International Journal of Biomedicine 15(2) (2025) 239-246
http://dx.doi.org/10.21103/Article15(2)_RA1

REVIEW ARTICLE

INTERNATIONAL JOURNAL OF BIOMEDICINE

Cardiac Filaminopathy: Prevalence, Clinical Features, and Genetic Insights in Saudi Arabia

Yaqob Samir Taleb[1,3,4*], Fatimah Alabdullah[2,3], Abdulkareem AlGarni[2,3,5], Muneera AlTaweel[3,4], Zafar Jan Muhammad Iqbal[2,3]

[1]Department of Basic Sciences, College of Applied Medical Sciences (CoAMS-A), King Saud Bin Abdulaziz University for Health Sciences, Al-Ahsa, Kingdom of Saudi Arabia
[2]Clinical Laboratory Sciences Program (CLSP), College of Applied Medical Sciences, King Saud Bin Abdulaziz University for Health Sciences, Al-Ahsa, Kingdom of Saudi Arabia
[3]King Abdullah International Medical Research Center, Al-Ahsa, Kingdom of Saudi Arabia
[4]Cardiac Science division, Department of Medicine, King Abdulaziz Hospital, MNGHA, Al-Ahsa, Kingdom of Saudi Arabia
[5]Hematology and Oncology division, Department of Medicine, King Abdulaziz Hospital, MNGHA, Al-Ahsa, Kingdom of Saudi Arabia

Abstract

Cardiac filaminopathy, resulting from mutations in the *FLNC* gene that encodes filamin C, is increasingly recognized as a significant cause of inherited cardiomyopathies, including dilated cardiomyopathy, hypertrophic cardiomyopathy, restrictive cardiomyopathy, and arrhythmogenic right ventricular cardiomyopathy. This review synthesizes current knowledge about the genetic basis, clinical manifestations, and prevalence of cardiac filaminopathy, with a specific focus on Saudi Arabia. The unique genetic landscape of the Saudi population, characterized by a high prevalence of consanguinity, suggests a potentially elevated burden of cardiac filaminopathy condition, although data remain limited. We highlight the need for more comprehensive genetic screening and research to understand better and manage cardiac filaminopathy in Saudi Arabia.(**International Journal of Biomedicine. 2025;15(2):239-246.**)

Keywords: cardiac filaminopathy • cardiomyopathy • filamin-C • clinical features • Saudi Arabia

For citation: Taleb YS, Alabdullah F, AlGarni A, AlTaweel M, Iqbal ZJM. Cardiac Filaminopathy: Prevalence, Clinical Features, and Genetic Insights in Saudi Arabia. International Journal of Biomedicine. 2025;15(2):xxx-xxx. doi:10.21103/Article15(2)_RA1

Abbreviations

ACM, arrhythmogenic cardiomyopathy; **DCM,** dilated cardiomyopathy; **FLNC,** filamin C; **HCM,** hypertrophic cardiomyopathy; **ICD,** implantable cardioverter defibrillator; **LV,** left ventricle; **RCM**, restrictive cardiomyopathy.

Introduction

Inherited cardiomyopathies are a diverse group of heart muscle diseases with significant clinical and genetic heterogeneity. Among these, cardiac filaminopathy, caused by mutations in the filamin C (*FLNC*) gene, has gained attention due to its role in various forms of cardiomyopathy. Filamin C (FLNC) is an essential actin-binding protein involved in cytoskeletal organization and signal transduction in cardiomyocytes. Mutations in the *FLNC* gene disrupt these processes, leading to a range of cardiac phenotypes, including dilated, hypertrophic, restrictive, and arrhythmogenic cardiomyopathies.[1] Unlike filamin A and filamin B, FLNC is widely expressed in skeletal and cardiac muscle tissues, where it is localized to the Z-disc, myotendinous junctions, sarcolemma, and intercalated discs.[2] While the mutations in

the *FLNC* gene are associated with distal and myofibrillar skeletal muscle disorders, the development of cardiomyopathy may occur independently of any skeletal muscle disease.[1,3,4]

Saudi Arabia presents a unique context for studying cardiac filaminopathy due to its high rate of consanguinity, which increases the risk of inherited genetic disorders. Despite this, the prevalence and impact of *FLNC* mutations in the Saudi population have not been extensively studied. Recently, a couple of cases in Saudi Arabia have been identified with mutations in the *FLNC* gene linked to dilated cardiomyopathy[5] and distal skeletal myopathy.[6] This growing body of evidence highlights the critical role that the *FLNC* gene plays in cardiac muscle function, suggesting a potential area of focus for future research and clinical interventions. These findings also emphasize the need for further genetic screening and investigation within the population to understand better the prevalence and impact of *FLNC* mutations on heart health in this region.

