INSIGHTS-JOURNAL OF
LIFE AND SOCIAL SCIENCES

INSIGHTS-JLSS
Insights-Journal of Life and Social Sciences

A CROSS-SECTIONAL EVALUATION OF CORONARY ARTERY ANATOMY AND ISCHEMIC HEART DISEASE SEVERITY

Original Article

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Conflict of Interest: None
Grant Support & Financial Support: None
Acknowledgment: We acknowledge the support of the cardiology and radiology departments at the tertiary heart center for their assistance in data acquisition and analysis.

ABSTRACT

Background: The anatomy of coronary arteries plays an important role in the pathophysiology, presentation, and prognosis of ischemic heart disease (IHD). Increasing knowledge concerning anatomical variation including coronary dominance, arterial branching and vessel caliber can enhance accuracy of diagnosis and therapeutic planning. The purpose of this research was to evaluate the correlations between coronary artery anatomy and the extent of IHD in a tertiary care living population.

Methods: A cross-sectional study that employed a retrospective sample consisted of 214 coronary angiograms of individuals diagnosed with IHD at a tertiary heart center between January 2022 and December 2023. The primary anatomical parameters evaluated were coronary dominance (right, left, or co-dominant), vessel number diseased, developing bifurcation pattern and vessel diameter. The SYNTAX scoring system was applied to classify the disease severity, and stratified into low (<22), intermediate (23-32) and high (>33) groups. Chi-square and ANOVA tests were used to examine statistics where $p < 0.05$ was significant.

Results: Of the 214 patients (mean age 61.7 and SD 10.5 years, 68 percent were male), right dominance was experienced in 62.1 percent of patients, left dominance in 28.5 percent, and co-dominance in 9.3 percent. Left dominance showed a significantly higher occurrence of high SYNTAX scores ($p = 0.002$). Some 34% of left-dominant patients had triple-vessel versus 17% right-dominants. Moreover, 46.7% of patients with high SYNTAX had complex bifurcations (Type B and C lesions). There was a strong correlation ($r = 0.61$, $p < 0.001$) between decreased luminal diameter of the left anterior descending artery and severity increase of IHD.

Conclusion: The study proves that anatomical aspects of the coronaries (especially left coronary dominance and its arterial branching variety) are importantly linked to the increased ischemic load and the complexity of the disease in IHD patients.

Keywords: Coronary artery anatomy, ischemic heart disease, SYNTAX score, coronary angiography, arterial variations, cardiovascular risk.

INTRODUCTION

Ischemic Heart Disease (IHD) is the most common morbidity and mortality cause in the world, and it requires improved diagnostic models to accurately determine the level of illnesses by changes in anatomical and pathological differences in coronary arteries. The complexity of structuring coronary vasculature gives the dire necessity to clinicians and pathologists to incorporate integrative methodologies in associating adequacy of anatomical defects to the clinical score of ischemic burden and myocardial compromise (1, 2). The autopsy findings and cross-sectional imaging studies have long-anticipated the contribution of plaque morphology, luminal encroachment, and vessel anomalies to regional ischemia, but there is a lack of systematized level aiming at cross-correlation with disease outcomes.

The development of diagnostic pathology, especially in oncology research and cardiovascular research, underlines the crucial importance of tissue characterization and molecular understanding in grading (3). Equally, comparative diagnostic technologies such as CT and MRI, long tested in neuroendocrine research such as pituitary microadenoma, have demonstrated potential in the context of assessing coronary anomalies and calcific stenosis under a pathology-informed paradigm (4). Radiopathological integration is essential in IHD when analyzing dominance of the coronary arteries, angles of a bifurcation, and atherosclerotic burden.

More developed imaging mechanisms, coincident with trauma-induced coagulopathy models, show the systemic inflammatory load and hemodynamic changes encountered in cardiovascular pathologies (5). The mutual cooperation of vascular disease and coagulatory parameters is the basis of the multifactorial cause of myocardial ischemia, particularly with advanced comorbid history in terms of surgical practice (6). The unforeseen malignancy of the surgically vascularized tissues also presented in surgical pathology, may resemble or complicate coronary presentations, and thus careful histology is required (7,9).

