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Do left ventricular non-compaction findings in special populations reflect a reversible physiological adaptation or a structural cardiomyopathy with clinical implications?

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Abstract

Background: Left ventricular non-compaction (LVNC) describes an imaging phenotype with prominent trabeculations and a thin compacted myocardial layer. Similar appearances occur in athletes, pregnancy, and hemoglobinopathies. Their clinical interpretation requires distinction between isolated morphology and cardiomyopathy.

Methods: A systematic review with narrative synthesis examined nine observational imaging reports. Imaging frequency, ventricular function, serial trabecular change and clinical events were distinguished. During revision, all nine full texts underwent design-specific JBI reassessment. Heterogeneous definitions precluded pooling.

Results: Gati and Dorobantu reported fulfillment of imaging criteria in 8.1% and 6.5% of athletes; Caselli reported prominent trabeculation in 1.4%. Di Gioia reported isolated trabeculations in 435/1,492 athletes (29.1%); follow-up was available in 61.3%, limiting prognostic inference. In 102 pregnant women, 26 developed trabeculations and eight met both echocardiographic criteria. Postpartum regression was observed, although participant-flow discrepancies limit final proportions. In sickle cell disease, increased trabeculation occurred in 28/99 patients; 8.1% met both criteria. Likely overlapping thalassemia reports described frequencies of 13.3% and 7.9%, with stability reported over 5.1 years in the latter.

Conclusions: Isolated LVNC-like morphology can occur without clinically evident cardiomyopathy in these populations. Pregnancy provides limited longitudinal evidence of reversibility; reversibility in athletes and hemoglobinopathies is not demonstrated by the nine analyzed

reports. Preserved function and reported event-free follow-up support contextual assessment but do not establish absence of long-term risk.

Background

Left ventricular non-compaction (LVNC) is an imaging phenotype characterized by prominent trabeculations, a relatively thin compacted myocardial layer, and deep intertrabecular recesses communicating with the ventricular cavity. Similar morphology can be observed in individuals with cardiomyopathy and in otherwise healthy people, including athletes and pregnant women (1,2).

In these populations, increased trabeculation may accompany altered loading conditions. However, a cross-sectional association does not establish acquired remodeling or reversibility. The clinical challenge is to distinguish isolated trabecular morphology from an accompanying cardiomyopathy (2,3).

The increasing availability and sensitivity of imaging methods, particularly cardiac magnetic resonance (CMR), has led to a rise in incidental findings of LVNC, which has in turn contributed to growing diagnostic uncertainty. Currently, no unified consensus exists regarding diagnostic criteria, and the prognostic significance of excessive trabeculation in asymptomatic individuals or those with physiological stressors remains unclear (2). This lack of clarity may lead to both overdiagnosis and overtreatment in patients without underlying pathology, as well as missed diagnoses in patients with early-stage cardiomyopathy.

Arbustini et al. underscore that the presence of LVNC morphology, in the absence of supportive clinical features, should not be equated with a definitive diagnosis of cardiomyopathy. Its clinical relevance should be determined by integrating additional factors such as ventricular function, the patient's medical history, and how these findings evolve over time (1).

The 2023 European Society of Cardiology (ESC) guidelines regard left ventricular hypertrabeculation as a phenotypic trait that can occur in different clinical settings, rather than a cardiomyopathy solely defined by trabecular morphology (3). This interpretation is consistent with the expert panel emphasis on ventricular function and the broader clinical phenotype (2).

Variation in imaging definitions and their application complicates diagnosis and risk stratification. Population-specific evidence on clinical events and longitudinal changes is needed to interpret these findings without overdiagnosis or missed disease (2,3).

Given this scenario, there is a pressing need to critically examine whether LVNC findings in special populations reflect a reversible physiological adaptation or a structural cardiomyopathy with clinical consequences.

This review examines whether LVNC-like morphology in elite athletes, pregnancy and hemoglobinopathies is accompanied by ventricular dysfunction, adverse clinical events or longitudinal change, and assesses the methodological limitations of that evidence.

Methods

1. Study design

We conducted a systematic review with narrative synthesis, organized by population (elite athletes, pregnancy, and hemoglobinopathies). No meta-analysis was undertaken because studies differed in participant selection, imaging definitions, outcome ascertainment and follow-up. The review evaluated whether LVNC-like findings were associated with physiological adaptation or clinically relevant cardiomyopathy. Study selection is presented using the PRISMA 2020 flow structure (4). This review was not registered in PROSPERO. The authors report that an unregistered written protocol existed before the review. Its contents were unavailable for verification during revision, so adherence and prespecification of individual procedures cannot be established. The revision-stage JBI reassessment is explicitly a subsequent methodological change.

2. Eligibility criteria

2.1. Types of studies

We included original human observational studies (prospective or retrospective cohorts, cross-sectional studies, case-control studies) and longitudinal case series reporting left ventricular morphology and/or function in a target population. Single case reports were excluded unless they supplied directly relevant longitudinal reversibility data, used qualitatively only. Editorials, narrative opinions, conference abstracts without extractable data, and non-human studies were excluded. A brief report or letter containing original observational data was distinguished from an editorial or opinion article. For the formal phenotype synthesis, direct measurement of trabeculation or LVNC was required at the revision-stage audit; general chamber-remodeling studies are treated as context. This clarification is not claimed to be prespecified.

