derived from apical 4- and 2-chamber views using the biplane Simpson method; LV ejection fraction (LVEF) and stroke volume were subsequently calculated. Left-atrial volume (LAV) was also assessed using the biplane method.

All measurements were made from a single cardiac cycle, using an inner-edge–to-inner-edge approach for linear dimensions and endocardial tracing (excluding trabeculations and papillary muscles) for volume

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calculations. Diastole was defined as the frame immediately before mitral valve opening, and systole as the frame immediately after mitral valve closure.

Statistical Analysis

Continuous variables were presented as mean±SD. Between-group comparisons were performed using independent samples *t*-tests. Prediction equations for cardiac parameters were developed using the SEAMLSS methodology (Figure 1). This stepwise approach models location (mean function), variance, scale (solution for variance pattern), and shape (Gaussian mapping to *Z* scores) to generate percentage predicted values if appropriate and *Z* scores. The analytical approach comprised 2 main phases (Figure 1).

SEAMLSS is a stepwise, least-squares implementation of the location–scale–shape modeling philosophy that underpins generalized additive models for location, scale, and shape and the least mean squares method used to construct pediatric growth and cardiac reference charts.[26,27] SEAMLSS differs from a conventional generalized additive models for location, scale, and shape fit in 3 respects that are material for reference-value derivation in athletic cohorts of moderate size. First, the location parameter is estimated by weighted least squares on the natural logarithmic scale, so that the fitted model retains a closed-form multiplicative allometric structure (predicted value=-constant × height raised to the allometric exponent × sex factor × discipline factor × RR interval raised to its exponent) that can be transcribed directly into a clinically usable equation rather than a smoothed spline that cannot. Second, the scale parameter is constrained a priori to proportional (multiplicative) variance and that constraint is then tested empirically across quantiles, rather than being estimated nonparametrically, which avoids overfitting the variance function when the sample size is modest. Third, the shape step uses an optimized piecewise linear mapping of ln(percentage predicted) onto Gaussian *Z* scores rather than assuming a parametric skew distribution.

The framework operationalizes the 3 requirements for reference equations set out by Altman and Chitty[19] and the allometric principles described by Nevill and Holder[20]: an unbiased mean function across the full

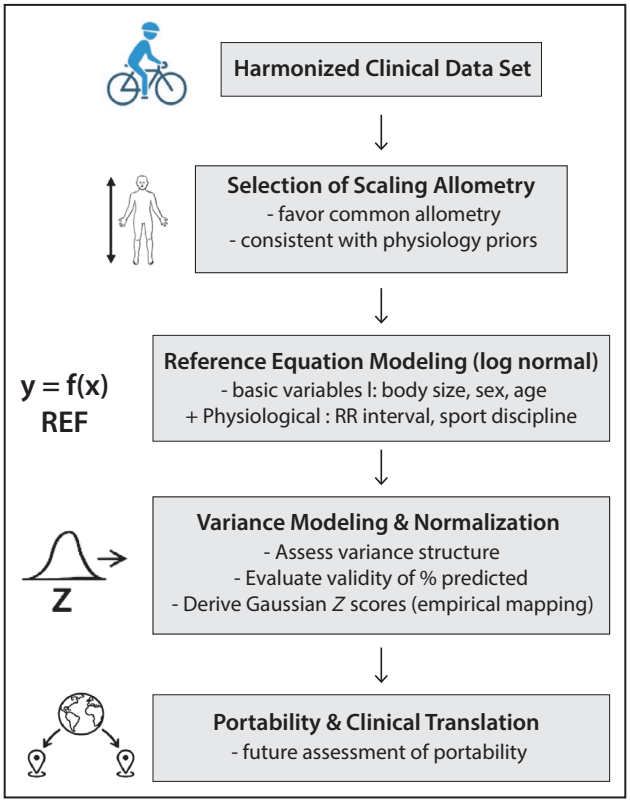


Figure 1. Development of equations for reference values. Systematic evaluation and allometric modeling using least squares scaling, stepwise framework used to derive reference equations including selection of allometric scaling, nested, modeling of mean structure, and assessment of variance properties. Derived reference equations are subsequently normalized to Gaussian *Z* scores.

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range of body size, homoscedastic residuals, and *Z* scores that map to fixed percentiles. Each step is reported in subsequent text, and the complete workflow is summarized in Figure 1. Covariates were retained only when they produced a statistically significant improvement in fit of the nested model ($P<0.05$).

Comparison of Scaling Approaches

Initial analyses compared different scaling strategies to identify the optimal anthropometric variable for allometric scaling. For each cardiac parameter, we evaluated scaling exponents using height, weight, and BSA independently. Weighted least squares regression determined the optimal power exponent (b) for each variable in the allometric equation: $Y=a\times X^b$, where Y represents the cardiac parameter and X represents the anthropometric variable. Models were compared using R^2 and systematic evaluation of residual patterns across the range of body sizes to identify the scaling variable providing the best fit with minimal bias.

Development of Sport-Specific Prediction Equations (SEAMLSS Methodology)

Height-based allometric equations incorporating sex, discipline, and heart rate generate percentage predicted values that stabilize variance across the predicted range. Piecewise linear transformation maps these to *Z* scores. Following selection of the optimal scaling variable, we applied our SEAMLSS approach to develop comprehensive prediction equations using a 3-step approach designed to ensure unbiased, clinically interpretable reference values:

Step 1: Location

We used weighted least squares allometric regression to model the location parameter (μ), with covariates (sex, discipline, heart rate) added sequentially and retained only when significantly improving prediction accuracy.

Step 2: Scale

To stabilize variance, we modeled the scale parameter (σ) using proportional variance, where SD equals a constant multiplied by the predicted value (SD=a×predicted), equivalent to percentage predicted values (observed/predicted ×100). When testing variance stabilization across quantiles, we employed binomial-adjusted *P* value thresholds ($p_0\times0.25/(p\times(1-p))$) to adapt significance levels to data density at each quantile.

Step 3: Shape

To ensure *Z* scores correspond to consistent percentiles, we applied nonparametric Gaussian mapping using optimized piecewise linear transformation on ln(percentage predicted). This approach, conceptually similar to achieving linearity in Q-Q plots, transforms empirical distributions into normalized *Z* scores without requiring parametric distributional assumptions beyond variance stabilization. For *Z* score transformation, we used the geometric mean of percentage predicted values. Piecewise mapping allows clinicians to inspect zones and adjust for edge cases, minimizing misclassification at distribution extremes. Outliers were excluded. Model performance was assessed using R^2. Statistical significance was set at $P<0.05$. Analyses were performed using Python 3.10.

