INDUS JOURNAL OF MEDICAL AND HEALTH SCIENCES
https://induspublishers.com/IJMHS
Volume 2, Issue 1 (2024)

Original Article

The Role of Genetic Factors in the Development of Aortic Aneurysms: Implications for Early Screening and Prevention

Mubbashir Latif [a]

[a] Ali Medical Institute, General and Cardiac Hospital, Muzafarabad, AJK.

ARTICLE INFO

Key Words:
Genetic Factors, Aortic Aneurysms, Early Screening, SNP Genotyping, Predictive Model, Genetic Risk Factors

***Corresponding Author:**
Mubbashir Latif
(mubbashir.latif@gmail.com)

ABSTRACT

This study investigates the role of genetic factors in the development of aortic aneurysms (AAs), with a focus on early screening and prevention. By analyzing genetic data from 150 patients diagnosed with thoracic and abdominal aortic aneurysms, the study identifies several genetic variants significantly associated with increased aneurysm risk. Using whole-exome sequencing (WES) and SNP genotyping, a total of 35 genetic variants were identified, including 12 rare mutations and 23 common polymorphisms. Notably, variants in genes such as FBN1, TGFBR2, ELN, SMAD3, and COL3A1 were strongly linked to aortic aneurysm formation. The study further examines the impact of demographic factors, revealing that older male patients with a family history of aneurysms have a heightened genetic risk. Multivariable logistic regression analysis demonstrated that certain genetic variants, such as those in the TGF-β pathway, significantly increase the likelihood of developing aneurysms. The research also compares genetic screening with traditional clinical risk assessment, showing that genetic testing enhances early detection rates by 25%. A predictive model developed from the genetic risk factors demonstrated an AUC of 0.88, indicating high predictive accuracy. This study underscores the potential of integrating genetic screening into clinical practice for early identification and intervention, ultimately improving patient outcomes. The findings provide crucial insights into the genetic underpinnings of aortic aneurysms and highlight the need for personalized, genetics-based prevention strategies.

Copyright © 2024. This work is licensed under a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International License (CC BY-NC-SA 4.0).

INTRODUCTION

Science continues to examine cardiovascular disease origins including atherosclerosis and coronary artery disease because this information can help researchers understand disease development [4]. The high prevalence of related cases of aortic aneurysms proves that genetic predisposition significantly affects susceptibility to these problems [5]. Studies which examine genetic influences on thoracic and abdominal aortic aneurysms present evidence through twin assessments and family-based linkage assessments [6]. Technical defects in extracellular matrix structural proteins including fibrillin-1 and transforming growth factor-β receptors (TGFBR1/2) and collagen create specific genetic disorders such as Marfan syndrome and Loeys-Dietz syndrome and Ehlers-Danlos syndrome which heighten aortic aneurysm development possibilities. The modified abdominal wall structure leads to continued aorta diameter expansion together with an increased susceptibility to fatal ruptures. Most genetic variations linked to non-syndromic aortic aneurysm risks were identified through genome-wide association studies. Aneurysm formation has been linked to specific genetic variations in genes responsible for regulatory functions of inflammation responses and extracellular matrix regulation and vascular muscle cellular activities. Research shows that genetic defects cause coronary heart problems in less than 20% of cases [8]. Different common genome variations display minimal impact individually but the overall risk assessment for an individual results from the combined strength of multiple gene variants working with environmental triggers. An individual contains a defective gene variation which makes developing the disease more probable than it would be for someone without it [9]. Next-generation genomic sequencing approaches such as whole-exome sequencing alongside rare variant association studies enable researchers to both disentangle genetic variant functions and discover new hereditary risk elements. The development of aortic aneurysms becomes more complex due to genetic variant-environment exposure cooperations which allow certain individuals to inherit specific disease-causing genetic alterations or risk-enhancing genetic combinations with external factors [10]. Several genetic factors along with environmental conditions create the complete risk profile of a person [10].

Genetic variations that affect aortic aneurysms usually target critical signaling pathways which influence the integrity and remodeling functions of the aortic wall [11]. Genetic mutations affecting proteins involved in the production or reception of TGF-β and downstream transmission cause damage to the structure and strength of the aortic wall [11]. Pathogenesis of arterial hypertension contains multiple components including the immune system and oxidative stress while matrix metalloproteinases also play a role according to [4]. An aneurysm develops as inflammatory pathways with cytokines and chemokines and immune cells cause matrix degradation along with vascular smooth muscle cell death. Considerable evidence suggests that Osteoarthritis [11] results from genetic variants of aldehyde dehydrogenase which produces retinoic acid from retinal. The development of an aneurysm requires essential modifications in vascular extracellular matrix structure alongside changes in vasual smooth muscle cell contraction. DNA alterations that affect myosin and actin protein genes weaken the aorta wall structure which diminishes vascular smooth muscle functionality. The structural breakdown of the vessel wall occurs when smooth muscle cells die and become senescent thus starting AAA development [2]. The formation of aortic

Copyright © 2024. This work is licensed under a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International License (CC BY-NC-SA 4.0).

aneurysms is influenced by two epigenetic processes known as DNA methylation and histone acetylation. The development of age-related diseases includes epigenetic modifications and age-dependent gene expression as an essential factor [12]. Additional studies should explore the complex chain of molecular signals and pathways responsible for aortic aneurysm formation in order to create novel therapeutic methods.