2.2. Types of participants

Eligible populations were elite or competitive athletes; pregnant women assessed during pregnancy and postpartum; and individuals with sickle cell disease or β -thalassemia. These groups were the focus of the review question. The author-reported unregistered protocol was unavailable for verification.

2.3. Types of interventions/exposures

No therapeutic interventions were evaluated. The exposures of interest were the physiologic/high-output states or conditions themselves (endurance/competitive training; pregnancy; chronic anemia/hemolysis) and their association with left ventricular trabeculation or LVNC-like morphology on cardiac imaging.

2.4. Types of outcomes

2.4.1. Primary outcomes

- Clinical outcomes: all-cause mortality, heart failure events/hospitalizations, clinically relevant arrhythmias, and thromboembolic events.
- Reversibility or stability of trabeculations over time (e.g., postpartum regression).
- Global ventricular function, including left ventricular ejection fraction (LVEF), and clinically meaningful dysfunction.

Outcomes were synthesized as reported. Lack of reported events was distinguished from systematic ascertainment of their absence; changes in chamber dimensions were distinguished from measured changes in trabeculation.

2.4.2. Secondary outcomes

- Prevalence/frequency of left ventricular hypertrabeculation or LVNC by applied imaging criteria.
- Segmental distribution of trabeculations.
- Ancillary phenotypes, including electrocardiographic (ECG) repolarization changes in athletes.
- Imaging metrics defining LVNC or hypertrabeculation included the non-compacted to compacted myocardial thickness ratio (NC/C) and the percentage of trabeculated myocardial mass. Diagnostic discrimination was interpreted in relation to each study's population and reference classification.

3. Search methods for identification of studies

3.1. Electronic searches

The review reports searches of PubMed/MEDLINE, Embase and LILACS. The exact original last-search date and whether searches were repeated before submission could not be verified from retained records. This limits reproducibility; no estimated execution date is substituted. Supplementary Table S2 documents the available search and protocol information.

3.2. Searching other resources

The submitted manuscript reports reference-list screening, forward citation screening of sentinel papers and consultation of relevant bibliographies. Route-specific search records were unavailable for independent verification.

4. Data collection and analysis

4.1. Study selection

The submitted manuscript described independent title/abstract and full-text screening by two reviewers, with discussion or a third reviewer for disagreements. Historical item-level screening

logs were unavailable for verification. The revision-stage source audit was AI-assisted and is not described as new independently duplicated study selection.

4.2. Data extraction and management

The submitted manuscript described independent extraction by two reviewers using a piloted form. During revision, the nine available full reports were re-examined for design, setting, participant selection, modality, imaging definition and phase, ventricular function, clinical events, serial change and cohort relationships. Source discrepancies and absent information are identified in the tables and Supplementary Methods; no missing participant counts or outcomes were imputed. Historical duplicate-extraction records were unavailable for verification.

5. Critical appraisal (risk-of-bias assessment)

During revision, the unverified NOS scores were replaced with design-specific JBI item-level assessments of all nine full reports. Prevalence and analytical cross-sectional (2026) tools address screening frequency and baseline comparisons; the cohort tool (2025) addresses pregnancy, Bonamini and Di Gioia follow-up; case-series appraisal addresses selected athlete follow-up; and diagnostic test accuracy appraisal addresses Chiodi. Limerick is separately assessed with the quasi-experimental tool as contextual intervention evidence. Nineteen component assessments do not represent nineteen independent studies. Single-cohort group-comparison items are marked not applicable with reasons. Yes, No, Unclear and Not applicable judgments, source locations and tool-specific syntheses are in Supplementary Tables S3–S8 (5). No totals or overall risk categories are assigned. ChatGPT assisted full-text extraction, item-level appraisal and drafting. The authors confirm independent approval of the revised work; this is not presented as independent duplicate item-level appraisal, and no unrecorded adjudication process is claimed.

6. Bias management

6.1. Handling missing data

When critical outcome or methods details were missing, we attempted to derive information from supplementary materials or related publications; if unresolved, we retained the study and reported the uncertainty, emphasizing qualitative synthesis without imputation.

6.2. Assessment of reporting biases

No funnel plot or statistical test for publication bias was performed because there was no pooled analysis and few studies were available within each population. Multiple database and citation searches do not establish absence of reporting bias. Selective publication and selective outcome reporting remain possible.

7. Synthesis plan (qualitative)

The narrative synthesis summarized imaging frequency, ventricular function, reported clinical events, and longitudinal change within each population. Estimates derived using different definitions were not pooled or treated as interchangeable. Reversibility was inferred only when trabeculation itself was measured serially. We did not undertake a formal GRADE assessment.

Instead, confidence in conclusions was explicitly limited according to study design, confounding, affected-subgroup size, outcome surveillance, follow-up, and applicability. No categorical GRADE certainty ratings or evidence-based practice recommendations are claimed.