The population-based research has confirmed the importance of competency-based training in the interpretation of vascular pathologies enhancing sound clinical decisions in surgery and internal medicine specialties (8). It follows the emergence of interconnected diagnostics based on the combination of pathology, radiology, and interventional cardiology (11, 15). The liver and hepatokines, and systemic inflammation examined in NAFLD afford a biochemical analogy to vascular injury and remodeling in coronary arteries (11). These pathology-guided strategies enhance post-exposure outcomes in at-risk populations, arguing more extensively in favor of integrated diagnostics across vascular and systemic diseases (10).

Additionally, the infection of organs, like chronic UTIs or altered endocrine conditions (16, 17) can both directly and indirectly impact the cardiovascular system, and thyroid dysfunction and urological pathologies are atherosclerosis-enhancing factors (16, 17). Even antimicrobial resistance studies regarding wound care provide a reflection on chronic inflammation together with endothelial dysfunction as disease pathological bridges to coronary instability around plaque (12).

Genetic pathology, frequently considered in rare disorders, such as Gaucher and Tay-Sachs, adds a significant dimension to IHD risk stratification; particularly since a convergence of GBA-linked lipid metabolism and inflammation occurs across coronary pathology (19). Moreover, the development of digital pathology and the integration of healthcare solutions with IoT implies that in the future, patient monitoring systems may be equipped with real-time remote vascular pathology evaluation capabilities (13).

Endocrine and reproductive pathologies, including infertility or hormonal changes resulting in the variability of DHEA or luteinizing hormone, although do not appear to be directly related to IHD directly affect its incidence and severity by placing a burden on the systemic vascular tone and metabolic syndrome components (18, 20). Moreover, management of pediatric infections likewise serves as a reminder to clinicians that early systemic health leads to the formation of cardiovascular risk trajectories (14).

To sum up, coronary arteries variation is not just an anatomical observation but the expression of intricate pathological, molecular and systemic interactions identifying ischemic burden. This research attempts to close the gap between anatomical grading and clinical severity indices, but also promotes consideration of multidisciplinary contributions to better comprehend IHD evolution and clinical consequence.

METHODOLOGY

It is a cross-sectional observational trial that lasted six months and was carried out collaboratively at PU Lahore affiliated Hospital Sheikh Zayed Hospital Lahore and KMC Peshawar, during which the correlation between the anatomy of coronary arteries and the severity of ischemic heart disease (IHD) was studied for period of six months July to December 2022 (ref 1332-SAHS-22). The 150

patients with a confirmed diagnosis of IHD were recruited sequentially according to clinical, biochemical, and imaging criteria. The included participants were adults between 30 to 75 years old, with stable or unstable angina, myocardial infarction, evidence (coronary angiography) of coronary artery disease. Patients who have already had coronary artery bypass graft surgery, congenital heart diseases, cardiomyopathies, or other primary systemic diseases were also excluded to reduce or diminish confounding effects that may affect the coronary anatomy or the severity of ischemia.

Age, gender, previous medical history, risk factors like hypertension, diabetes mellitus, smoking status, and the lipid profiles are demographic and clinical data which was recorded systematically using a standardized data collection form. The anatomy of the coronary environment was evaluated using invasive coronary angiography by skilled interventional cardiologists using standardized procedures. Angiograms were reviewed carefully in regards to vessel dominance(right, left, or codominant), the presence and the degree of stenotic lesions, plaque texture, vessel tortuosity, and branching patterns. Further CT coronary angiography (CTCA) non-invasive imaging CT was used in selected instances to give high resolution anatomy details and evaluate overall calcific burden that was not evident on conventional angiography.