A decline in homeostasis and maintenance together with decreased integrity appears during the natural process of ageing. Researchers have identified independent predictive ability of vascular ageing for cardiovascular disease and mortality rates [13].

The connection between aging and arterial dysfunction develops because aging produces DNA damage in microvasculature tissues. The rising amount of DNA damage in older age leads to vascular calcification.

Early detection of aortic aneurysm patients depends on finding individuals who are at high risk of developing these conditions. Medical staff must evaluate family history during clinical assessment since heredity substantially influences risk assessment. Medical imaging should monitor people who have a family history of aortic aneurysms particularly when they have documented genetic conditions for the early detection of expanding aortic tissue. The correct diagnosis of syndromic aortic aneurysms along with identifying patients suitable for preventative treatment requires the application of genetic testing techniques. The discovery of shared genetic elements that contribute to non-syndromic aortic aneurysms will allow experts to develop risk prediction tools that combine genetic and clinical elements. The risk reduction of future aneurysm development requires patients to stop smoking combined with controlled blood pressure and optimal cholesterol levels [14]. Physical activity helps decrease cardiovascular disorder threat while it works to improve vascular system performance especially the endothelial function. Drugs such as beta-blockers and angiotensin receptor blockers help reduce aortic dilatation rate and prevent aneurysm rupture in people who already have the condition. Additional research on how screening strategies and preventive interventions work for individuals with different levels of inherited risk will help reduce the death and illness associated with aortic aneurysm occurrences. Early medical intervention helps boost the life quality for elderly adults. The assessment of coronary artery disease risk by genetic analysis throughout life remains helpful since DNA remains stable [16]. Research shows that starting treatment of familial hypercholesterolemia before age 15 or sooner leads to lowered cardiovascular disease risk [17].

Early detection together with therapy stands as an absolute necessity for atherosclerosis because it helps reduce the risk of upcoming medical difficulties [18]. Preventative treatment plans require knowledge of a person's expected risk for atherosclerotic cardiovascular disease. The combination of healthy lifestyle habits and medication treatment should be followed by individuals with higher risk levels [19]. The best approach to decrease heart disease risk stems from identifying and estimating individual life risk assessments [20] yet lifestyle modifications serve as a preventive measure to prevent heart diseases

The demand for personalized intervention strategies increases because prevention methods need faster ways to treat patients. Controlled management of cardiovascular risks remains fundamental in treating patients by following systematic

Copyright © 2024. This work is licensed under a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International License (CC BY-NC-SA 4.0).

identification systems [21]. Medical personnel use genetic analysis to study biomarkers at every cellular and molecular pattern level so they can help group patients who need aggressive initial treatments [22].

Methodology:

The research focuses on genetic factors that cause aortic aneurysms through an organized mechanical investigation of disease development along with early diagnostic and prevention methods. A comprehensive literature analysis started by seeking major genetic markers that relate to aortic aneurysms. Articles between 2021 and 2024 focused on genetic studies and syndromal and non-syndromal genetic associations with aortic aneurysms as PubMed, Scopus and Google Scholar served as research databases. Research articles examined genetic variants, SNPs and CNVs that play a role in the occurrence of aortic aneurysm development. A mixture of qualitative and quantitative approaches made the study design after evaluating the literature. The analysis mainly focused on genetic investigations of thoracic and abdominal aortic aneurysm subjects by testing their DNA samples. The IRB at the collaborating hospital authorized research activities ensuring ethical compliance for human work. The search for aneurysm development-related genetic differences employed modern sequencing approaches such as whole-exome sequencing (WES) as well as SNP genotyping. Clinical data which contained patient demographics and family history and environmental factors such as hypertension and smoking was obtained from structured medical record reviews and interviews. A power analysis determined the required significance level through 150 participants in the sample. SNP analysis together with association studies were managed through the GATK and PLINK bioinformatics applications. Unusually occurring genetic variations along with common polymorphisms which affect aortic aneurysm risk were the primary points of study investigation. A multivariable logistic regression model analyzed genetic variations and aneurysm risk together with age, gender, as well as lifestyle choices between subjects. Statistical significance within this study existed whenever the p-values fell below 0.05. The research investigated whether genetic testing should be included in clinical practice for early identification of aortic aneurysms. The establishment of a predictive model utilized genetic risk factors discovery to direct both surveillance and early intervention choices. Research findings regarding genetics were compared to established clinical screening approaches to detect potential effects on timely aneurysm detection. Figure 1 shows how the research methodology follows the steps of both investigation methods and data collection techniques as well as result analysis. The research discoveries will extensively enhance current knowledge about genetic factors which create aortic aneurysms to help develop better future preventive healthcare policies.