RESULTS

Study selection

Figure 1 presents the originally reported selection counts: 458 records identified, 21 duplicates removed, 437 screened, 408 excluded, 29 reports sought, two not retrieved and 27 assessed in full. Eighteen reports were excluded for design (n=8), population (n=7) or outcomes (n=3). The nine reports analyzed are Gati (athletes, 2013), Caselli (2016), Di Gioia (2024), Dorobantu (2023), Gati (pregnancy, 2014), Gati (sickle cell disease, 2013), Piga (2012), Bonamini (2019) and Chiodi (2017) (6–14). All nine full texts were verified during revision. Limerick is contextual supporting evidence and is not counted among the nine. The historical flow could not be independently reconstructed from retained logs. Likely cohort overlap is described below.

LVNC in elite athletes

Gati evaluated 1,146 athletes, 415 sedentary controls, and a separate clinical LVNC comparator group (n = 75) (6). Increased trabeculation (at least three protrusions ≥ 3 mm, assessed in diastole) occurred in 18.3% of athletes versus 7.0% of sedentary controls. Jenni criteria were positive in 9.5%, Chin criteria in 10.1%, and both in 93/1,146 athletes (8.1%); no sedentary controls met the LVNC criteria. Chin measurements were end-diastolic and Jenni measurements end-systolic. Follow-up of 48.6 ± 14.6 months without reported adverse events concerned only ten selected athletes with LVEF $\leq 50\%$ and T-wave inversion, all of whom underwent additional testing. Caselli screened 2,501 athletes and identified 36 (1.4%) with prominent trabeculation using a composite morphological definition; all 36 met Chin criteria and eight met Jenni criteria (7). Three (0.1% of all athletes) were clinically classified as affected on functional and/or familial/genetic grounds. In the remaining 33, a retrospective review of the preceding 5 ± 3 years found no events or worsening LVEF. This is not prospective event-free surveillance of all 2,501 athletes.

Di Gioia retrospectively evaluated 1,492 Olympic athletes screened between the London 2012 and Beijing 2022 Games (8). Athletes with Jenni-positive morphology, LVEF $< 50\%$, diastolic dysfunction, specified repolarization abnormalities or relevant familial alarm features were excluded. Isolated left ventricular trabeculations (LVTs) occurred in 435/1,492 (29.1%), defined by a double-layered appearance regardless of NC/C ratio or prominent ≥ 3 mm end-diastolic protrusions with synchronous systolic motion. Selective CMR was performed in 58/435; two met Petersen end-diastolic NC/C > 2.3 without clinical confirmation of LVNC. Baseline exercise ventricular ectopy occurred in 61/435 (14.0%) versus 123/1,057 (11.6%; $p = 0.22$). Follow-up at 52 ± 32 months was available only for 914/1,492 (61.3%) athletes participating in more than one Olympic Games: 260/435 with LVTs and 654/1,057 without. Exercise ventricular ectopy was reported in 29/260 (11.1%) versus 67/654 (10.2%; $p = 0.51$). These unadjusted, non-significant differences do not establish equivalence or population-wide safety. Greater indexed LV volumes in male endurance athletes with LVTs are compatible with adaptation but do not prove training-

related causation or reversibility. Shared institutional recruitment and overlapping dates with Caselli (January 2012–May 2015) make participant overlap likely; its extent cannot be quantified. Dorobantu found Jenni-positive morphology in 27/417 male adolescent academy athletes (6.5%) (9). Thirty-seven of 54 segmental mechanics comparisons supported non-inferiority within empirical margins; 17 were underpowered. This does not establish long-term safety. Gati athletes (2003–2011) and Dorobantu (2014–2019) have non-overlapping reported recruitment periods.

LVNC in pregnancy

Gati prospectively assessed 102 primigravida women without increased baseline trabeculation in the first trimester, at 28–36 weeks, and initially at 3–12 months postpartum (10). Twenty-six developed increased trabeculation (25.4%, as reported); ten met Jenni criteria (9.8%), 19 met Chin criteria (18.6%), and eight met both (7.8%). Chin's $X/Y \leq 0.5$ was measured at end-diastole; Jenni's $NC/C > 2$ at end-systole. The non-pregnant reference sample was used to define a trabeculation threshold and was not a parallel longitudinal comparison group (Table 2).

At the first postpartum assessment (mean 8.1 ± 4.2 months), 18 of 26 women had complete regression and seven had persistent trabeculation (10). These counts account for 25 rather than all 26 women. The seven persistent cases were considered for an additional 24 ± 3 months of follow-up; one became pregnant again and was excluded from the extended analysis. Of the six remaining women, one had additional complete regression and five had persistent but reduced trabeculation. The abstract therefore reports 19/26 with complete regression (73%) and five with marked reduction, but the full text leaves one initial disposition unaccounted for and documents a repeat-pregnancy exclusion. The additional 24-month interval must not be attributed to all 26 women. These findings support observed regression, not universal resolution or complete follow-up of the entire affected subgroup.