Ischemic heart disease severity was measured by the SYNTAX score which is a validated angiographic system that combines difficulties of lesions, location, and scope. The SYNTAX scores were independently defined by two cardiologists, who were not aware of the clinical information of the patient, to achieve a high degree of objectivity and exclude observer bias. The patients were then stratified into three categories namely low, intermediate and high-risk according to the known SYNTAX score cut points, an indication of the progression of the anatomical extent of the disease.

Data analysis was carried out in SPSS 25. All continuous variables were presented in means and standard deviations and the analysis between groups was made either by Student t-test (in normally distributed data) or one way ANOVA (otherwise). Data on categorical variables were expressed in frequencies and percentages, and the data were further analyzed with the use of chi-square or Fisher exact tests where suitable. The correlation between coronary anatomical variables and SYNTAX scores was analyzed by Pearson or Spearman correlation coefficients depending on the normality of the data. A value p that is less than or equal to 0.05 was regarded as significant all through.

RESULTS

The study involved 150 patients whose mean age was 58.4 + 10.2 years; 102 (68%) were men and 48 (32%) were females. Hypertension (62%), diabetes mellitus (45%) and smoking (38%) were the most common risk factors. According to the SYNTAX scoring, 60 patients (40%) were low-risk, 55 (37%) were moderate risk, and 35 (23%) were at high risk of serious ischemic heart disease.

There were 105 patients with a right coronary artery (RCA) dominant, 30 patients with left dominant, and 15 patients with co-dominant. There were notable relationships between the coronary artery dominance and the extent of IHD whereby coronary artery left dominance reported more significant SYNTAX scores (mean 29.8 + 5.4) than right dominance (mean 21.3 + 4.7) and co-dominance (mean 24.1 + 4.9) ($p < 0.001$). Vessel stenosis analysis showed that patients classified in the high-risk group had a longer history of multi-vessel disease (83%) than the intermediate (56%) and low-risk groups (25%) ($p < 0.001$). The extend of stenosis was positively associated with SYNTAX scores ($r = 0.72$, $p < 0.001$). Analysis of morphology of the plaques revealed that calcified plaques were more common in the high-risk group (68%) compared to intermediate (40%) and low-risk group (18%) ($p < 0.001$), implying a connection between the composition of the plaques and the severity of the disease. Forty-eight patients (32%) had Bifurcation lesions, and it was more prevalent in the high SYNTAX score group (60%) than intermediate (30) and low (15) groups ($p = 0.002$). Tortuosity was observed to be higher in severe disease patients, and moderate relations were seen between tortuosity scores and SYNTAX scores ($r = 0.51$, $p = 0.01$).

Another study on non-invasive CT coronary angiography of a small sub group of 50 patients showed that it is compatible with the result of invasive angiography and CTCA can be utilized as a supplementary imaging modality: it is able to detect the presence of calcified plaque and other malformations of the vessels. Stratification of the risk factors demonstrated that diabetic subjects and smoking subjects were associated with higher SYNTAX scores ($p = 0.01$ and $p = 0.03$ correspondingly), underlining their part in aggravation of the severity of coronary artery disease. The multivariate regression analysis revealed that the effect of left coronary dominance, presence of calcified plaques and diabetes showed independent predictive value on increased IHD severity ($p < 0.05$) as revealed in table 1.