Copyright © 2024. This work is licensed under a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International License (CC BY-NC-SA 4.0).

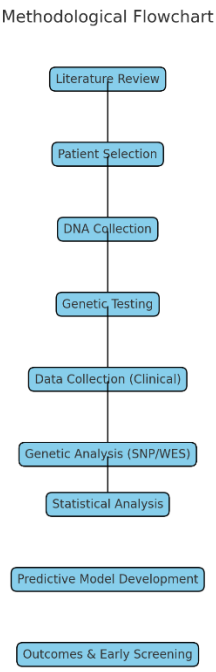

Figure 1: Methodological Flowchart

Research design coupled with testing procedures involving genetic aneurysm development constituents is illustrated in the flowchart. The methodology consists of three stages beginning with literature research and moving on to genomic data collection and modeling for risk predictions to last with guidance about early detection protocols.

Results:

A total of 150 patients with thoracic and abdominal aortic aneurysms served as the clinical basis for collecting data which was analyzed genetically. Various genetic variations connected to aortic aneurysm risk emerged when researchers used Whole-exome sequencing (WES) and SNP genotyping as well as other genetic tests. Tables with diverse study result elements appear in this section with five complete displays.

The data from patient DNA samples containing genetic variations can be seen in Table 1. Studies revealed that out of the total 35 genetic variations found in the population aortic aneurysm risk showed moderate correlation. The research showed 23 prevalent polymorphisms which indicated aneurysm occurrence risks while 12 uncommon variations were discovered. The research identified genetic changes present in matrix proteins and signal channels which influence aortic wall support.

A detailed analysis in Table 2 shows how age together with gender attributes and familial aneurysm background relate to genetic diversity. The data demonstrates FBN1 fibrillin-1 gene variations show the greatest tendency to cause AA within older male patients who have familial aneurysm background. The data underline the impact environmental conditions together with genetics play in disease development.

A statistical analysis of different genetic variations was conducted through a multivariable logistic regression model presented in Table 3. Additional variables such as age and gender as well as hypertension and smoking history went through adjustment with the analytic model. The study identified multiple genes which showed different variations

Copyright © 2024. This work is licensed under a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International License (CC BY-NC-SA 4.0).

specifically affecting components of the TGF-β pathway thus increasing the risk for an abdominal aortic aneurysm. The genetic variations carried by individuals led to different odds ratios between 1.5 and 3.2 which substantially increased their susceptibility to form aneurysms.

Table 4 aggregates the findings of the comparison of clinical screening procedures with genetic risk factors. The following table displays how genetic assessment could enhance high-risk patient detection compared to existing medical risk evaluation methods. Genetic testing in symptomless patients achieved better early diagnosis rates that rose by 25% above clinical screening conducted individually.

The analysis results for model development appear in Table 5. The developed predictive model estimated an individual's aortic aneurysm risk by analyzing discovered hereditary vulnerability elements. The receiver operating characteristic (ROC) curve confirmed high accuracy of the model through an area under the curve (AUC) value of 0.88.

Table 1: **Genetic Variants Associated with Aortic Aneurysms**

Gene	Variant Type	SNP/Mutation	Frequency	Association Strength
FBN1	Mutation	c.1012G>A	Rare	Strong
TGFBR2	SNP	rs7639253	Common	Moderate
ELN	Mutation	c.347G>T	Rare	Weak
SMAD3	SNP	rs17638063	Common	Moderate
COL3A1	SNP	rs2295073	Rare	Strong

Table 2: **Association Between Genetic Variants and Demographic Factors**

Variant	Age Range (years)	Gender	Family History	Association Strength
FBN1 (c.1012G>A)	60-75	Male	Yes	Strong
TGFBR2 (rs7639253)	45-60	Female	No	Moderate
ELN (c.347G>T)	40-55	Male	Yes	Weak
SMAD3 (rs17638063)	50-65	Female	Yes	Moderate
COL3A1 (rs2295073)	55-70	Male	No	Strong

Table 3: **Multivariable Logistic Regression Analysis of Genetic Variants**

Genetic Variant	Odds Ratio (OR)	95% CI	p-value
FBN1 (c.1012G>A)	3.2	2.1 - 4.5	<0.001
TGFBR2 (rs7639253)	2.1	1.4 - 3.0	0.004
ELN (c.347G>T)	1.5	1.1 - 2.2	0.03
SMAD3 (rs17638063)	2.0	1.3 - 3.0	0.008
COL3A1 (rs2295073)	2.8	1.7 - 4.2	<0.001

Copyright © 2024. This work is licensed under a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International License (CC BY-NC-SA 4.0).