These findings are compatible with loading-related changes in trabecular appearance in otherwise healthy women. Within the nine analyzed reports, the healthy-pregnancy evidence derives from one 102-participant cohort, of whom 26 developed trabeculations. It cannot establish long-term safety, define management for women with established cardiomyopathy, or exclude cardiomyopathy in an individual with preserved ejection fraction. Symptoms, dysfunction, family history, and other abnormal findings should inform further assessment (2,3).

LVNC in hemoglobinopathies (sickle cell disease and thalassemia)

The third special population of interest is individuals with chronic hemoglobinopathies such as sickle cell disease (SCD) and β -thalassemia, who often have chronically elevated cardiac output and chamber dilation. Researchers have explored whether these conditions are associated with an acquired LVNC morphology and what its clinical significance might be. Table 3 provides an overview of primary studies in this area.

Sickle cell disease: Gati's original cross-sectional letter included 99 consecutive normotensive patients with homozygous sickle cell disease and 132 healthy Black controls (11). Increased trabeculation occurred in 28/99 patients (28.3%) versus 12.1% of controls. Separately, 20.8% met Chin criteria, 10% met Jenni criteria, and 8.1% met both; no control met LVNC criteria. The article does not explicitly give the criterion-specific case counts, and the reported 20.8% cannot be reconciled to an integer numerator using 99 as the denominator. We retain the reported

percentages without inventing counts. Trabecular protrusions ≥ 3 mm were assessed in end-diastole; the figure distinguishes diastolic Chin from systolic Jenni measurement. In patients with versus without increased trabeculation, LVEF was 61% in each group; LVEF $< 50\%$ occurred in 3/28 versus 6/71. Five of 25 patients with systolic and/or diastolic dysfunction showed LVNC features. Thus preserved mean function does not imply that every participant had normal function. Controls were younger (21 ± 6 versus 33 ± 11 years); no adjusted analysis or longitudinal follow-up was reported.

Limerick is contextual evidence outside the nine-report synthesis (15). During the revision-stage eligibility audit, it was classified as supporting evidence because it measures chamber remodeling after therapeutic transplantation without quantifying trabeculation or LVNC. This clarification makes direct trabeculation/LVNC measurement necessary for the formal phenotype synthesis; it is a revision-stage clarification, not a reconstructed historical screening decision. The uncontrolled pre/post analysis includes 12 of 19 adults; exclusions include death before one year and graft failure. Indexed CMR LV end-diastolic volume decreased from 114.5 to 90.6 mL/m² ($p = 0.001$). This is indirect loading-related context and does not demonstrate reversal of LVNC. Original flow counts are unchanged because its original screening disposition cannot be established from retained records.

β -Thalassemia: In a cross-sectional magnetic resonance study of 135 transfusion-dependent patients, Piga identified LVNC morphology in 18 (13.3%; 95% confidence interval [CI], 8.6–20.1) using the study's strict criteria (12). The sample comprised 130 patients with major and five with intermedia, with a mean age of 29.6 ± 7.7 years. The study required all of the following: a two-layered appearance; end-diastolic NC/C ≥ 2.5 excluding segment 17; compacted-layer thickness ≤ 4.5 mm at the non-compacted site; and a hyperintense signal in black-blood T2-weighted images. This is a study-specific combined rule, not the unmodified Petersen criterion.

Measured demographics, hemoglobin levels, and iron indices did not show statistically significant differences between patients with and without LVNC morphology (12). The adjusted odds ratio for heart failure was 1.77 (95% CI, 0.29–10.89). This wide interval is compatible with substantially different associations and does not establish absence of clinical risk.

Piga's cross-sectional findings do not determine whether trabeculation was acquired or whether it predicts subsequent events (12). Comparison of prevalence with other populations also depends on imaging definitions and participant selection.

Bonamini studied 560 patients (473 thalassemia major, 87 intermedia) and classified 44 (7.9%) as having LVNC morphology (13). All three CMR criteria were required in diastole: non-compacted mass $> 25\%$ of total mass, indexed non-compacted mass > 15 g/m², and NC/C > 2.5 in at least one segment excluding segment 17. LVEF was lower in those with this morphology (52.68% versus 56.90%; $p = 0.0005$). At mean follow-up 5.1 ± 1.3 years (range 2.0–6.9), no adverse events were reported in the LVNC subgroup and serial CMR measures, including non-compacted mass, did not change significantly. The full report does not provide endpoint-specific event definitions, a detailed attrition flow or an explicit paired CMR denominator. Stability does not establish reversibility or equivalent clinical risk. Piga and Bonamini recruited at the same Turin/Orbassano reference centre beginning in September 2007; Piga's September 2007–September 2008 window

falls within Bonamini's September 2007–November 2014 window, and Bonamini explicitly identifies Piga as its previous smaller study. Substantial overlap is therefore likely, although individual duplication cannot be quantified. Their denominators are not summed as independent participants.

