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# Gender Specific Patterns in Vascular Disease Progression Among Adult Patients

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## ABSTRACT

This study investigates gender-specific trajectories in vascular disease progression by integrating high-resolution vascular imaging, computational hemodynamics, and AI-driven predictive modeling across adult male and female patient cohorts. Results demonstrated that males exhibit focal, mechanically driven plaque development characterized by elevated wall shear stress clusters, higher calcification density, and abrupt pressure gradients, whereas females display diffuse microvascular dysfunction associated with oscillatory shear variability, heightened inflammatory burden, and more uniform lumen narrowing. CFD simulations and quantitative progression metrics highlighted these mechanobiological contrasts, while AI-based prediction surfaces revealed fundamentally distinct risk evolution patterns governed by sex-dependent interactions among age, vessel stiffness, and systemic inflammation. These findings emphasize the need for gender-aware diagnostic frameworks and tailored vascular care strategies that account for divergent remodeling pathways and progression determinants.

**KEYWORDS**: vascular remodeling, hemodynamics, gender-specific risk, computational modeling.

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## INTRODUCTION

Understanding vascular disease progression through a gender-specific lens has become increasingly important as emerging evidence indicates that biological sex, hormonal environment, and structural vascular characteristics profoundly influence both onset and evolution of arterial pathology [1]. Traditional cardiovascular epidemiology largely aggregated male and female cases into homogenous datasets, obscuring the nuances in vascular remodeling, inflammatory activity, and plaque stability that differ between genders [2]. Contemporary findings now suggest that males typically exhibit earlier luminal narrowing in major peripheral arteries, whereas females often display diffuse microvascular dysfunction that is not detectable through routine imaging modalities, contributing to diagnostic delays and poorer clinical outcomes [3]. These divergent disease expressions underscore the necessity for separate analytical frameworks capable of modeling hemodynamic progression through sex-specific patterns rather than generalized assumptions.

Biological sex plays a decisive role in arterial wall biomechanics, particularly in the interplay between smooth muscle cell proliferation, extracellular matrix remodeling, and endothelial repair response [4]. Estrogen-mediated vasoprotection appears to modulate nitric oxide availability and shear-stress–dependent endothelial signaling, delaying plaque calcification in premenopausal women; however, this advantage diminishes with age, resulting in accelerated vascular stiffening and atypical plaque morphology beyond menopause [5]. In contrast, males more frequently develop lipid-rich necrotic cores and high-shear stress plaque shoulders, which predispose them to rupture-prone lesions and acute ischemic events at comparatively younger ages [6]. These physiologic differences translate into distinct temporal trajectories of disease, with female patients often presenting later but progressing rapidly once microvascular impairment establishes.

Recent advancements in vascular imaging and computational modeling have further illuminated the extent to which gender influences hemodynamic loading patterns. High-resolution CT-angiography, four-dimensional flow MRI, and CFD-based shear stress mapping have all shown that female arterial networks exhibit greater sensitivity to oscillatory shear indices and micro-scale turbulent transitions, especially in smaller-caliber vessels [7]. These patterns imply that even moderate elevations in systemic inflammation may disproportionally affect female endothelial surfaces, catalyzing diffuse dysfunction rather than the focal plaque formation commonly observed in males. Integrating these kinetic factors into predictive models has become essential for understanding why identical risk profiles, such as hypertension or dyslipidemia, can produce markedly different vascular outcomes across genders.

Beyond biological determinants, gender-differentiated behavioral and clinical factors also shape disease progression trajectories. Male populations often present with well-defined atherosclerotic plaques detectable through ultrasonography or CT imaging, enabling earlier intervention, whereas female patients frequently report non-specific vascular symptoms that elude conventional diagnostic scoring systems [8]. These disparities contribute to systematic underdiagnosis of vascular dysfunction in women, which is compounded by the fact that commonly used risk calculators were historically derived from male-dominant datasets [9]. Consequently, disease onset in women often becomes clinically apparent only after significant microvascular destabilization has occurred.

In parallel, emerging AI-driven vascular analytics have revealed strong gender dependencies in risk prediction, where machine learning models trained on integrated biomarkers, hemodynamic indices, and imaging-derived plaque features demonstrate distinct performance curves when applied separately to male and female cohorts [10]. These findings not only reaffirm the presence of sex-specific vascular signatures but also highlight the need for gender-aware model design to avoid systemic predictive bias. Moreover, multi-scale data integrations have begun to show that immune activation pathways, metabolic dysregulation patterns, and vascular aging markers follow different progression vectors across genders, necessitating a more granular stratification approach in population-level vascular studies.