Validation Cohort

To assess the portability and accuracy of our sport-specific reference equations, we performed external validation using an independent cohort of 62 elite male endurance cyclists from professional cycling teams. This cohort was recruited separately from the development cohort and underwent equivalent echocardiographic assessment protocols.

Model performance in the independent validation cohort was assessed by applying the developed prediction equations to calculate *Z* scores for each cardiac parameter. Calibration was assessed by comparing the observed proportion of cyclists falling beyond prespecified *Z* score thresholds with the proportion expected under a standard normal distribution. For each threshold, a 95% CI for the observed proportion was calculated using the Wilson score interval,[28,29] which is obtained by inverting the score test for a binomial proportion and, unlike the Wald interval, retains reliable coverage for small samples and for proportions close to 0 or 1. Calibration was considered adequate when the expected proportion fell within this interval. The mean±SD of the *Z* scores were also examined. Finally, we compared the proportion of cyclists classified as abnormal using ASE/BSE guideline thresholds with the proportion classified as abnormal by our *Z* score-based approach (*Z* score>1.96 or<–1.96).

RESULTS

Study Population and Baseline Characteristics

The study cohort comprised 181 elite international-level cyclists (105 men, 76 women) with a mean age of 22.7±5.5 years and predominantly White race (96%) (Table 1). Cyclists were categorized by discipline into endurance 128 (70%, 66 male/62 female) and sprint 53 (29%, 39 male/14 female) groups.

Male endurance cyclists exhibited significantly larger absolute cardiac dimensions across

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Table 1. Baseline Demographic, Hemodynamic, and Echocardiographic Characteristics of Male and Female Participants

Characteristic	Male sex (n=105)	Female sex (n=76)	Effect size
Age, y	22.7±6.0	22.5±4.7	…
Height, m	1.80±0.07	1.65±0.06	−2.1
Weight, kg	76.0±9.5	63.05±6.7	−1.5
Body surface area, m^2	1.94±0.1	1.70±0.1	−1.8
Race	White 95.2%	White 97.3%	…
Systolic blood pressure, mm Hg	125.6±12.3	118.3±13.4	−0.5
Diastolic blood pressure, mm Hg	71.3±8.9	70.6±8.7	…
LV end-diastolic volume, mL	159.4±27.7	119.4±20.5	−1.5
LV end-systolic volume, mL	67.4±16.6	47.1±9.9	−1.4
LV stroke volume, mL	91.8±18.0	72.3±16.3	−1.1
Left atrial volume, mL	58.3±15.7	49.5±13.3	−0.5
LV mass, g	186.2±40.3	134.8±21.8	−1.5
Relative wall thickness	0.32±0.04	0.31±0.03	−0.44
Mean wall thickness, mm	8.6±0.8	7.5±0.6	−1.43
Cardiac output, L/min	4.9±0.9	4.1±1.1	−0.7
LV diastolic diameter, mm	55.0±3.7	50.5±3.2	−1.2
LV systolic diameter, mm	36.9±3.8	33.3±2.9	−1.0
LV ejection fraction, %	58.5±5.0	61.2±5.1	0.5

Data are presented as mean±SD. Cohen's d effect sizes with 95% CIs are reported for significant differences between sexes. Nonsignificant effect sizes where not reported. LV indicates left ventricular.

all parameters. LVEDV (159.4±27.7 mL versus 119.4±20.5 mL), LVESV (67.4±16.6 mL versus 47.1±9.9 mL), LVM (186.2±40.3 g versus 134.8±21.8 g). and LAV (58.3±15.7 mL versus 49.5±13.3 mL) in men and women respectively (P<0.001 for all). LVEF was higher in women (61±5% versus 58±5%, P<0.001) (Table 1). Distribution analysis with kernel density estimation revealed clear separation between male and female cyclists, with men demonstrating higher BSA-indexed (standard linear) values across sex-matched disciplines (Figure 2, Figure S1). The overlapping distributions between disciplines, contrasted with the clear separation by sex, underscores the importance of sex-specific reference values within cycling discipline-specific populations.

Application of Society Guidelines in Cyclists

A substantial proportion of elite cyclists exceeded established guideline thresholds. Using the ASE 2015 reference values, 69.6% of cyclists exceeded the upper limit of normal for LVEDV indexed to body surface area (LVEDVi), 62.9% for LVESV indexed to body surface area (LVESVi), and 14.9% for LVM index. Application of the BSE 2020 guidelines yielded similar findings, with 50.8% exceeding thresholds for LVEDVi, 56.3% for LVESVi, and 18.2% for LVM index (Table 2).

Sex-stratified analysis of BSA-indexed values revealed persistent differences between male and female cyclists despite adjustment for body size. Male cyclists demonstrated higher LVEDVi (81.8±13.3 versus 70.4±11.4 mL/m^2, P<0.001), LVESVi (34.5±7.9 versus 27.8±5.7 mL/m^2, P<0.001), LVM index (95.5±19.7 versus 79.6±12.7 g/m^2, P<0.001), and LAV index (30.0±8.1 versus 29.3±7.8 mL/m^2, P=0.56) compared with women. Large effect sizes persisted for volumetric parameters (Cohen's d: LVEDV 1.59, LVESV 1.42, LVM 1.52) but not for LAV (Cohen's d−0.59), where no statistically significant difference was observed by sex when indexed to BSA (Table S1).