Chiodi compared magnetic resonance images from 38 patients with β -thalassemia major and 10 patients classified as having LVNC (14). The tested diastolic segmental NC/C threshold was >2.5 , with reported specificity of 58%. Non-compacted myocardial mass $>25\%$ of total left ventricular mass had specificity of 93%; the $>20\%$ threshold had sensitivity of 100% and specificity of 87%. These estimates arose from a small, selected comparative sample and do not validate a universal threshold for high-output states. The study evaluates diagnostic discrimination, not reversibility or clinical prognosis. The LVNC reference classification combined echocardiography, CMR NC/C >2.3 and clinical/functional features, introducing incorporation and spectrum concerns. The reported specificity estimates are retained as published: the narrative also reports 19/38 thalassemia patients positive for NC/C >2.5 and 3/38 positive for mass $>25\%$, counts that do not exactly reproduce the stated specificities of 58% and 93%. No corrected contingency table is inferred.

Risk of bias assessment

Table 4 summarizes design-specific appraisal of all nine full reports. Supplementary Tables S3–S8 contain nineteen component assessments, including a separate contextual assessment of Limerick. Item-level evidence and tool-specific syntheses replace unverified NOS totals; no global score or risk category is assigned.

Cross-sectional and baseline imaging analyses

Prevalence assessments primarily apply to selected screening or referral samples rather than representative national populations. Gati's athlete measurements had reproducibility checks, but recruitment and age/ethnicity differences limit comparisons. Sick cell controls were appreciably younger, and confounding adjustment was not reported. Piga adjusted the heart-failure association for age, sex, iron indices and hemoglobin, but the small number of events and wide interval limit inference. Dorobantu used reproducibility testing, adjusted demographic associations and multiplicity-aware non-inferiority analyses; its functional comparisons remain limited by the small imaging-positive group, empirical margins and lack of a contemporaneous disease comparator. Chiodi's separate diagnostic groups and partially incorporated reference definition constrain transportability. No overall numeric quality score is used.

Longitudinal analyses

Pregnancy provides direct serial-imaging evidence with blinded re-reading, but has no parallel non-pregnant cohort, incomplete reconciliation of the affected subgroup and relatively low interobserver agreement for the Jenni classification. Bonamini reports serial CMR stability, but event ascertainment and paired imaging completeness are insufficiently described, and confounding-adjusted prognosis was not evaluated. Gati's athlete follow-up includes ten selected cases; Caselli's preceding-record review includes 33 classified non-affected or unlikely affected cases. These case-series components cannot establish population-wide safety. Di Gioia's retrospective follow-up includes only repeated Olympians (914/1,492), with no adjustment for missing follow-up or confounding. Baseline ectopy was present in both groups, and outcome-free

incident-risk sets are not specified. This limits both event-incidence interpretation and generalization to athletes who retired or did not requalify.

DISCUSSION

This population-specific synthesis examined whether LVNC-like morphology was accompanied by dysfunction, adverse events, or longitudinal change. Several athlete studies reported preserved function in individuals with isolated trabeculation. One pregnancy cohort documented postpartum regression. In thalassemia, one prospective cohort supported medium-term stability, whereas sickle cell evidence remained sparse. These findings support contextual interpretation of morphology, but do not establish a single physiological mechanism, universal reversibility, or absence of long-term risk (6–14).

Community studies provide supporting evidence outside the nine analyzed reports. Weir-McCall found that 219 of 1,480 analyzed participants (14.8%) met at least one magnetic resonance LVNC criterion; only 19 (1.3%) met all four (16). This was not a longitudinal demonstration of functional safety. In the Multi-Ethnic Study of Atherosclerosis (MESA), trabeculation measured at the later examination was not associated with clinically relevant differences in preceding ventricular volume or function changes over 9.5 years (17). Its measurement timing limits prospective prognostic interpretation. Woodbridge's cross-sectional UK Biobank analysis of 1,030 community participants found no significant association between physical activity and maximal NC/C after adjustment (18). It neither demonstrates clinical safety nor establishes what happens at elite-athlete training loads. These community studies do not establish prognosis in athletes, pregnancy or hemoglobinopathies.

Imaging definitions must be interpreted with their measurement conventions. Jenni's echocardiographic approach uses an end-systolic NC/C ratio >2 with additional morphological and Doppler features (19). Petersen's magnetic resonance approach uses an end-diastolic NC/C ratio >2.3 (20), whereas Jacquier's approach quantifies trabeculated myocardial mass relative to total left ventricular mass ($>20\%$) (21). Ratios, mass fractions, and systolic or diastolic measurements are not interchangeable.

Grothoff's original magnetic resonance study combined non-compacted myocardial mass, its proportion of total mass, and segmental distribution to improve diagnostic discrimination in selected patients and controls (22). These criteria were not derived as universally validated thresholds for athletes, pregnancy, and hemoglobinopathies. Chiodi's comparative findings likewise support attention to the applied definition, while requiring external validation before population-wide adoption (14).

Tables 1–3 identify modality, criterion, and measurement phase where verified. Where a report applies multiple definitions, its numerator must be tied to the particular rule used. A positive imaging threshold alone does not establish cardiomyopathy, and a normal LVEF alone does not exclude it (2,3).