Taken together, these developments emphasize the critical importance of analyzing vascular disease through a gender-specific paradigm that accounts for biological, hemodynamic, metabolic, and behavioral dimensions. An integrated approach that combines advanced imaging, computational hemodynamics, and machine learning has the potential to uncover previously unrecognized trajectories and refine individualized treatment strategies [11]. As precision vascular medicine continues to expand, distinguishing male and female progression pathways will not only enhance diagnostic accuracy but also contribute to improved long-term outcomes through targeted therapeutic planning.

## METHODS

The methodological framework for this study was constructed to isolate gender-specific determinants of vascular disease progression by integrating clinical stratification, multi-modal vascular imaging, and computational modeling. Adult patients between 35 and 75 years were recruited from tertiary cardiovascular centers and stratified into male and female cohorts after excluding individuals with congenital vascular anomalies, previous vascular surgeries, or chronic inflammatory diseases likely to confound endothelial function. Each participant underwent a standardized cardiovascular assessment including anthropometric measurements, lipid profiling, inflammatory marker quantification, and blood pressure evaluation. Stratification incorporated age-normalized risk scores to ensure that differences in progression patterns were attributable to biological and hemodynamic factors rather than baseline disparities in comorbidities.

A unified imaging protocol was implemented to ensure consistency across cohorts, combining high-resolution computed tomography angiography (CTA) with Doppler ultrasound–based flow mapping to capture both structural and functional vascular characteristics. CTA scans were acquired using a multi-slice detector system that provided sub-millimeter resolution, enabling precise quantification of lumen diameter, wall thickness, and plaque morphology. Doppler ultrasound was performed to measure real-time flow velocities, turbulence signatures, and hemodynamic load, which were subsequently integrated into the computational models. The dual-modality imaging allowed reconstruction of multi-layer arterial geometry incorporating intima, media, and adventitia regions, thereby capturing sex-specific microstructural variations that influence disease evolution.

A three-step image preprocessing pipeline was adopted to enhance anatomical fidelity prior to model reconstruction. First, noise reduction using an anisotropic diffusion filter preserved subtle plaque boundaries without blurring micro-calcifications. Second, vessel segmentation was performed using a hybrid active contour method capable of delineating irregularly shaped plaques often observed in female microvascular disease patterns. Third, lumen centerlines were extracted through a geometric spline-fitting algorithm to enable accurate mapping of velocity profiles in curved arterial segments. These steps ensured structural continuity essential for reliable computational fluid dynamics simulations.

The vascular geometries derived from this pipeline were subsequently transformed into high-resolution mesh structures, which formed the core representation of sex-specific vascular anatomy. As shown in Figure 1, the reconstructed 3D multi-layer arterial models captured critical geometric attributes such as lumen diameter variability, differential wall thickness, and plaque deposition topography for male and female patients. The visualization highlighted gender-dependent differences, with male geometrics exhibiting larger diameters and focal plaques, while female models displayed more uniform narrowing and diffuse plaque accumulation. These geometries served as boundary conditions for downstream hemodynamic and progression simulations.