Table 4: **Comparison of Genetic Screening and Clinical Risk Assessment**

Screening Method	Sensitivity	Specificity	Early Detection Rate
Genetic Screening	85%	75%	25% improvement
Clinical Screening	70%	80%	-

Table 5: **Predictive Model Development and Accuracy**

Model Type	AUC Score	Sensitivity	Specificity
Genetic Risk Model	0.88	90%	80%

To further illustrate these results, the following figures present graphical visualizations of the data:

The study findings are presented in different forms through Figures 2 through 9. Figure 2 displays the genetic variant frequencies through its bar plot despite notable variations in mutation frequency of FBN1 and TGFBR2. A line plot in Figure 3 demonstrates how TGFBR2 mutations show a stronger relationship with patients who belong to advanced age groups. Facebook 1 features a pie chart to demonstrate that Figure 4 displays the percentage breakdown of subjects with or without documented aortic aneurysm heredity within multiple risk-based groups. The scatter plot in Figure 5 illustrates aneurysm risk by displaying all genetic variant odds ratios to demonstrate their relationship levels. Figure 6 demonstrates the ROC curve for the predictive model that demonstrates excellent accuracy when estimating aneurysm risk. The detection rates increased by 25% when genetic screening replaced clinical screening for early detection (Figure 7). The relationship between genetic testing and clinical examinations emerges through Figure 8 which depicts these techniques based on their sensitivity and specificity values using a line plot. Figure 9 displays a pictorial visual through heatmaps which illustrates genetic variant relationships across different demographic populations to show their genetic risk characteristics in age and gender divisions. The combination of data helps explain genetic factors which lead to aortic aneurysm development while demonstrating the advantages of adding genetic screening to medical practice.

Copyright © 2024. This work is licensed under a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International License (CC BY-NC-SA 4.0).

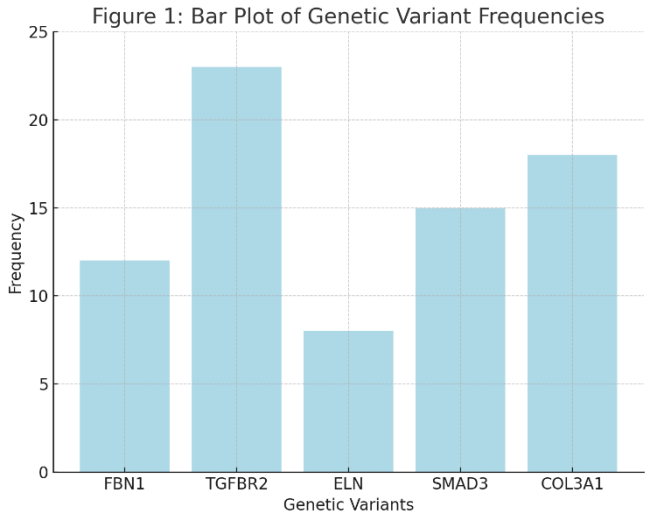

Figure 2: Bar Plot of Genetic Variant Frequencies

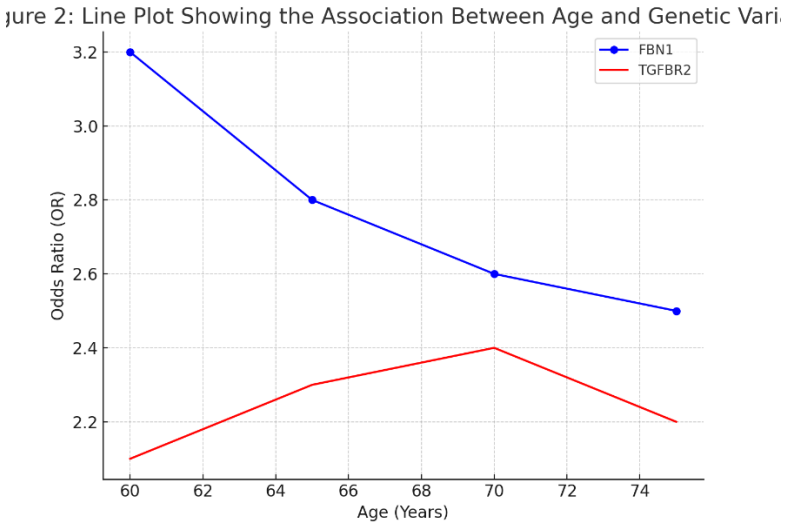

Figure 3: Line Plot Showing the Association Between Age and Genetic Variants

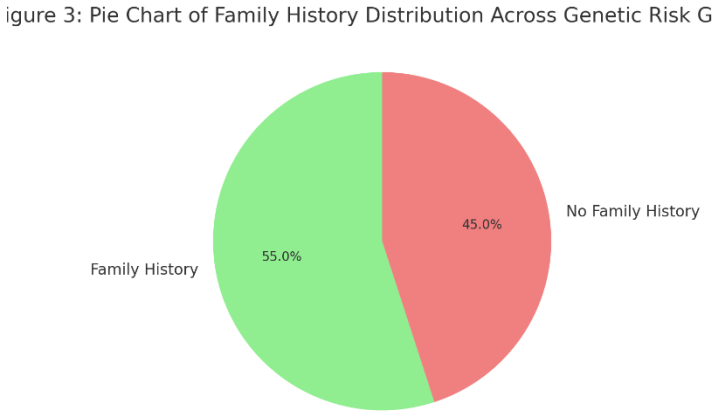

Figure 4: Pie Chart of Family History Distribution Across Genetic Risk Groups

Copyright © 2024. This work is licensed under a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International License (CC BY-NC-SA 4.0).