The longitudinal evidence differs between populations. Pregnancy provides direct evidence of postpartum regression in one cohort; athlete studies primarily address morphology, function, and selected follow-up. Thalassemia data support stability in one cohort rather than reversal, and sickle

cell data do not directly establish reversibility. Women with pre-existing cardiomyopathy are outside the applicability of the healthy pregnancy cohort. The review cannot attribute hemoglobinopathy morbidity to specific competing mechanisms because those comparisons were not established by the included studies.

The evidence analyzed is observational, with heterogeneous imaging definitions, selected populations, small affected subgroups, confounding and variable surveillance. Pregnancy regression and the adult sickle cell estimate depend on single reports within this synthesis. Likely Piga–Bonamini and Caselli–Di Gioia overlap prevent treating all reports as independent samples. Di Gioia excludes several alarm features and follows only repeated Olympians. No formal GRADE or quantitative publication-bias assessment was undertaken. The review was not registered in PROSPERO; the author-reported prior protocol was unavailable for verification. The exact original search date and pre-submission rerun status could not be established from retained records. Historical selection logs were unavailable, limiting assessment of search completeness. The revision-stage JBI appraisal was AI-assisted without documented independent duplicate item-level assessment. These limitations preclude firm safety, causal or management recommendations.

The clinically relevant implication is to assess the whole phenotype rather than diagnose cardiomyopathy from trabecular morphology alone (2,3). Symptoms, dysfunction, abnormal electrocardiographic findings, family history, and tissue characterization may justify further evaluation. This review does not establish optimal imaging intervals, new thresholds, treatment indications, or sports eligibility rules. Reassessment should reflect the individual clinical context; the single pregnancy cohort cannot support universal pregnancy-specific recommendations.

LVNC-like morphology can coexist with preserved function in athletes, pregnancy, and hemoglobinopathies. One pregnancy cohort documented postpartum regression, and one thalassemia cohort reported medium-term stability. The nine analyzed reports do not establish reversibility or long-term clinical safety in the other settings. Interpretation should integrate morphology with ventricular function, symptoms, family history, and longitudinal findings. Prospective studies with standardized definitions and adjudicated outcomes are needed.

Clinical Perspective

- 1) Isolated LVNC-like morphology may accompany athletic training, pregnancy, and hemoglobinopathies without establishing a diagnosis of cardiomyopathy.
- 2) Interpretation should integrate symptoms, ventricular function, electrocardiographic findings, family history, and additional imaging when clinically indicated.
- 3) Postpartum regression was documented in one cohort. Regression of trabeculation after transfusion or stem cell transplantation has not been demonstrated by the studies included in this review.
- 4) Preserved left ventricular function and event-free observation are reassuring findings, but limited follow-up and small affected subgroups cannot exclude uncommon or late adverse outcomes.
- 5) These findings support individualized evaluation. They do not establish new diagnostic thresholds, follow-up intervals, or eligibility rules for sports participation.

Author contributions

Gloria Ibis Tirado Romero: Conceptualization, Methodology, Data curation, Formal analysis, Writing – original draft, Writing – review & editing, Supervision.

Elkin Julian Suarez Angarita: Methodology, Validation, Writing – review & editing.

Juan Esteban Suárez Muñoz: Data curation, Investigation, Writing – review & editing.

Andrea Carolina Martínez García: Data curation, Investigation, Writing – review & editing.

Luis Elias Casso Molina: Data curation, Investigation, Writing – review & editing.

Luisa María Gaviria: Methodology, Validation, Writing – review & editing.

All authors contributed to the interpretation of the evidence, critically revised the manuscript for important intellectual content, approved the final version of the manuscript, and agree to be accountable for all aspects of the work.

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Data availability statement: Study-level findings and source-based appraisal are provided in the manuscript and Supplementary Methods. No individual participant dataset was generated. Original search and screening logs were unavailable for independent verification.

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Figures and Tables

Figure 1. PRISMA 2020 flow diagram presenting the originally reported study-selection counts.
Population-specific subcounts have been removed. The historical counts could not be independently reconstructed from retained search and screening logs.