Methods

We conducted a comprehensive literature search on PubMed for inherited cardiomyopathies associated with *FLNC* mutations, focusing particularly on their phenotypic characteristics and potential prevalence within the Saudi Arabian population. Different keyword combinations were inserted: "cardiac filaminopathy" AND "filamin-C" OR "FLNC" AND "inherited cardiomyopathy" AND "cardiomyopathy" AND "Saudi Arabia" AND "clinical features." The relevance of the articles was selected for each cardiomyopathy.

Results

Filamin C (FLNC), encoded by the *FLNC* gene, is a critical component of the cardiac Z-disc, where it contributes to the mechanical stability and signal transduction pathways that regulate muscle contraction. The protein's role in maintaining the structural integrity of the sarcomere and its interactions with various signaling molecules underline its importance in cardiac function. Mutations in *FLNC* can lead to the development of cardiomyopathies through mechanisms such as impaired mechanotransduction, altered signaling pathways, and disrupted cytoskeletal architecture.[1] Also, FLNC is believed to be involved in crosslinking filamentous actin (F-actin), although the precise mechanisms underlying this interaction remain unclear. Recently, Ohiri et al. revealed FLNC functions as an actin crosslinking protein. They justified the potential key role of FLNC in regulating cellular responses, such as stress and injury. For example, FLNC is observed to accumulate at injury sites within skeletal myofibers and cardiomyocytes during exercise, where it contributes to repair mechanisms, including sarcomere rebuilding.[7] FLNC is known to be predominantly localized to key structural regions within cardiomyocytes, including the Z-discs, sarcolemma, and intercalated discs (Figure 1).

Many proteins can interact with FLNC, including Z-disc-associated proteins such as Titin, Calsarcin, Myotilin, Nebulette, and other proteins.[10]Also, other protein complexes known to interact with FLNC, such as the β1A integrin subunit and the sarcoglycan complex at the costamere, are anchored to the sarcolemma of cardiomyocytes.[11] Moreover, FLNC associates with the structures of intercalated discs, which are composed of gap junctions, adherens junctions, and desmosomes. Thus, FLNC localization at intercalated discs supports mechanical and electrical coupling between adjacent cardiomyocytes. Given that FLNC can interact with various proteins linked to inherited cardiomyopathy, it may contribute to the manifestation of diverse cardiomyopathy phenotypes.[12]

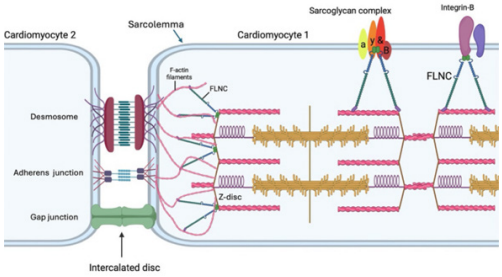

Fig. 1. *FLNC interacts with Z-disc proteins and costamere proteins (sarcoglycans) through its C-terminal region. This interaction facilitates the linkage between Z-disc proteins and sarcolemma. FLNC actin-binding protein can also interact with F-actin filaments. [8] FLNC is also localized at the intercalated disc, and thereby any disruption in FLNC function could impair the cell-cell mechanical force transduction. Figure is adapted from Ortiz-Genga et al.[9] and Zhou et al.[8] and created by BioRender. FLNC, filamin C.*

Genetic Mutations and Pathogenesis

The *FLNC* gene mutations associated with cardiac filaminopathy can be classified into truncating and missense mutations, each leading to distinct cardiomyopathy phenotypes. Truncating mutations often result in a loss of protein function, contributing to the development of dilated cardiomyopathy (DCM) and arrhythmogenic cardiomyopathy (ACM), characterized by ventricular arrhythmias, left ventricular fibrosis, and a high risk of sudden cardiac death.[13-15] On the other hand, missense mutations that disrupt the dimerization and proper folding of the protein are known to result in the formation of protein aggregates within the sarcomere that are more commonly associated with hypertrophic (HCM) and restrictive cardiomyopathies (RCM), which can lead to abnormal thickening of the ventricular walls and impaired diastolic function.[1]

In addition, the *FLNC* truncating variants were defined as nonsense, frameshift, or canonical splice site variants.[14, 16] These truncating variants compromise the structural integrity of FLNC, which may exacerbate the susceptibility to cardiac dysfunction and contribute to various cardiomyopathic phenotypes.[17] Understanding the specific impact of these mutations is essential for elucidating the molecular mechanisms underlying FLNC-related cardiomyopathies.