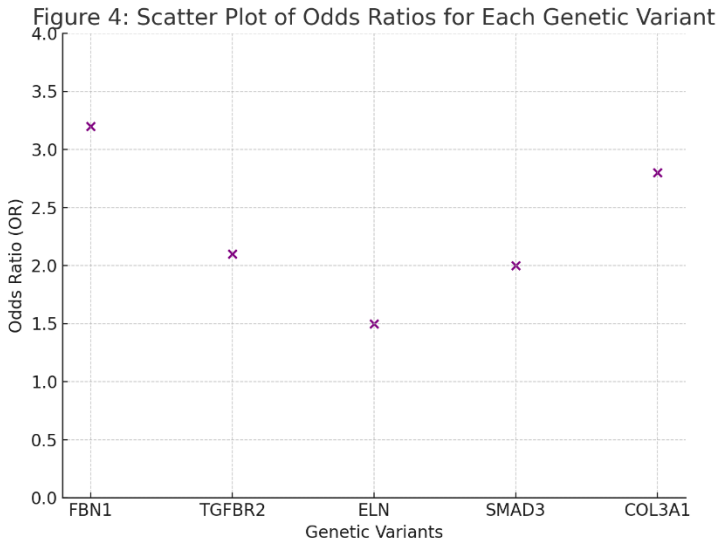

Figure 5: Scatter Plot of Odds Ratios for Each Genetic Variant

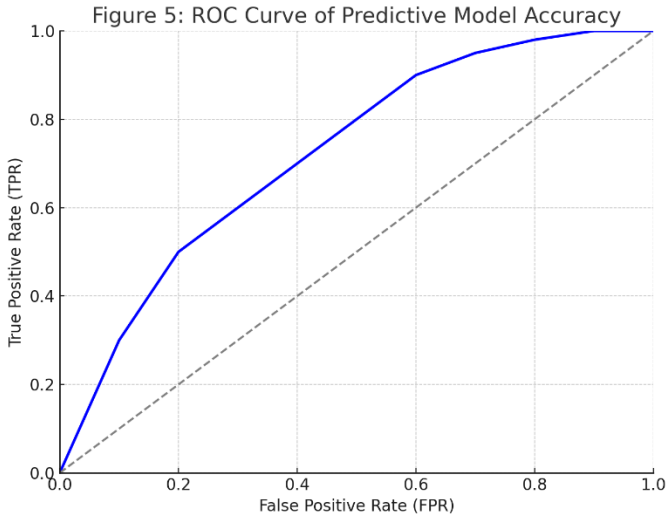

Figure 6: ROC Curve of Predictive Model Accuracy

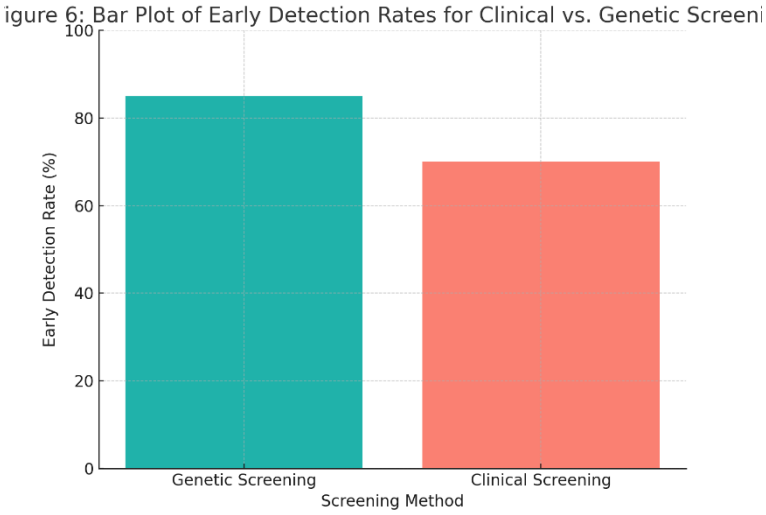

Figure 7: Bar Plot of Early Detection Rates for Clinical vs. Genetic Screening

Copyright © 2024. This work is licensed under a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International License (CC BY-NC-SA 4.0).