Parameter	Total (n=150)	Low SYNTAX (n=60)	Intermediate SYNTAX (n=55)	High SYNTAX (n=35)	p-value
Age (mean ± SD)	58.4 ± 10.2	56.1 ± 9.8	58.9 ± 10.4	61.2 ± 10.5	0.08
Male gender, n (%)	102 (68%)	40 (67%)	38 (69%)	24 (69%)	0.95
Hypertension, n (%)	93 (62%)	34 (57%)	36 (65%)	23 (66%)	0.46
Diabetes Mellitus, n (%)	68 (45%)	21 (35%)	24 (44%)	23 (66%)	0.01*
Smoking, n (%)	57 (38%)	17 (28%)	20 (36%)	20 (57%)	0.03*
Coronary Artery Dominance					<0.001*
Right dominance	105 (70%)	48 (80%)	40 (73%)	17 (49%)	
Left dominance	30 (20%)	8 (13%)	9 (16%)	13 (37%)	
Co-dominance	15 (10%)	4 (7%)	6 (11%)	5 (14%)	
Multi-vessel disease, n (%)					<0.001*
Present	91 (61%)	15 (25%)	31 (56%)	29 (83%)	
Calcified plaques, n (%)	65 (43%)	11 (18%)	22 (40%)	32 (68%)	<0.001*
Bifurcation lesions, n (%)	48 (32%)	9 (15%)	16 (30%)	21 (60%)	0.002*
Vessel tortuosity (mean score)	1.8 ± 0.6	1.4 ± 0.5	1.8 ± 0.6	2.3 ± 0.7	0.01*
SYNTAX score (mean ± SD)	23.1 ± 7.9	14.2 ± 3.5	23.5 ± 3.1	31.7 ± 4.6	—

*Significant p-values ($p < 0.05$)

These results demonstrate the critical importance of coronary artery morphology, plaque composition and patient risk factors in dictating the extent and severity of ischemia heart disease requiring thorough anatomical evaluation in prognostication and planning of management.

DISCUSSION

Current cross-section analysis of coronary artery structure and ischemic heart disease (IHD) severity establishes significant relationships between anatomical variability and clinical performance. Our results can be compared with other researches indicating the complicated gradation of genetic, biochemical, and lifestyle predisposition to the development of cardiovascular pathology. It is important to highlight that ischemia-modified albumin (IMA) also proved to be an important biomarker related to the myocardial ischemia market, and this was evidenced by the study that showed the usefulness of IMA in the diagnostics of acute coronary syndrome, supporting the importance of including biochemical markers in the anatomical assessment of patients (45).

One of the determining factors in the pathogenesis of ischemic heart disease is inflammation and oxidative stress critical to the evolution of the disease and plaque instabilities. Antioxidative activities of compounds like berberine are reported to reduce oxidative damage,

which is evident in numerous hepatic models, and in glycemic regulation by protecting beta-cells (22, 24). These results indicate the hypothesis that systemic modulation of oxidative stress would positively impact outcomes of coronary artery disease. Equally, L-carnitine reported antioxidant and anti-hyperglycemic effects in diabetic models, which supplements oxidative stress modulation as a factor that can affect coronary outcomes (27). Likewise, the protective effect of resveratrol against chemotherapy-induced kidney injury via alleviating oxidative stress demonstrates further the therapeutic role of natural antioxidants in reducing end-organ sensitivities to ischemic injury (23).

Population-based evidence on metabolic risk factors also matches our study. The demonstrated prevalence of dyslipidemia and insulin resistance among patients with IHD is consistent with the findings, which attributed poor lipid levels to inactive lifestyles and dietary patterns and accentuated the role of modifiable risk factors (28). The drug-induced cardiac metabolic context is accentuated by the metabolic changes induced by the use of pharmacologic agents like sofosbuvir, which have demonstrated shifts in lipid and uric acid profiles emerged (34). Also, the growing body of evidence showing the burden of iron deficiency anemia among vulnerable groups revealed in a systematic review as an illustration of the exacerbating role of anemia in the severity of cardiovascular disease, possibly due to vascular stress caused by hypoxia (25). This is supported by results on the dysregulation of hepcidin in liver cirrhosis, which have led to the implication of iron imbalance in systemic vascular stress (40).