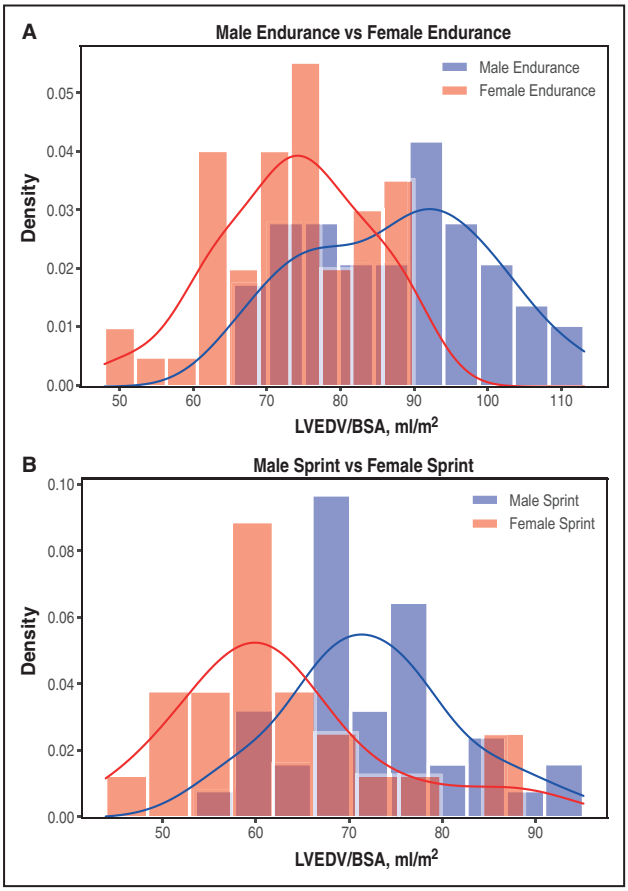


Figure 2. LVEDV/BSA in male and female endurance and sprint athletes.
A, Sex comparison within male and female endurance athletes reveals. **B**, Sex comparison within male and female sprint athletes. BSA indicates body surface area; and LVEDV, left ventricular end-diastolic volume.

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Table 2. Count and Proportion of Subjects With Values Above Guideline Thresholds

Variable (n=180)	Sex	ASE 15 limits	BSE 20 limits	Abnormal by ASE n (%)	Abnormal by BSE n (%)
LV end-diastolic volume index	Male Female	34–74 mL/m^2 29–61 mL/m^2	30–79 mL/m^2 29–70 mL/m^2	126 (69.6)	92 (50.8)
LV end-systolic volume index	Male Female	11–31 mL/m^2 8–24 mL/m^2	9–31 mL/m^2 8–27 mL/m^2	114 (62.9)	105 (56.3)
Left atrial volume index	Both	34 mL/m^2	34 mL/m^2	52 (28.7)	52 (28.7)
LV diastolic diameter index	Male Female	22–30 mm/m^2 23–32 mm/m^2	37–56 mm/m^2 35–51 mm/m^2	45 (24.8)	65 (35.9)
LV systolic diameter index	Male Female	13–21 mm/m^2	11–41 mm/m^2 20–37 mm/m^2	36 (19.8)	22 (12.1)
LV mass index	Male Female	115 g/m^2 95 g/m^2	33–99 g/m^2	27 (14.9)	33 (18.2)
Relative wall thickness	Both	0.42	0.42	1 (0.5)	1 (0.5)
LV ejection fraction	Both	50%	50%	5 (2.7)	5 (2.8)

Number and percentage of cyclists with echocardiographic measurements exceeding sex-specific guideline thresholds. ASE indicates American Society of Echocardiography; BSE, American Society of Echocardiography; and LV, left ventricular.

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Determination of Optimal Allometric Scaling Exponents

Multivariable weighted least squares allometric regression was performed to identify the optimal scaling variable and exponent for each cardiac parameter. Height provided scaling characteristics compared with weight or BSA across all volumetric and dimensional measurements. For LVEDV, the allometric exponent for height was 1.80, yielding an adjusted coefficient of determination (R^2) of 0.57 after accounting for sex. In comparison, for LVEDV, BSA showed an exponent of 0.89 and weight an exponent of 0.38. Complete allometric coefficients and R^2 are shown in Table 3 and Table S2 Both height and BSA provided numerically higher R^2 values, whereas weight allometry was systematically lower than the other scaling variables. This led to the selection of height for scaling with a simple coefficient consistent with literature and within our CI.

Similar patterns were observed for LVESV, where height scaling (exponent 1.94, SE 0.40) achieved R^2 of 0.49, numerically higher than both weight and BSA. For LV mass, height scaling (exponent 1.78, SE 0.39) yielded R^2 of 0.41. For LAV, height scaling (exponent 1.96, SE 0.50) yielded an R^2 of 0.29, again numerically higher than weight (R^2 0.24) and BSA (R^2 0.26). Similar patterns of numerically higher R^2 values for height-based scaling were observed across functional indices (LVEF, LV stroke volume, and cardiac output). The numerically higher R^2 values for height-based scaling, combined with simpler exponents consistent with literature, led to the selection of height as the primary scaling variable (Table 3).

Development of Multivariable Prediction Equations

Following selection of optimal scaling exponents, prediction equations were developed incorporating

Table 3. Multivariable Allometric Coefficients

Variable	Height	Weight	BSA
LV end-diastolic volume	1.80 (0.29)	0.38 (0.10)	0.89 (0.16)
LV end-systolic volume	1.94 (0.40)	0.50 (0.14)	1.09 (0.23)
Left atrial volume	1.96 (0.50)	0.26 (0.16)†	0.74 (0.28)
LV stroke volume	1.57 (0.36)	0.29 (0.12)	0.71 (0.20)
Cardiac output	1.71 (0.38)	0.32 (0.13)	0.78 (0.22)
LV mass	1.78 (0.39)	0.23 (0.13)†	0.72 (0.22)
LV diastolic diameter	0.65 (0.12)	0.14 (0.04)	0.33 (0.07)
LV systolic diameter	0.64 (0.18)	0.15 (0.06)	0.34 (0.10)
LV ejection fraction	−0.04 (0.16)†	−0.03 (0.05)†	−0.05 (0.09)†

Weighted least squares allometric scaling coefficients for echocardiographic parameters relative to height, weight, and body surface area adjusted by sex and RR interval. Values in parentheses represent SEs. Adjusted values are corrected for sex. All variables reached statistical significance, except the ones marked with †. BSA indicates body surface area; and LV, left ventricular.