Clinical Features of Cardiac Filaminopathy

The clinical spectrum of cardiac filaminopathy is broad, ranging from asymptomatic carriers to individuals with severe, life-threatening cardiac conditions. Recent studies have shown that variants in *FLNC* can be associated with various cardiomyopathies, including dilated cardiomyopathy (DCM),

hypertrophic cardiomyopathy (HCM), arrhythmogenic cardiomyopathy (ACM), and restrictive cardiomyopathy (RCM),[18] and can also lead to distinct phenotypes.[1,19]

Dilated Cardiomyopathy (DCM)

Truncating mutations of *FLNC* have been found in 1%-5% of patients with the DCM phenotype.[20] Dilated cardiomyopathy is a severe cardiac condition characterized by left ventricular dilation and impaired systolic function, often leading to heart failure, arrhythmia, and sudden cardiac death. Emerging research has established a strong association between DCM and pathogenic mutation in *FLNC*. There are different genes closely associated with DCM, including titin, desmin, lamin A/C (*LMNA*), desmoplakin, desmin, β-myosin heavy chain (*MYH7*), Bcl2-associated athanogene 3 (*BAG3*), and *FLNC*. The clinical manifestations of DCM during its early stages may include fatigue, dyspnea, dizziness, syncope, and edema. However, abnormal skin pigmentation, skeletal myopathy, and neurosensory disorders may appear in severe cases.[21] A recent study genetically characterized DCM patients who underwent cardiac transplantation in a Chinese population using whole-exome sequencing and showed that *FLNC* truncation could lead to severe clinical symptoms in DCM patients, suggesting an urgent need for appropriate treatment of this complex cardiomyopathy.[22]

Hypertrophic Cardiomyopathy (HCM):

This phenotype is characterized by asymmetric septal hypertrophy, leading to left ventricular outflow tract obstruction, diastolic dysfunction, mitral regurgitation, myocardial ischemia, autonomic dysfunction, and an increased risk of arrhythmias. Patients may present with symptoms such as chest pain, dyspnea, palpitations, and syncope. Variants in sarcomere-related structures have been linked to causing left ventricular (LV) hypertrophy,[23] but the two most common pathogenic gene mutations are *MYH7* and *MYBPC3*.[24] The identification of the *MYH7* gene, which encodes the beta-myosin heavy chain—a key component of the sarcomere thick filament—was indeed a major step in understanding the genetic basis of HCM, especially the non-syndromic form of the disease. Subsequent familial studies have revealed pathogenic variants in additional sarcomeric genes, including *MYBPC3* (myosin-binding protein C), *TNNT2* (troponin T), and *TNNI3* (troponin I). Recent research methodologies have also uncovered variants in non-sarcomeric genes that display moderate to strong associations with HCM. Noteworthy among these are *JPH2* (junctophilin), *CSRP3* (cysteine and glycine-rich protein 3), *FHOD3* (formin homology 2 domain-containing 3), *ALPK3* (alpha-protein kinase 3), *TRIM63* (tripartite motif containing 63, exhibiting autosomal recessive inheritance), *PLN* (phospholamban), and *FLNC*.[25]

The severity of HCM in patients with *FLNC* mutations can vary widely, from mild to severe forms[26] requiring medical intervention or implantable cardioverter-defibrillators (ICDs). Missense variants of *FLNC* are predominantly linked to HCM, with prevalence rates ranging from 1.3% to 8.7% in HCM cohorts. However, some studies found no significant excess of rare missense variants in HCM patients compared to controls, raising questions about the role of *FLNC* missense variants in this condition. Of the 54 identified missense variants, only 13 are considered (likely) pathogenic based on additional evidence, such as functional studies or familial segregation. The remaining variants are classified as variants of uncertain significance (VUS) according to current diagnostic criteria. Notably, there is significant clustering of missense variants within the ROD2 domain of *FLNC*, a region crucial for cell signaling, suggesting that variants located in this domain have a higher likelihood of being pathogenic for HCM.[17]

Restrictive Cardiomyopathy (RCM)

Restrictive cardiomyopathy (RCM) is marked by a stiffening of the ventricular walls, resulting in impaired diastolic filling, atrial enlargement, and the development of heart failure with preserved ejection fraction (HFpEF). Patients with RCM often present with symptoms of heart failure, such as fatigue, dyspnea, edema, and ascites.[27] This phenotype is particularly severe and is associated with a poor prognosis.[28,29] RCM typically follows an autosomal dominant inheritance pattern. Genes related to RCM include *TNNI3*, *TNNT2*, *MYH7*, *MYBPC3*, *LMNA*, desmin, and *FLNC* (Table 1). Most identified mutations occur within genes that encode sarcomeric proteins, while others are found in proteins that can associate with the sarcomere, such as small heat-shock proteins like crystallin αB, or their interacting partners, like BAG3 proteins. The dysfunction of these proteins may contribute to the accumulation of aggregated proteins.[29] Recently, several reports have shown that missense mutations in *FLNC* may lead to exclusively RCM phenotype or overlapping with other cardiomyopathies such as hypertrophic cardiomyopathy or left-ventricular non-compaction.[26,30,31]