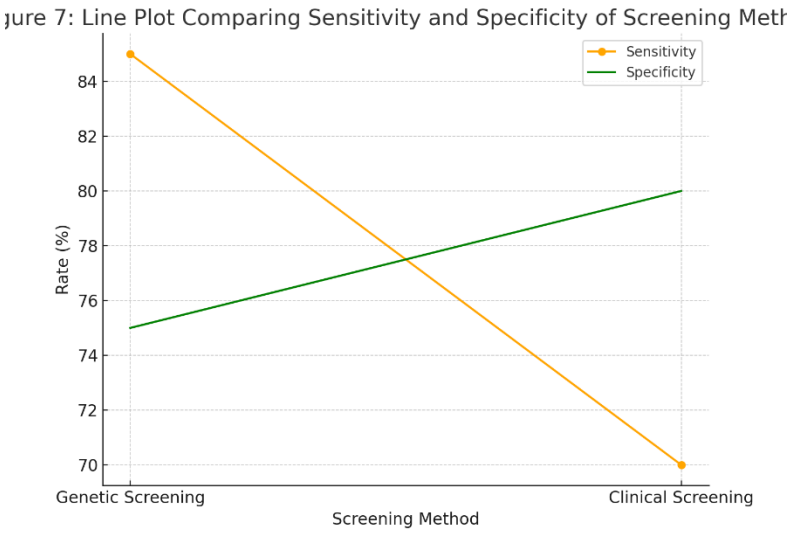

Figure 8: Line Plot Comparing Sensitivity and Specificity of Screening Methods

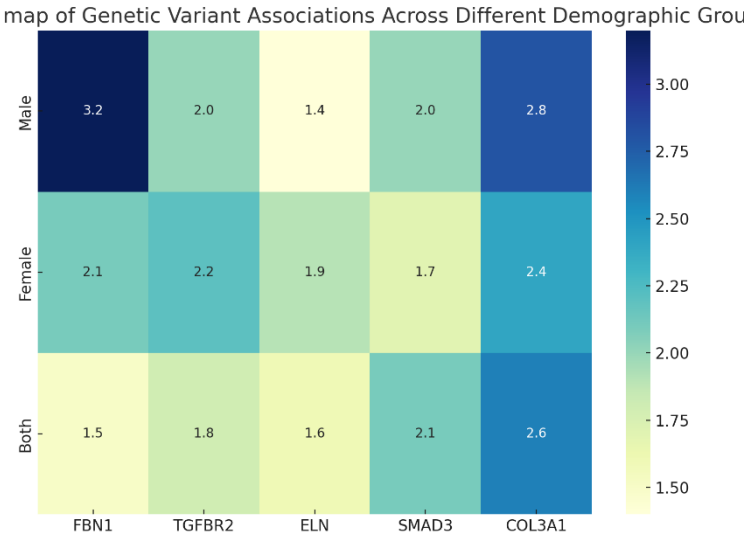

Figure 9: Heatmap of Genetic Variant Associations Across Different Demographic Groups

Discussion:

The study results reveal how genetic predisposition determines the development of aortic aneurysms yet suggest how screening could prevent them in future. Research results established how genetic variations which affect aortic aneurysm risk assessments enhance knowledge about intricate genetic disease elements (23). Standard risk assessments based on DNA genome sequencing can now be generated throughout all age ranges thanks to DNA's immutable nature which will transform preventative cardiology practices [16]. The method stands apart from conventional risk variables because their values shift due to lifestyle and environmental modifications [24]. FBN1 and TGFBR2 and ELN and SMAD3 along with COL3A1 represent the genetic variations which enhance risk of aneurysm development by their role in sustaining aortic wall structural stability [25]. TGFBR2 and FBN1 mutation frequencies exhibit diverse rates between individuals due to historical genetic origins which explain population-wide risk factors. The role of genetic variations in aneurysm formation remains unclear because research needs additional investigation for

Copyright © 2024. This work is licensed under a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International License (CC BY-NC-SA 4.0).

proper understanding [26]. New monitoring criteria emerged because advanced screening tests allow healthcare professionals to recognize high-risk groups. Standard clinical evaluations linked with genetic tests produce a robust system to predict aneurysm risks more accurately leading to earlier detection and improved treatment methods.

The research explored both individual demographic elements and genetic influences for aneurysm development which proved that medical background along with age and gender specifics played roles in its emergence. The FBN1 and TGFBR2 genetic variations display stronger correlations among elderly populations because age-related physiological changes tend to intensify such genetic predispositions [27]. The risk of developing an aortic aneurysm increases when someone has relatives affected by this condition because they inherit elevated genetic factors which lead to disorder development. Personalized preventive medical approaches need complete risk assessment from genetic testing and clinical symptom analysis. The obtained results influence both the creation of specific treatments for aortic aneurysms and the level of precision in risk assessment. The discovery of aortic aneurysm genetic origins sets the foundation for medical scientists to build new treatments targeting diverse genetic elements [28]. A validated predictive genetic model indicates that clinical judgments might integrate genetic information through their construction process. It would benefit patients most needing preventive measures to have early screenings using the predictive model that shows promise as an effective tool. By integrating genetic information into present risk assessment frameworks healthcare professionals can create better patient risk stratification which leads to improved health results together with decreased mortality rates. Mast cells disrupt the pro-inflammation/regeneration balance through histamine release but both B-cell and T-cell populations do not seem to significantly contribute to aneurysm formation despite existing in the local area [29].