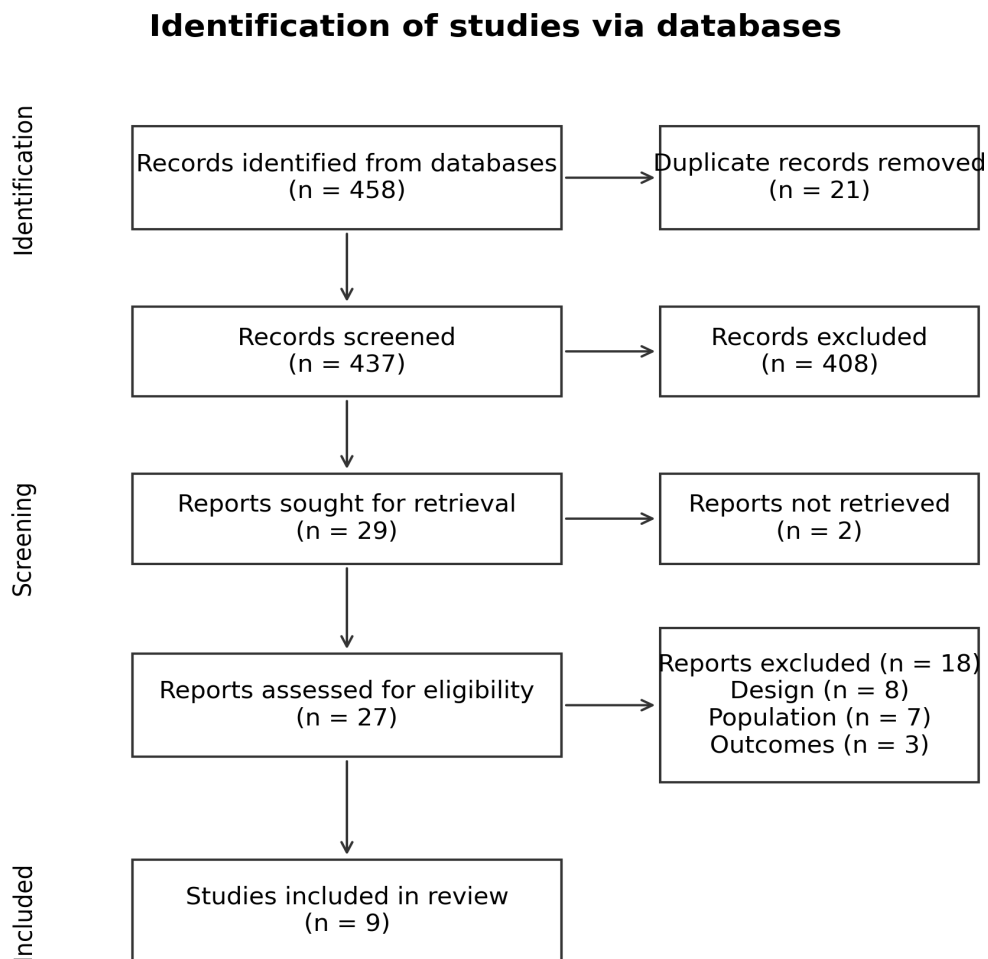


Table 1. Imaging findings in athletes. Abbreviations: LVNC, left ventricular non-compaction; LVT, left ventricular trabeculation; LVEF, left ventricular ejection fraction; CMR, cardiac magnetic resonance; NC/C, non-compacted to compacted myocardial thickness ratio; ED, end-diastole; ES, end-systole; EF, ejection fraction; STE, speckle-tracking echocardiography; TOST, two one-sided tests. Imaging definitions, phases and follow-up denominators are study-specific.

Study/component	Sample	Imaging definition and phase	Frequency	Follow-up / interpretation
Gati 2013 (6) Cross-sectional + selected series	1,146 athletes; 415 sedentary controls; 75 clinical LVNC comparators	≥3 protrusions ≥3 mm in diastole; Chin ED; Jenni ES; both criteria distinguished	Increased: 18.3% vs 7.0%. Jenni 9.5%; Chin 10.1%; both 93/1,146 (8.1%); no control LVNC	Ten selected cases only: 48.6 ± 14.6 months, no events reported. No detraining demonstration.
Caselli 2016 (7) Screening + selected record review	2,501 competitive athletes	Two layers; >3 protrusions >3 mm in ED; synchronous movement; Doppler filling. Chin ED; Jenni ES; selective further tests	Prominent: 36/2,501 (1.4%); all 36 Chin-positive, eight Jenni-positive. Clinical LVNC: three (0.1%)	Preceding records, 5 ± 3 years, in 33 classified normal/unlikely; no events/worsening reported. Not whole-cohort prospective follow-up.
Di Gioia 2024 (8) Retrospective baseline + follow-up	1,492 Olympic athletes, 2012–2022; clinical/morphologic alarm exclusions	Double layer regardless of NC/C or ≥3 mm ED protrusions; Jenni ES-positive excluded. Selective Petersen ED CMR	435/1,492 (29.1%) isolated LVTs; 58 CMR, two Petersen-positive without clinical LVNC	Followed 914/1,492:260/435 vs654/1,057. VEB29/260 vs67/654, p=.51;52 ±32months. Repeated Olympians only; likely Caselli overlap.
Dorobantu 2023 (9) Cross-sectional mechanics	417/447 eligible male academy athletes; 2014–2019	Jenni: ES NC/C >2 in SAX segment, prominent trabeculations/recesses. STE	27/417 (6.5%)	37/54 segmental comparisons statistically non-inferior; 17 underpowered. Usual-care follow-up not a defined long-term event cohort.

Table 2. Serial imaging findings in pregnancy. Abbreviations: LVNC, left ventricular non-compaction; LVEF, left ventricular ejection fraction; NC/C, non-compacted to compacted myocardial thickness ratio. Chin measurements are end-diastolic and Jenni measurements end-systolic; initial and extended postpartum follow-up are distinguished.