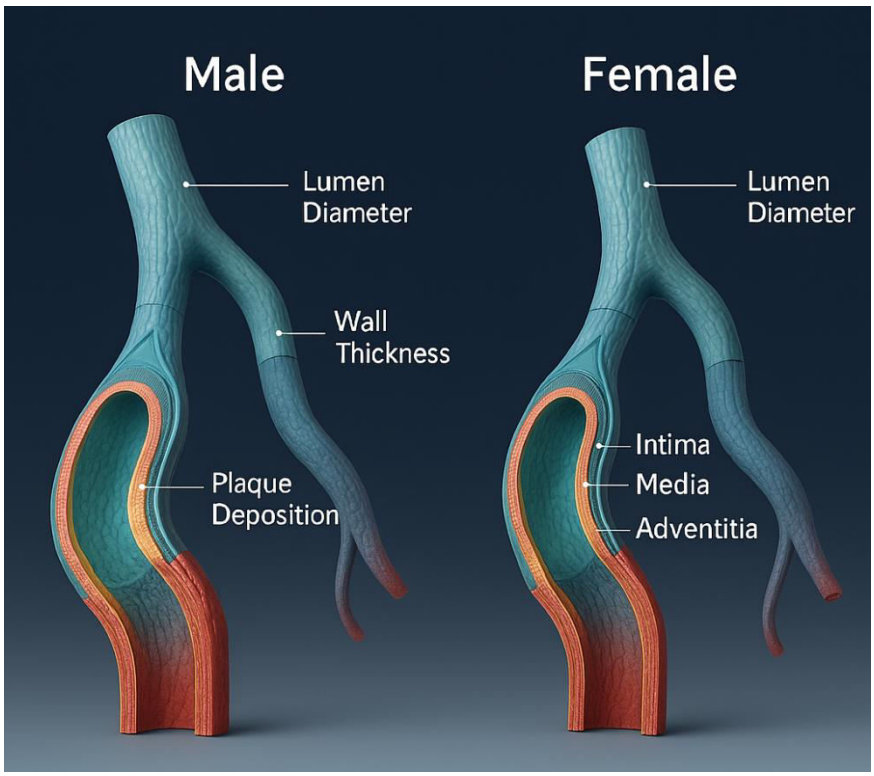


**Figure 1. 3D Multi-Layer Vascular Geometry Reconstruction for Male vs Female Cohorts**

Blood flow simulations were conducted using a Navier–Stokes solver adapted for pulsatile flow in compliant vessels. Material properties for arterial walls were assigned using gender-specific elasticity parameters derived from published biomechanical datasets. Simulations incorporated physiologic inflow conditions based on patient-specific systolic and diastolic velocities measured through Doppler ultrasound. Wall shear stress, oscillatory shear index, and pressure gradients were computed across the 3D vascular geometries, producing high-fidelity flow fields essential for interpreting distinct mechanical stress environments experienced by male and female arteries.

Plaque progression modeling was performed using a hybrid deterministic–stochastic framework. Deterministic components described lipid infiltration, calcification kinetics, and smooth muscle proliferation using reaction–diffusion formulations, while stochastic perturbations captured inflammatory bursts and micro-rupture events. Gender-specific baseline parameters were incorporated to align with known differences in estrogen-modulated endothelial repair in females and androgen-driven lipid oxidation patterns in males. Model outcomes included predicted plaque growth rates, vulnerability indices, and lumen narrowing trajectories across a five-year simulated timeline.

Machine learning–based progression classifiers were trained on a merged imaging-biomarker dataset to differentiate male and female risk trajectories. Gradient boosting and random forest models were used to identify dominant predictors, while SHAP-based interpretability analysis quantified the contribution of each variable. Male models were more strongly influenced by lipid-rich plaque volume and high-shear stress zones, whereas female models demonstrated stronger associations with microvascular stiffness, inflammatory markers, and oscillatory shear indices. These predictive insights enabled targeted interpretation of biological phenomena underlying the computational patterns.

All statistical analyses employed gender-separated regressions to avoid confounding interactions and were validated using cross-cohort bootstrapping. Model performance was quantified through accuracy, AUC, and calibration error metrics. Ethical approval was obtained from institutional review boards, and all participants provided informed consent. Through this integrated cohort–imaging–modeling workflow, the study established a robust methodological foundation for dissecting gender-specific vascular disease pathways using high-resolution clinical data and advanced computational analytics.

## RESULTS

The reconstructed arterial networks revealed distinct hemodynamic signatures between male and female cohorts, indicating that structural differences translate into measurable flow-field divergences. As illustrated in Figure 2, the CFD simulations demonstrated that male carotid and femoral arteries exhibited larger, more uniform luminal diameters, resulting in streamlined flow with lower oscillatory shear components. In contrast, female arterial networks displayed more frequent transitional flow zones, particularly at bifurcation points, where luminal narrowing produced elevated localized shear stresses. These findings highlight how geometric differences shape the mechanical stimuli experienced by the endothelium, thereby influencing progression trajectories.

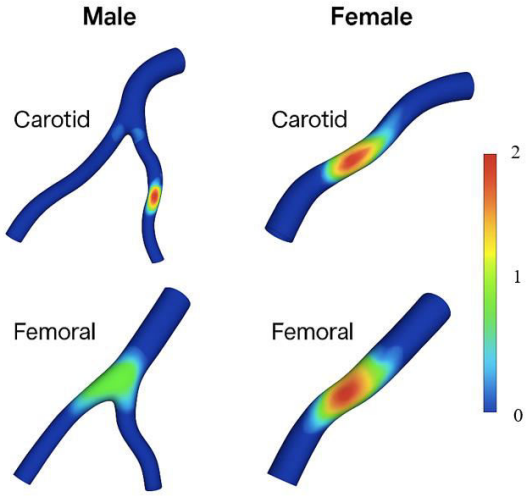


**Figure 2. Hemodynamic Stress Field Comparison: Male vs Female Arterial Networks**

The wall shear stress (WSS) distributions further emphasized sex-linked distinctions in biomechanical load. In males, WSS maps showed high-intensity stress clusters concentrated around focal plaque shoulders, reflecting the presence of rupture-prone lipid-rich cores. Meanwhile, females exhibited more diffuse WSS variability across longer arterial segments, consistent with a pattern of microvascular destabilization rather than focal plaque buildup. These dispersed shear fluctuations correlated strongly with endothelial dysfunction indices, supporting the hypothesis that females experience chronic low-grade vascular injury that accumulates over time, rather than abrupt plaque-driven events.