Table 4. Allometric Prediction Equations for Left Heart Structure and Function in Elite Cyclists

Variable	Constant	Height allometry	Male factor (×)	Endurance factor (×)	RR allometry	R^2	σ log
LV end-diastolic volume index	46.38	1.7	1.15	1.09	0.30	0.65	0.13
LV end-systolic volume index	19.09	1.7	1.19	1.05	0.30	0.53	0.19
Left atrial volume index	18.04	1.7	…	1.17	0.50	0.33	0.23
LV ejection fraction	60.36	…	0.96	1.01	…	0.08	0.08
LV stroke volume	27.07	1.7	1.13	1.14	0.27	0.52	0.16
Cardiac output	1.89	1.7	1.06	1.05	…	0.27	0.19
LV mass index	50.99	1.7	1.22	1.14	0.07	0.55	0.17
LV diastolic diameter index	35.70	0.6	1.03	…	…	0.41	0.06
LV systolic diameter index	24.02	0.6	1.04	…	…	0.28	0.09

Predictive equations for echocardiographic parameters incorporating allometric scaling with height, sex, RR interval, and discipline (endurance vs sprint). All models had proportional variance. LV indicates left ventricular. LAVi left atrial volume index; LVdi, left ventricular; LVEDVi, left ventricular end-diastolic volume index; LVEF, left ventricular ejection fraction; LVESVi, left ventricular end-systolic volume index; LVMi, left ventricular mass index; LVsi, left ventricular systolic diameter index; LVSV, left ventricular stroke volume; R^2, coefficient of determination (systematic evaluation and allometric modeling using least squares scaling observed vs predicted); RR, R-R interval (sec); and σlog, residual SD on the natural log scale.

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clinically relevant covariates. Table 4 presents the allometric prediction equations in a structured format, displaying for each cardiac parameter the constant, height allometric exponent, multiplicative sex and discipline factors, RR allometric exponent, coefficient of determination (R^2), and residual SD (σ log). The complete equation form including *Z* score transformation coefficients is provided in Table S3. Sex emerged as a significant determinant across all cardiac parameters, with men demonstrating larger dimensions after accounting for height. Discipline-specific effects were also identified, with endurance cyclists showing larger volumes and mass compared with sprint cyclists. RR interval contributed significantly across all cardiac parameters, with longer RR intervals associated with greater dimensions and mass.

Validation plots demonstrated good agreement between measured and predicted values across the physiological range for all echocardiographic measures evaluated. Residual analysis confirmed homoscedastic distribution, and percentage predicted values showed appropriate spread around 100% across the range of body sizes and cardiac dimensions, validating the absence of systematic bias in the prediction models (Figures 3–5 and Figures S2–S6A–C).

Establishment of Reference Intervals and *Z* Score Transformation

To enable clinical interpretation, percentage predicted values were transformed to *Z* scores. This transformation successfully normalized the empirical distribution, allowing calculation of percentile-based reference intervals. Piecewise linear regression was used to map percentage predicted values to *Z* scores for consistency. The 95% reference interval (2.5th to 97.5th percentiles) and their corresponding percentage predicted values mapped from the piecewise linear transformation are shown in Table 5. Piecewise linear regression plots confirmed successful normalization, with quantile regression lines converging toward theoretical Gaussian percentiles (Table 5). When the final prediction equations were applied to the study cohort, *Z* scores demonstrated a near-normal distribution centered around zero for all cardiac parameters (Table S4).

External Validation in Independent Cohort

The validation cohort comprised 62 elite male endurance cyclists from professional teams with mean age 27.9±4.6 years, height 1.80±0.06 m, and BSA 1.89±0.11 m^2 (Table 6). When conventional ASE 2015 guidelines were applied, 90.3% of cyclists exceeded thresholds for LVEDVi, 83.9% for LVESVi, and 58.1% for LAV index. Similarly, BSE 2020 guidelines classified 77.4% as abnormal for LVEDVi and 83.9% for LVESVi (Figure 6, Table S5).

In contrast, application of our sport-specific *Z* score reference equations demonstrated substantially improved classification. Only 6.5% of cyclists had LVEDVi *Z* scores >1.96, 6.5% for LVESVi, and 9.7% for LAV index. Wilson calibration analysis confirmed excellent distributional properties of the *Z* scores, with the expected proportions at the 5th and 95th percentile thresholds falling within the Wilson 95% CIs for the observed proportions for the majority of cardiac parameters (Table S6). Mean *Z* scores across the validation cohort ranged from −0.43 to 0.03, with SDs between 0.99 and 1.08, indicating minimal systematic bias and appropriate variance calibration.

Detailed results for all cardiac parameters, including optimal scaling exponents, prediction equations,