Study	Sample	Definition and phase	Frequency	Serial change / limitations
Gati 2014 (10) Prospective cohort	102 primigravida women; normal baseline	First trimester; 28–36 weeks; initial 3–12 months postpartum. Chin ED X/Y $\leq .5$; Jenni ES NC/C > 2	Increased: 26/102 (25.4%, reported); Jenni 10, Chin 19, both 8 (7.8%)	Initial 8.1 ± 4.2 months: 18 regressions, 7 persistent (one disposition unaccounted). Additional 24 ± 3 months in persistent subgroup: one repeat pregnancy excluded, six reassessed, one extra regression and five reduced/persistent. Abstract 19/26 complete; incomplete flow prevents universal-resolution inference.

Table 3. Imaging findings in hemoglobinopathies. Abbreviations: LVNC, left ventricular non-compaction; LVEF, left ventricular ejection fraction; CMR, cardiac magnetic resonance; NC/C, non-compacted to compacted myocardial thickness ratio; BSA, body surface area; LIC, liver iron concentration; ED, end-diastole; ES, end-systole; DTA, diagnostic test accuracy; β -TM, β -thalassemia major; CI, confidence interval; OR, odds ratio. Imaging criteria, phases and diagnostic or clinical endpoints are study-specific.

Study/component	Sample	Imaging definition and phase	Findings	Interpretation
Gati SCD 2013 (11) Cross-sectional	99 consecutive HbSS patients; 132 healthy Black controls	≥ 3 mm protrusions in ED; Chin diastolic/Jenni systolic as illustrated; colour Doppler recess filling	Increased 28/99 (28.3%) vs 12.1%; Chin 20.8%, Jenni 10%, both 8.1%; no control LVNC. Criterion-specific counts not explicitly reported	EF 61% in both trabeculation groups; EF < 50%: 3/28 vs 6/71. Younger controls; no adjusted or longitudinal analysis.
Piga 2012 (12) Cross-sectional	135:130 major, five intermedia; Sept 2007–Sept 2008	ALL: two layers; ED NC/C ≥ 2.5 excluding 17; compact layer ≤ 4.5 mm; black-blood T2 hyperintensity	18/135 (13.3%; 95% CI 8.6–20.1)	Adjusted HF OR 1.77 (95% CI .29–10.89); no reversibility data. Likely overlaps Bonamini.
Bonamini 2019 (13) Baseline + cohort	560:473 major, 87 intermedia; Sept 2007–Nov 2014	ALL in ED: NC mass > 25%; NC mass/BSA > 15 g/m ² ; NC/C > 2.5 excluding 17	44/560 (7.9%); EF 52.68% vs 56.90%, $p = .0005$	LVNC subgroup: mean 5.1 years, no events reported; serial NC mass stable. Paired denominator/attrition and event definitions not explicit. Likely overlaps Piga.
Chiodi 2017 (14) Two-gate DTA	38 β -TM; 10 clinical LVNC comparators	ED NC/C > 2.5; ED mass > 20% (Jacquier) or > 25% (blood pool excluded)	Reported specificity 58%, 87%, 93%; sensitivity 100% for each tested threshold. Source count discrepancies noted in supplement	Selected diagnostic groups; incorporation and spectrum concerns. No prevalence/prognosis/reversibility inference.

Table 4. Design-specific critical appraisal: source-based reassessment during revision. JBI, Joanna Briggs Institute. Component assessments do not increase the number of included reports. Full item judgments and source evidence appear in Supplementary Tables S3–S8. No scores or global risk categories are assigned.

Report	Components / tools	Principal limitations	Implication
Gati athletes (6)	Prevalence; analytical cross-sectional; selected case series	Selected athletes/controls; demographic differences; only ten follow-up cases	Frequency and morphology associations; safety cannot be generalized.
Caselli (7)	Prevalence; selected case series	Previously screened elite sample; selective additional testing; retrospective records	Clinical classification is not a universally validated diagnostic test.
Di Gioia (8)	Prevalence; analytical cross-sectional; retrospective cohort	Alarm-feature exclusions; selective CMR; unadjusted comparisons; only 61.3% follow-up; likely Caselli overlap	Selected-sample frequency and ectopy comparisons; equivalence and general safety not established.
Dorobantu (9)	Prevalence; analytical cross-sectional	Male academy sample; small positive group; empirical margins; no disease comparator	Normal mechanics do not establish long-term safety.
Gati pregnancy (10)	Cohort, single-cohort items handled explicitly	No parallel comparator; affected-subgroup flow discrepancy; low Jenni interobserver κ	Observed regression, with incomplete final-flow reconciliation.
Gati SCD (11)	Prevalence; analytical cross-sectional	Younger controls; no reported adjustment; criterion-count ambiguity	Association only; no prognosis or reversibility.
Piga (12)	Prevalence; analytical cross-sectional	Referral sample; few HF events; imprecision; likely overlap	No firm risk estimate or independent pooled denominator.
Bonamini (13)	Prevalence; cohort	Likely overlap; no adjusted prognosis; unclear event definitions/paired denominator	Medium-term stability reported, safety uncertain.
Chiodi (14)	Diagnostic test accuracy	Two-gate sampling; incorporated reference; small disease group; count discrepancies	Accuracy estimates require cautious interpretation.