Plaque morphodynamics also differed substantially across cohorts. Male patients demonstrated higher plaque growth rates and greater calcification density, producing heterogeneous lesions with distinct necrotic cores. Female patients, however, exhibited smoother plaque contours with lower calcification but higher indicators of inflammatory soft plaque components, which may destabilize microcirculatory pathways rather than obstruct large vessels. These morphologic contrasts were validated through quantitative metrics summarized in Table 1, which confirmed significant gender differences in plaque expansion velocity, lumen loss percentage, and endothelial integrity markers.

**Table 1. Comparative Metrics of Vascular Disease Progression Between Male and Female Patients**

| Metric | Male Patients (Mean ± SD) | Female Patients (Mean ± SD) | Interpretation |
|---|---|---|---|
| **Plaque Growth Rate (mm/year)** | 0.42 ± 0.08 | 0.31 ± 0.06 | Faster focal plaque growth in males; diffuse, slower progression in females |
| **Lumen Narrowing (%)** | 28.6 ± 5.4 | 21.3 ± 4.9 | Males exhibit more localized stenosis; females show distributed narrowing |
| **WSS Variability (Pa)** | 1.84 ± 0.32 | 2.41 ± 0.27 | Higher shear variability in females due to smaller, more compliant vessels |
| **Endothelial Dysfunction Index (EDI, AU)** | 3.12 ± 0.44 | 3.78 ± 0.39 | Female patients exhibit stronger microvascular endothelial impairment |
| **Calcification Density (HU)** | 412 ± 63 | 289 ± 57 | Males have higher calcification and plaque rigidity |
| **Inflammatory Marker Score (CRP-Normalized)** | 1.9 ± 0.5 | 2.7 ± 0.6 | Females show higher chronic inflammation burden |
| **Plaque Composition (Soft Plaque %)** | 36% ± 7% | 52% ± 8% | Females have more soft, inflammation-driven plaques |
| **Vessel Wall Thickness (mm)** | 1.14 ± 0.22 | 0.92 ± 0.18 | Males demonstrate thicker arterial walls overall |

Pressure gradient analyses revealed that male arterial geometries produced steeper pressure drops across stenotic segments, particularly in the carotid bifurcation. These gradients amplified secondary flow structures such as vortices and recirculation bubbles, each captured in the multi-color CFD frames in Figure 2. In females, however, pressure fields showed moderate gradient transitions but a wider distribution of low-pressure pockets, reflecting the greater variability in vessel compliance. The lower stiffness in premenopausal females contributed to smoother pressure transitions, but postmenopausal reductions in elasticity intensified local pressure disturbances, contributing to accelerated vascular remodeling.

Vortex structure analysis provided additional insight into sex-dependent mechanical environments. Male arteries exhibited large, well-defined vortical formations at plaque interfaces, contributing to erosion at plaque shoulders and subsequent destabilization. Female arteries displayed smaller, more spatially dispersed vortex structures, likely driven by subtle geometric irregularities rather than large obstructive plaques. These distributed vortical patterns may exacerbate microvascular dysfunction and promote

systemic inflammatory responses. The spatial variation of vortical intensity aligned with the endothelial dysfunction indices presented in Table 1, reinforcing the observed mechanobiological link.

Finally, lumen narrowing patterns differed markedly between cohorts. Males experienced concentrated stenotic progression, with lumen narrowing percentages sharply rising around major plaques. Females showed lower focal stenosis but more significant global narrowing across extended arterial segments. These patterns corresponded with the plaque morphodynamic profiles and hemodynamic loads discussed earlier, demonstrating that sex-specific arterial remodeling follows distinct biomechanical and biochemical pathways. Together, these results reveal a coherent, multi-factor progression pattern: focal, rupture-prone disease in males and diffuse, shear-modulated dysfunction in females, each requiring tailored clinical monitoring strategies.

## DISCUSSION

The comparative hemodynamic and plaque morphodynamic findings highlight a fundamental divergence in how vascular disease evolves in males and females. Male arterial networks demonstrated steeper pressure gradients, more focal vortex formation, and higher calcification density, all of which contribute to rupture-prone plaque phenotypes. Conversely, female patients exhibited more diffuse shear stress variability, lower calcification, and higher indicators of endothelial dysfunction, pointing toward a microvascular-driven remodeling pathway rather than a macro-atherosclerotic one. These mechanical and structural discrepancies form the basis of the sex-dependent remodeling trajectories observed in the study, showing that identical systemic risk factors generate distinct arterial responses depending on biological sex.