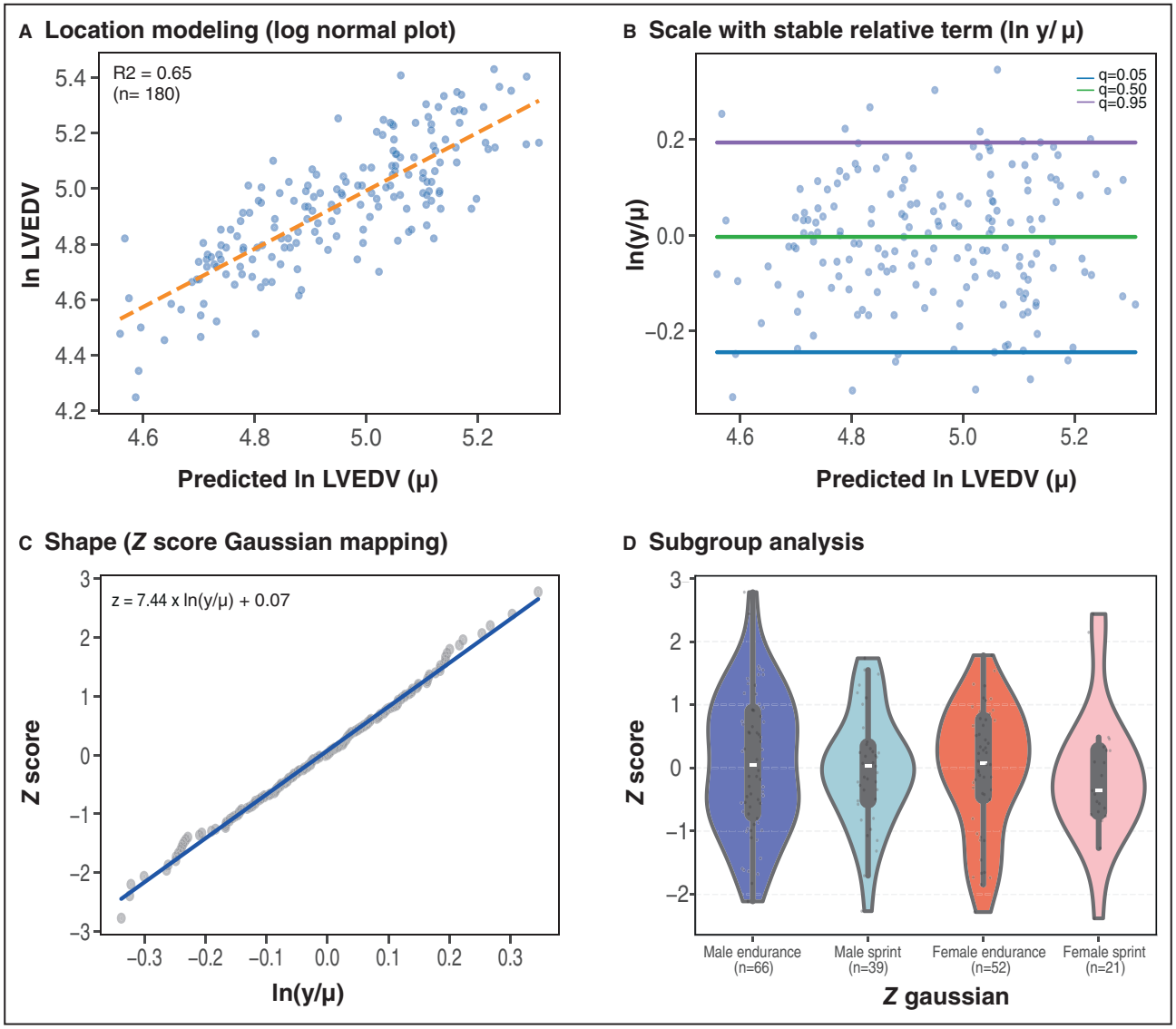


Figure 3. Validation and diagnostic performance of LVEDV.
A, Location parameter model fit. Scatter plot showing the relationship between observed ln(LVEDV) and predicted ln(LVEDV). **B**, Scale parameter assessment. Residual plot displaying ln(y/μ) αγαινστ πρεδιχτεδ λν(ΛϛΕΔϛ). **C**, Shape parameter with Gaussian mapping. Q-Q plot showing *Z* scores against LVEDV ln(pp) to assess normality of residuals after Gaussian transformation. **D**, Violin plots comparing the distribution of Gaussian Z-scores across athlete subgroups. ln indicates natural logarithm; LVEDV, left ventricular end-diastolic volume; PP%, percentage predicted; and q, quantile. *Homoscedasticity tests (Breusch–Pagan / White) *P*>0.05, *Z* shift=0.0.

validation plots, and reference intervals, are provided in the supplementary materials (Tables S1–S6 and Figures S1–S6).

DISCUSSION

This study addresses a challenge in sports cardiology: distinguishing between physiological cardiac remodeling in athletes and pathological enlargement. Our research provides reference equations for left heart structure and function in elite cyclists, incorporating key determinants such as body size, sex, heart rate, and cycling discipline. These equations yield percentage predicted values and *Z* scores, enabling standardized interpretation within cyclist-specific reference intervals and offering important implications for PPCS.

In this cohort, a substantial proportion of elite cyclists exceeded ASE guideline thresholds when conventional BSA indexing was applied to LV and LA structural parameters. These findings reinforce prior observations that nonathlete reference values often create diagnostic ambiguity and may misclassify healthy athletes as having pathological cardiac enlargement.[18,30,31] We also observed persistent sex-related differences in BSA-indexed values, with male cyclists demonstrating significantly higher LVEDVi, LVESVi, and LVM index

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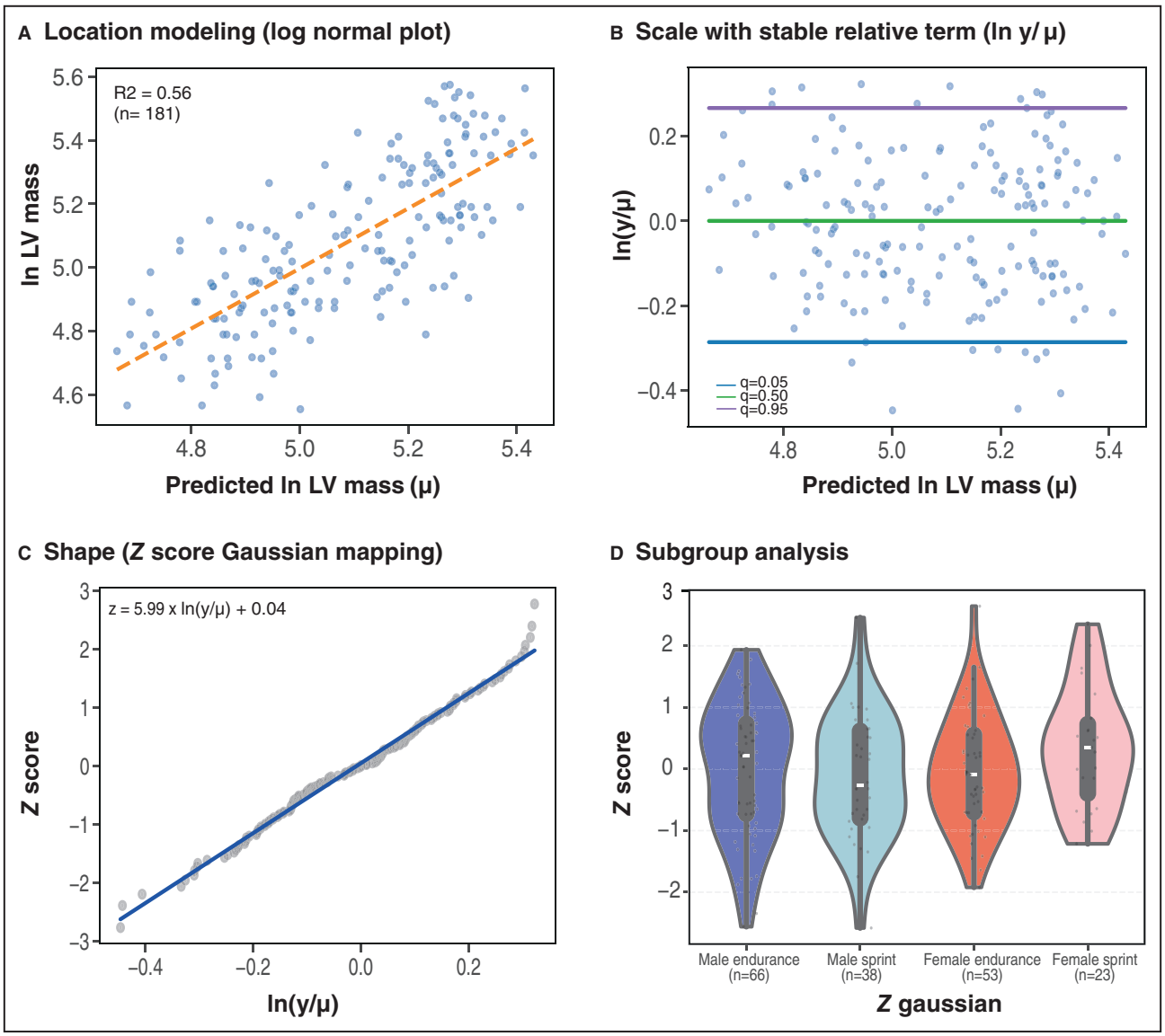