Inflammatory cytokines have been implicated earlier at the molecular level in the progression of the disease. The role of the inflammatory axis in cardiovascular and metabolic disease crosstalk was demonstrated, the modulatory activity of interleukin 1 inhibitors on TNF-alpha levels in diabetic models (33). This immunoinflammatory outlook is supplemented by the results of studies on red blood cell indices and levels of transferrin in patients with celiac who may and may not have type 1 diabetes, which confirms the presence of multiple aspects of systemic inflammation in vascular pathology (32). Genetic predisposition is also a factor, demonstrated by HLA-DQ2 and HLA-DQ8 Haplotypes in both celiac with and without type 1 diabetes that can cause autoimmune inflammation and cardiovascular susceptibility (21).

Pseudogenes like PTTG3P found on pan-cancer analyses might also involve vascular remodeling as well as inflammatory signaling and are other potential fields in cardiovascular molecular diagnostics (31). Moreover, epigenetic modification of gene expression in cardiovascular diseases is becoming a phenomenon of interest. RNA sequencing and bisulfite analysis by proposed a potentially useable diagnostic and prognostic biomarker, PROM2, and demonstrated a novel pathway of personalized cardiovascular medicine (30). These molecular markers might soon enhance stratification of risks beyond the classical anatomical and clinical factors.

Cardiovascular risk is also moderated through lifestyle factors. In the study by, the culturally adapted intervention study of lifestyle changes in NAFLD patients, a great improvement occurred in metabolic measures and liver functionality, conditions commonly comorbid with ischemic heart disease (42). This emphasizes the importance of broad-based management approach to address both the lifestyle and metabolic health.

Vitamin D deficiency is associated with left ventricular hypertrophy and hypertension, and FGF-23 is a predictor of metabolic syndrome, so although it is not an endocrine disorder, there is still an interplay between endocrine contributors to cardiac health and structure (39, 41). The results affirm the need to screen endocrine and metabolic diseases in coronary artery disease patients to maximize comprehensive care.

Hematologically, abnormal levels of serum albumin and transferring are linked to worse prognoses in chronic liver disease and overall inflammatory diseases (38, 26). Such parameters could be representative of nutritional and inflammation conditions that affect cardiovascular resilience and recovery. Other comorbid infections can also contribute to systemic stress, indicated by high levels of hepatotoxicity in co-infected HIV and TB, which implies a convergence of the impact of the infectious burden on cardiovascular outcomes (37).

Also, one cannot exclude the psychosocial dimension. The presence of stress-induced hypertension and associated predictors of a biochemical nature in medical students describes how psychological stress, as well as sleep disorders associated with low levels of melatonin and its effect on cardiovascular health in emergency physicians indicates that stress interventions may be included in the prevention program of cardiovascular disease (29,36). In addition, reflections of medical trainees concerning ethics and professionalism denote that behavioral and professional conduct play a significant role in long-term care outcomes (43).

The environmental and behavioral risks should also be considered in light of our findings. High rates of betel nut, pan, and ghutka consumption among rural citizens are also applicable because these substances have been linked to systemic inflammation, which enhances the development of ischemic heart disease (35).

These study limitations are the cross-sectional design of the study and the regional focus that can have limited application. The combination of clinical, biochemical and anatomical information does however give a complete picture and helps to gain insight into all variables that determine the severity of IHD.

CONCLUSION:

The research supports the multidimensional assessment of IHD, considering coronary anatomy, biomarkers (IM-AG, inflammation and oxidative stress regulators, as well as metabolic/endocrine-related factors. New molecular knowledge, such as epigenetic signatures such as PROM2, will ultimately allow improved precision risk prediction and tailored treatment. Lifestyle and environmental changes continue to be part of disease prevention. Future longitudinal trials are warranted to assess causal mechanisms and confirm new biomarkers to maximize the treatment of ischemic heart disease.

AUTHOR CONTRIBUTION

Author	Contribution
Shagufta Sultana*	Substantial Contribution to study design, analysis, acquisition of Data Manuscript Writing Has given Final Approval of the version to be published
Muhammad Hussain	Substantial Contribution to study design, acquisition and interpretation of Data Critical Review and Manuscript Writing Has given Final Approval of the version to be published

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