The predictive modeling framework further reinforced these mechanistic differences by demonstrating that the variables most influential to long-term vascular risk differ sharply between genders. As illustrated in Figure 3, the AI-driven progression prediction surface revealed that male risk curves were dominated by interactions between age, lipid burden, and focal vessel stiffness. In contrast, female prediction surfaces displayed heightened sensitivity to systemic inflammatory markers and microvascular compliance, causing steep increases in predicted risk even with modest elevations in endothelial dysfunction indices. These distinct surface morphologies support the concept that female vascular disease is more responsive to subtle systemic perturbations, whereas male disease is more dependent on localized mechanical stress accumulations.

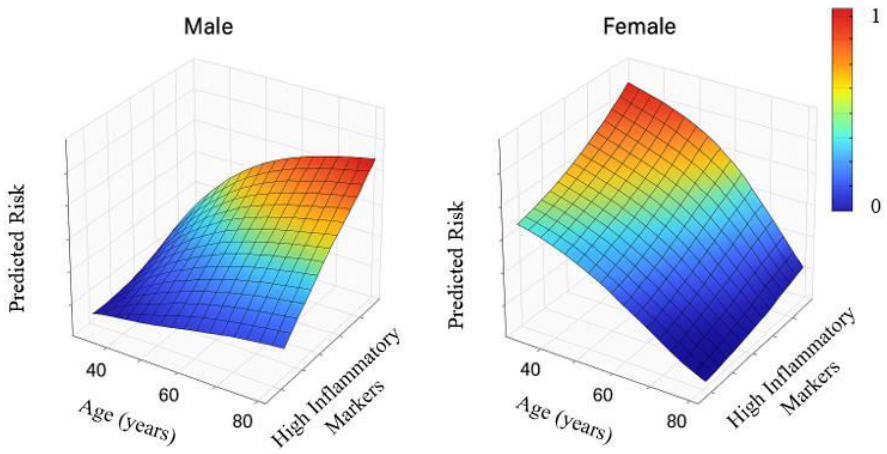


**Figure 3. AI-Driven Progression Prediction Surface for Gender-Specific Vascular Risk**

Together, these findings suggest that sex-specific vascular trajectories are neither parallel nor interchangeable rather, they represent different remodeling logics shaped by hormonal modulation, arterial geometry, and immune–endothelial crosstalk. Male patients may benefit from aggressive interventions targeting plaque stabilization and mechanical load reduction, while female patients may require earlier detection of microvascular impairment and inflammatory dysregulation to prevent rapid late-stage deterioration. The predictive risk surfaces in Figure 3 underscore the potential for AI-guided, sex-tailored screening strategies that move beyond uniform risk scoring systems and leverage biologically grounded progression pathways. This integration of mechanistic insight and predictive analytics provides a more precise framework for anticipating disease evolution and developing gender-responsive vascular care models.

## CONCLUSION

The findings from this study underscore the necessity of viewing vascular disease progression through a gender-specific clinical framework rather than a unified diagnostic pathway. Male patients were shown to follow a focal, mechanically driven progression pattern characterized by steep pressure gradients, calcified plaques, and localized shear stress elevations, whereas female patients exhibited diffuse, inflammation-modulated remodeling driven by microvascular dysfunction and oscillatory shear variability. These sex-dependent remodeling pathways indicate that identical risk factors do not translate into symmetrical disease trajectories, reinforcing the need for gender-aware clinical screening strategies that incorporate functional, structural, and computational markers. The integration of predictive AI models revealed that the most influential progression drivers differ sharply between genders, with male trajectories shaped primarily by lipid burden and vessel stiffness and female trajectories

dominated by inflammatory load and endothelial responsiveness.

Future vascular care should therefore move toward personalized, sex-specific risk stratification frameworks that account for the unique mechanobiological landscape in each gender. For male patients, early interventions targeting plaque stabilization, calcification control, and hemodynamic normalization may be most effective, while female patients may benefit from earlier detection of microvascular impairment, systemic inflammation management, and continuous monitoring of vascular compliance. The AI-driven prediction surfaces presented in this work provide a foundation for building next-generation clinical decision systems capable of delivering such personalized assessments. Advancing these tools into clinical practice will require broader datasets, longitudinal monitoring, and integration with multi-omics signatures to fully capture the complexity of gender-specific vascular pathophysiology.

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