Figure 4. Validation and diagnostic performance of LV mass.
A, Location parameter model fit. Scatter plot showing the relationship between observed ln(LV mass) and predicted ln(LV mass). **B**, Scale parameter assessment. Residual plot displaying ln(y/μ) αγαινστ πρεδιχτεδ λν(Λς Μασσ). **C**, Shape parameter with Gaussian mapping. Q-Q plot showing *Z* scores against LV mass ln(pp) to assess normality of residuals after Gaussian transformation. **D**, Violin plots comparing the distribution of Gaussian *Z* scores across athlete subgroups. ln indicates natural logarithm; LV mass, left ventricular mass; PP%, prediction percentage; and q, quantile. *Homoscedasticity tests (Breusch–Pagan/White) P >0.05, Z shift=0.0.

than women, highlighting the need to account for sex as a factor within prediction models.

Our allometric analysis examined height, weight, and BSA as scaling variables for cardiac dimensions. For volumetric and mass measurements, height-based scaling yielded higher exponents of ~1.7 to 1.8, whereas BSA-based scaling yielded exponents close to 1.0, which also fell within our CIs. We selected height-based scaling for several reasons. First, height is simpler to measure and less influenced by body composition variability. Second, given that the elite cyclists have low body fat with minimal variability, weight (and consequently BSA) captures less meaningful variation in body size. Third, height-based scaling yielded consistently higher nominal R^2 values across all cardiac parameters. Finally, height-based scaling aligns with prior studies in young athletic populations,[24,32,33,34] Although previous studies report varying sport-specific allometric coefficients, establishing a common allometric framework, as Sejersen et al. suggest,[35] would support standardization while allowing for sport-specific adjustments through covariates. Our approach uses a consistent exponent across cardiac parameters and incorporates discipline-specific and physiological modifiers, balancing generalizability with sport specificity.

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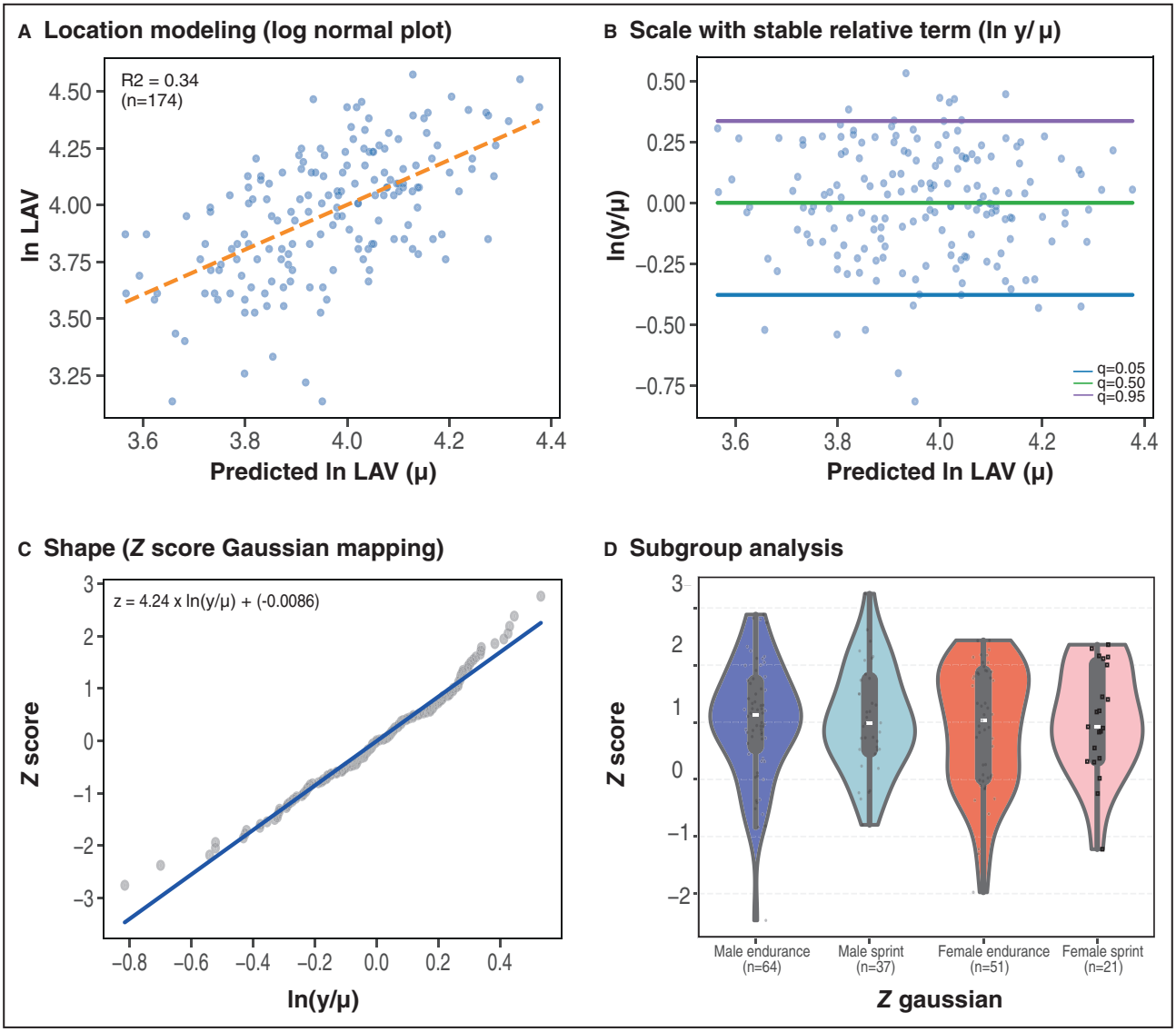


Figure 5. Validation and diagnostic performance of LAV.
A, Location parameter model fit. Scatter plot showing the relationship between observed ln(LAV) and predicted ln(LAV). **B**, Scale parameter assessment. Residual plot displaying ln(y/μ) αγαινστ πρεδιχτεδ λν(ΛΑς). **C**, Shape parameter with Gaussian mapping. Q-Q plot showing *Z* scores against LAV ln(pp) to assess normality of residuals after Gaussian transformation. **D**, Violin plots comparing the distribution of Gaussian *Z* scores across athlete subgroups. ln indicates natural logarithm; LAV, left atrial volume; PP%, prediction percentage; and q, quantile. *Homoscedasticity tests (Breusch–Pagan/White) *P* >0.05, Z shift=0.0.