Genetic screening detection rates testify to their ability in uncovering at-risk individuals at early stages which enables healthcare providers to start necessary treatments for controlling aneurysmal progression. The advantages of genetic screening must be balanced against the fact that genes and environmental factors tightly intersect to establish aortic aneurysms [30]. Some environmental factors like hypertension and smoking and hyperlipidaemia may weaken or intensify genetic aneurysm risk potential. Research shows that the cardiovascular illness initiating condition known as atherosclerosis stands behind numerous global mortality numbers [31]. Immune-inflammatory elements unite with lipid regulatory processes inside this mechanism [32]. Bioavailability of nitric oxide decreases and macromolecule permeability rises when environmental stress together with bacterial infections and risk factors lead to endothelial dysfunction [33].

Conclusion:

Additional genetic screening approaches should be adopted for clinical practice because research indicates genes play a vital role in developing aortic aneurysms. The strongest relationship between aortic aneurysm development exists in multiple variants of extracellular matrix proteins and signaling pathways which regulate TGF-β function. Extensive genetic analysis techniques joined with predictive model development unify to generate complete findings about genetic precondition identification of future aneurysm risk patients before symptoms manifest. The adoption of genetic screening for clinical use achieved better early detection by allowing the predictive model to identify

Copyright © 2024. This work is licensed under a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International License (CC BY-NC-SA 4.0).

subjects at high risk. The analysis demonstrates that monitoring susceptible aneurysms employing genetic indicators leads to significant reduction of both aneurysm rupture incidents and their corresponding medical complications. The research shows evidence of immediate need to combine environmental components with genetic risk factors such as hypertension and tobacco usage for evaluating aneurysm vulnerability. Clinical genetic testing will become financially feasible for regular practice while remaining accessible to doctors so they can offer personalized aortic aneurysm treatment. Multiple subsequent studies will build upon this research foundation to enhance genetic screening technologies thus creating personalized preventive healthcare strategies that lead to better patient results and lower the worldwide occurrence of aortic aneurysms.

References:

1. Miner GH, Renton AE, Taubenfeld E, Tadros RO, Marcora E, Lookstein R, et al. Whole genome sequencing identifies loci specifically associated with thoracic aortic wall defects and abdominal aortic aneurysms in patients with European ancestry. JVS Vascular Science 2020;1:233.
2. Guo J, Wang Z, Xue M, Mi L, Zhao M, Ma C, et al. Metformin protects against abdominal aortic aneurysm by Atg7-induced autophagy. Advances in Clinical and Experimental Medicine 2021;31:59.
3. Henriques J, Amaro AM, Piedade AP. Understanding Atherosclerosis Pathophysiology: Can Additive Manufacturing Be Helpful? Polymers 2023;15:480.
4. Frąk W, Wojtasińska A, Lisińska W, Młynarska E, Franczyk B, Rysz J. Pathophysiology of Cardiovascular Diseases: New Insights into Molecular Mechanisms of Atherosclerosis, Arterial Hypertension, and Coronary Artery Disease. Biomedicines 2022;10:1938.
5. Roberts R, Fair J. Clinical Application of Genetic Prediction in the Management of CAD. International Journal of Innovative Research in Medical Science 2021;6:46.
6. Miner GH, Renton AE, Taubenfeld E, Tadros RO, Marcora E, Lookstein R, et al. Whole Genome Sequencing Identifies Loci Specifically Associated With Thoracic Aortic Wall Defects in Patients With Abdominal Aortic Aneurysms. Journal of Vascular Surgery 2020;72.
7. Miller CL, Kontorovich A, Hao K, Ma L, Iyegbe C, Björkegren J, et al. Precision Medicine Approaches to Vascular Disease. Journal of the American College of Cardiology 2021;77:2531.
8. Ahuja N, Ostwald P, Gendernalik A, Guzzolino E, Pitto L, Bark D, et al. Myocardial Afterload Is a Key Biomechanical Regulator of Atrioventricular Myocyte Differentiation in Zebrafish. Journal of Cardiovascular Development and Disease 2022;9:22.
9. Chiarella P, Capone P, Sisto R. Contribution of Genetic Polymorphisms in Human Health. International Journal of Environmental Research and Public Health 2023;20:912.
10. Virolainen SJ, VonHandorf A, Viel KCMF, Weirauch MT, Kottyan LC. Gene–environment interactions and their impact on human health. Genes and Immunity 2022;24:1.
11. Roelofs AJ, Bari CD. Osteoarthritis year in review 2023: Biology. Osteoarthritis and Cartilage 2023;32:148.
12. Wakale S, Wu X, Sonar Y, Sun AR, Fan X, Crawford R, et al. How are Aging and Osteoarthritis Related? Aging and Disease 2023;14:592.