The developed models include sex, RR interval, and discipline as multiplicative factors, recognizing that robust reference equations require not only appropriate allometric scaling but also incorporation of key physiological determinants. These variables interact with body size in determining cardiac dimensions, and their inclusion substantially improves predictive accuracy beyond scaling alone. This approach aligns with current statistical methods for developing reference equations in cardiology.[21,22,36]

Sex was a significant determinant of cardiac dimensions, with men showing 15% to 22% larger absolute volumes and masses than women after adjusting for height and other covariates. These differences remained after allometric scaling, indicating fundamental sex-related variation beyond body size. The effect sizes were substantial, with Cohen's d values from 0.91 to 1.59 for BSA-indexed parameters, confirming large differences between male and female athletes.[37]

A key contribution of this study is the inclusion of RR interval as a covariate in prediction equations. The positive association between RR interval and the evaluated cardiac parameters reflects the complex association between heart rate and chamber size. Training induced increased vagal tone results in bradycardia, where longer diastolic filling times promote greater

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Table 5. Left Ventricle Percentage Predicted

PP (%)/*Z* score	2.5/–1.96	5.0/–1.65	50/0.0	95/1.65	97.5/1.96
LV end-diastolic volume index	76.7	79.7	100	124.2	129.2
LV end-systolic volume index	67.1	72.1	100	137.3	146.3
Left atrial volume index	62.9	66.9	100	146.7	158.7
LV ejection fraction	85.0	87.0	100	114.1	117.1
LV stroke volume	70.4	74.4	100	133.7	141.8
Cardiac output	67.1	71.1	100	139.3	148.3
LV mass index	71.5	75.5	100	130.9	138.9
LV diastolic diameter index	88.9	89.9	100	109.9	112.9
LV systolic diameter index	83.0	85.0	100	117.0	120.0

Distribution of percentage predicted values for echocardiographic parameters across selected percentiles (2.5th, 5th, 50th, 95th, and 97.5th). Values represent the ratio of observed to predicted measurements based on allometric scaling models. LV indicates left ventricular; and PP (%), percentage predicted.

chamber dilation and compensatory hypertrophy. Conversely, increased preload and chamber dilation result in a higher resting stroke volume and subsequent slower resting heart rate while maintaining adequate cardiac output. Previous physiological studies have highlighted this phenomenon, in that resting heart rate is inversely correlated with stroke volume and cardiac dimensions in endurance athletes.[6]

The discipline-related differences we observed align with previous studies in cycling populations. Abergel et al. reported substantial variation in chamber dimensions across cycling specializations.[38] Finocchiaro et al. also found significant variation in LV adaptation across sports, with endurance athletes showing the greatest chamber dilation.[39] These discipline-specific differences reflect distinct training-induced physiological adaptations. Endurance training imposes volume overload, promoting eccentric LV remodeling. Sprint training generates pressure overload during brief maximal efforts, but with limited volume stimulus duration. Including discipline-specific modifiers in our prediction equations reflects fundamental differences in training stimuli and resulting cardiac adaptation in the same sport. These discipline-specific reference values are especially valuable in PPSC contexts, where distinguishing physiological adaptation from pathology depends on knowing the expected range for each discipline.[23,40] The inclusion of functional parameters in our prediction equations provides critical diagnostic value, enabling clinicians to distinguish physiological adaptation from pathological conditions such as dilated cardiomyopathy. Stroke volume and cardiac output scaled appropriately with body size and training discipline, confirming that structural enlargement supports enhanced cardiovascular performance rather than maladaptation.

External Validation and Clinical Utility

A critical strength of our study is the external validation in an independent cohort of 62 elite male endurance cyclists from professional teams. This validation demonstrates the generalizability of our reference equations beyond the development cohort. The Wilson calibration analysis confirmed excellent distributional properties, with *Z* scores maintaining their intended probabilistic interpretation in this external population. Importantly, the dramatic reduction in abnormal classifications, from 90% using conventional ASE guidelines to ~6.5% using our *Z* score approach, underscores the clinical utility of sport-specific reference values.

This improved specificity allows clinicians to more confidently distinguish physiological adaptation from potential pathology in elite cyclist populations, reducing unnecessary investigations and athlete anxiety while maintaining appropriate sensitivity for detecting abnormalities. Clinicians can interpret *Z* scores using standard thresholds: values between –1.96 and+1.96 represent the central 95% of the reference population, whereas values outside this range warrant careful evaluation as statistically unusual findings for the cyclist's body size, sex, discipline, and heart rate. *Z* scores enable precise quantification rather than binary classification—instead of simply labeling dimensions as "large," clinicians can determine exact SD units from the mean (e.g., *Z*=+2.5 indicates 2.5 SD above mean, approximately 99th percentile). This standardization provides objective, sport-specific metrics that support clinical decision-making and represents an important step toward integration into routine practice and athlete cardiac screening programs.