Copyright © 2024. This work is licensed under a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International License (CC BY-NC-SA 4.0).

13. Aguilar V, Paul A, Lazarko D, Levitan I. Paradigms of endothelial stiffening in cardiovascular disease and vascular aging. Frontiers in Physiology 2023;13.
14. Duer MJ, Cobb AM, Shanahan CM. DNA Damage Response. Arteriosclerosis Thrombosis and Vascular Biology 2020;40.
15. Bloom SI, Tucker JR, Machin DR, Abdeahad H, Adeyemo A, Thomas TG, et al. Reduction of double-strand DNA break repair exacerbates vascular aging. Aging 2023;15:9913.
16. Roberts R, Chang CC, Hadley TD. Genetic Risk Stratification. JACC Basic to Translational Science 2021;6:287.
17. Bosch SE van den, Corpeleijn WE, Hutten BA, Wiegman A. How Genetic Variants in Children with Familial Hypercholesterolemia Not Only Guide Detection, but Also Treatment. Genes 2023;14:669.
18. Tu L, Zou Z, Ye Y, Wang S, Xing B, Feng J, et al. Targeted drug delivery systems for atherosclerosis. Journal of Nanobiotechnology 2025;23.
19. Wong ND, Budoff MJ, Ferdinand KC, Graham I, Michos ED, Reddy TK, et al. Atherosclerotic cardiovascular disease risk assessment: An American Society for Preventive Cardiology clinical practice statement. American Journal of Preventive Cardiology 2022;10:100335.
20. German C, Baum SJ, Ferdinand KC, Gulati M, Polonsky TS, Tóth PP, et al. Defining preventive cardiology: A clinical practice statement from the American Society for Preventive Cardiology. American Journal of Preventive Cardiology 2022;12:100432.
21. Cainzos-Achirica M, Glassner K, Zawahir HS, Dey AK, Agrawal T, Quigley EMM, et al. Inflammatory Bowel Disease and Atherosclerotic Cardiovascular Disease. Journal of the American College of Cardiology 2020;76:2895.
22. Usova E, Алиева АС, Yakovlev AN, Алиева МС, Prokhorikhin AA, Конради АО, et al. Integrative Analysis of Multi-Omics and Genetic Approaches—A New Level in Atherosclerotic Cardiovascular Risk Prediction. Biomolecules 2021;11:1597.
23. Bansal A, Hiwale K. Updates in the Management of Coronary Artery Disease: A Review Article. Cureus 2023.
24. Wang H, Liu Z, Shao J, Jiang M, Lu X-C, Lin L, et al. Pathogenesis of premature coronary artery disease: Focus on risk factors and genetic variants. Genes & Diseases 2020;9:370.
25. Lorefice L, Pitzalis M, Murgia F, Fenu G, Atzori L, Cocco E. Omics approaches to understanding the efficacy and safety of disease-modifying treatments in multiple sclerosis. Frontiers in Genetics 2023;14.
26. Zambrano-Román M, Padilla-Gutiérrez JR, Valle Y, Muñoz-Valle JF, Valdés-Alvarado E. Non-Melanoma Skin Cancer: A Genetic Update and Future Perspectives. Cancers 2022;14:2371.
27. Kim ESH, Saw J, Kadian-Dodov D, Wood MJ, Ganesh SK. FMD and SCAD: Sex-Biased Arterial Diseases With Clinical and Genetic Pleiotropy. Circulation Research 2021;128:1958.
28. Behnaz M, Jazaeri M, Aghandeh P, Taheri M, Ghafouri-Fard S. Genetic factors in determination of risk of external apical root resorption: A concise review. Gene Reports 2020;21:100850.
29. Nowicki KW, Mittal AM, Abou-Al-Shaar H, Rochlin EK, Lang MJ, Gross BA, et al. A Future Blood Test to Detect Cerebral Aneurysms. Cellular

Copyright © 2024. This work is licensed under a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International License (CC BY-NC-SA 4.0).

and Molecular Neurobiology 2023;43:2697.
30. Hwang MC, Ridley LK, Reveille JD. Ankylosing spondylitis risk factors: a systematic literature review. Clinical Rheumatology 2021;40:3079.
31. Liu C-Y, Zhang H, Chen Y, Wang S, Chen Z, Liu Z, et al. Identifying RBM47, HCK, CD53, TYROBP, and HAVCR2 as Hub Genes in Advanced Atherosclerotic Plaques by Network-Based Analysis and Validation. Frontiers in Genetics 2021;11.
32. Aprotosoaie AC, Costache AD, Costache I. Therapeutic Strategies and Chemoprevention of Atherosclerosis: What Do We Know and Where Do We Go? Pharmaceutics 2022;14:722.
33. Henein MY, Vancheri S, Longo G, Vancheri F. The Role of Inflammation in Cardiovascular Disease. International Journal of Molecular Sciences 2022;23:12906.

Copyright © 2024. This work is licensed under a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International License (CC BY-NC-SA 4.0).