Methodological Considerations: Piecewise Transformation and *Z* Score Normalization

A key contribution of our study is the comprehensive methodology developed for creating robust reference equations. By developing multiplicative allometric equations, we ensure body-size-independent scaling using a single equation across height, sex, and sport

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Table 6. Baseline Characteristics of the Validation Cohort

Characteristic	Validation cohort (n=62)
Age, y	27.9±4.6
Height, m	1.80±0.06
Weight, kg	71.0±6.2
Body surface area, m^2	1.89±0.11
Race	White 100%
Heart rate, bpm	51.0±8.0
LV end-diastolic volume, mL	161.9±18.0
LV end-systolic volume, mL	70.6±11.6
LV stroke volume, mL	91.3±12.5
Left atrial volume, mL	66.9±16.1
LV mass, g	209.0±30.9
Relative wall thickness	0.36±0.04
Mean wall thickness, mm	9.9±0.8
Cardiac output, L/min	4.6±0.9
LV diastolic diameter, mm	54.8±3.8
LV systolic diameter, mm	36.5±3.0
LV ejection fraction, %	56.4±5.0

Validation cohort consisting of elite male endurance cyclists from professional teams. Values are presented as mean±SD unless otherwise specified. LV indicates left ventricular.

discipline, eliminating the need for separate reference tables. We demonstrated that percentage predicted values effectively stabilize variance across all cardiac metrics, with residual variance falling within binomial error bounds even at higher quantiles. This transformation provides equal precision across the physiological range, avoiding the problem of heteroscedasticity in clinical reference equations. For *Z* score calculation, we showed that optimized piecewise linear mapping transforms percentage predicted values into Gaussian-distributed *Z* scores, ensuring that the same *Z* score always corresponds to the same percentile. This is critical for facilitating clinical communication, where consistent interpretation is essential. Piecewise mapping also allows clinicians to inspect zones and adjust parameters, minimizing the chance of edge cases and misclassification at distribution extremes. This 3-step framework can be extended to develop reference values for other athletic populations and the general population, providing a standardized approach to clinical normative data.

LIMITATIONS

Several limitations should be noted. The cohort comprised predominantly White British athletes from a single national program, limiting generalizability to other populations and a cross-sectional design prevents assessment of longitudinal changes. In addition, classification as endurance or sprint simplifies the training spectrum but maintains a broad reflection of

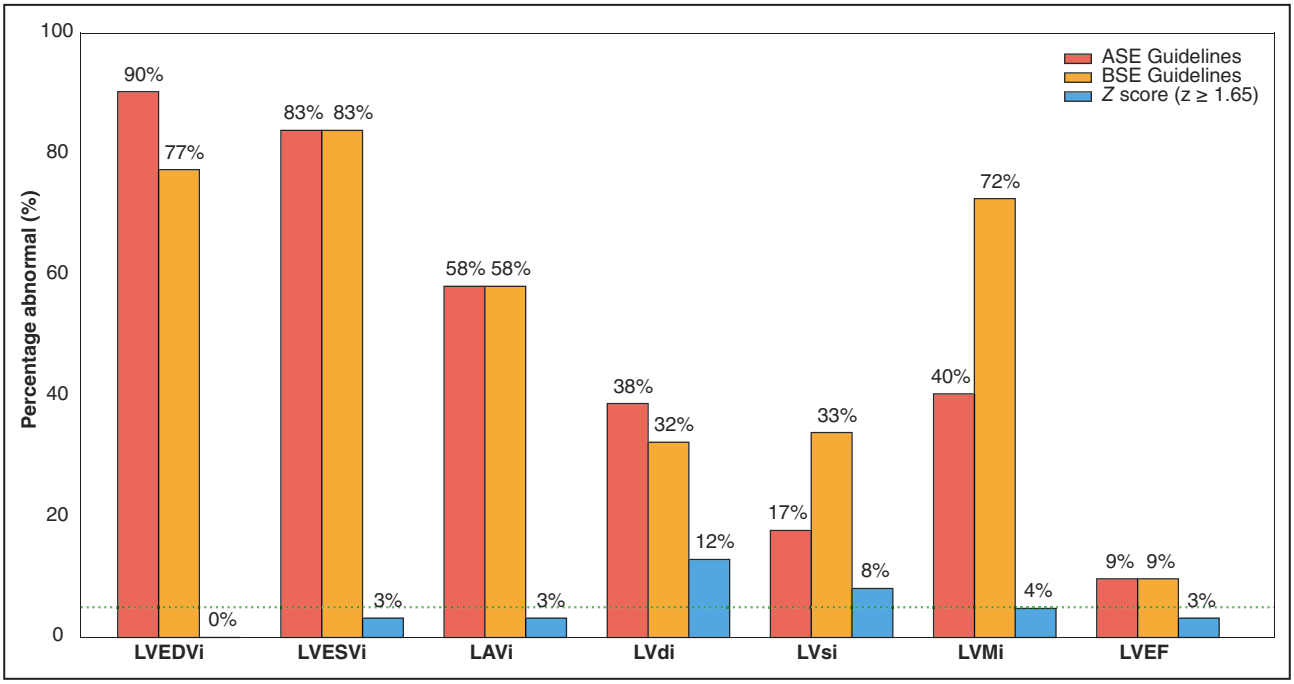


Figure 6. Proportion of elite cyclist classified as abnormal by ASE guidelines, BSE guidelines, and *Z* score from predicted equations developed in the validation cohort.
ASE indicates American Society of Echocardiography; BSE, American Society of Echocardiography; LAVi, left atrial volume index; LVdi, left ventricular diastolic diameter index; LVEDVi, left ventricular end-diastolic volume index; LVEF, left ventricular ejection fraction; LVESVi, left ventricular end-systolic volume index; LVMi, left ventricular mass index; and LVsi, left ventricular systolic diameter index.

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cycling-specific disciplines. It is important to also acknowledge that these allometric models are based on the training regimes of elite, professional cyclists and therefore may not be applicable to cyclists of lower training volumes. Further studies are required to elucidate bespoke allometric models across sporting disciplines and cardiorespiratory fitness/training volumes.

Finally, this study focused solely on the left heart only. Although right heart evaluation is also important in the PPCS setting, we considered it beyond the scope of the present analysis and better addressed in a separate report.[41] Larger multicenter cohorts would improve precision and enable detailed subgroup analyses.

CONCLUSIONS

This study provides sport-specific reference equations with percentage predicted values and *Z* scores for PPCS in elite cyclists. We demonstrated that conventional ASE and BSE guideline thresholds misclassify substantial proportions of healthy cyclists when using BSA indexing. Height-based allometric scaling provided superior fit compared with weight or BSA for cardiac dimensions. Sex, training discipline, and RR interval were identified as essential determinants of cardiac structure beyond body size. These cycling-specific reference values enable more accurate distinction between physiological adaptation and pathology.

ARTICLE INFORMATION

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Disclosures

None.

Supplemental Material

Figures S1-S6

Tables S1-S6
STROBE checklist

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