Arrhythmogenic Cardiomyopathy (ACM)

Arrhythmogenic cardiomyopathy (ACM) is a genetic heart disease resulting from mutations in proteins that constitute the intercalated disc, including both desmosomal (plakophilin-2, desmoplakin, desmoglein-2, and desmocollin) and non-desmosomal proteins (titin, PLN, DES, LMNA, and FLNC).[32] Recent studies have revealed that mutations in *FLNC* may cause the ACM phenotype.[19,33,34] Arrhythmogenic cardiomyopathy (ACM) is associated with an increased risk of ventricular arrhythmias and sudden cardiac death. Truncating *FLNC* mutations are often implicated in this phenotype, which is characterized by fibrofatty infiltration of the myocardium, left ventricular dilation, and a high incidence of arrhythmias. Sudden cardiac death may be the first manifestation of the disease in some patients, particularly in young adults.[35] More recently, Marinas et al.[36] have identified rare variants of *FLNC* across 22 index cases (15 males, median age of 45), of which 16 harbored ‘radical’ variants (comprising 8 deletions/insertions, 6 nonsense variants, and 2 splice site variants) classified as pathogenic or likely pathogenic. Additionally, 6 cases carried missense variants classified as variants of unknown significance (VUS). The left-dominant form of ACM was present in 63.6% of index cases. Interestingly, the 2020 Padua Criteria for ACM were able to distinguish 8 ACM patients with traditional right ventricular involvement from 14 ACM patients with the left ventricular form among *FLNC* carriers, estimating the disease penetrance at around 71%.

Table 1 presents the list of disease-causing genes and their most commonly associated phenotype.

Table 1.
List of disease-causing genes and their most commonly associated phenotype.

Location within the cell/function	Protein	Gene	Common Phenotype	References
Sarcomere proteins	Myosin-binding protein C	*MYBPC3*	HCM	[37-39]
	Troponin C	*TNNC1*	HCM	[40]
	Beta-myosin heavy chain	*MYH7*	HCM	[41]
	Essential myosin light chain	*MYL3*	HCM	[42,43]
	Troponin T	*TNNT2*	HCM, DCM	[44,45]
	Troponin I	*TNNI3*	HCM, RCM, DCM	[46-48]
	Actin	*ACTC1*	RCM, HCM	[48]
	Regulatory myosin light chain	*MYL2*	HCM	[43]
	Tropomyosin	*TPM1*	DCM, HCM	[43,49]
Z-disc proteins	Titin	*TTN*	DCM	[45,49]
	Desmin	*DES*	DCM	[50]
	Filamin-C	*FLNC*	DCM, ACM	[50-52]
	α-actinin 2	*ACTN2*	HCM	[50,53]
	Cysteine and glycine-rich protein-3	*CSRP3*	HCM	[50,54]
	Telethonin (T-cap)	*TCAP*	HCM, DCM	[50,55]
	Myopalladin	*MYPN*	DCM	[50]
	Nebulette	*NEBL*	HCM, DCM	[50]
	Nexilin	*NEXN*	DCM	[50,56]
	Obscurin	*OBSCN*	HCM, DCM	[50,57]
Calcium handling Proteins	Ryanodine receptor 2	*RYR2*	HCM, ACM	[58-60]
	Calmodulin	*CALM*	HCM	[61]
	Phospholamban	*PLN*	DCM, HCM	[62,63]
Desmosome	Desmoplakin	*DSP*	DCM, ACM	[64-66]
	Plakophilin-2	*PKP2*	ACM	[65,67,68]
	Plakoglobin	*JUP*	ACM	[36,65,69]
	Desmocollin-2	*DSC2*	ACM	[65,69,70]
	Desmoglein-2	*DSG2*	ACM	[65,69,71]
Ion channel	Sodium channel protein type 5 subunit alpha	*SCN5A*	DCM, ACM	[72,73]
	Delayed rectifier inward potassium channel alpha-subunit	*KCNQ1*	DCM	[74,75]

Prevalence and Genetic Landscape in Saudi Arabia

The prevalence of *FLNC*-related cardiomyopathies in Saudi Arabia has not been comprehensively studied. However, the high rate of consanguinity in the population suggests that inherited cardiomyopathies, including those caused by *FLNC* mutations, may be more common than in populations with lower consanguinity rates.[76]A limited number of case reports and genetic studies have begun to shed light on the burden of *FLNC* mutations in Saudi Arabia.[3,5,6] In addition, a previous study conducted in a Saudi Arabian cohort identified several families with severe cardiac phenotypes linked to genetic mutations. In these families, 23 marriages (62%) were consanguineous, and DCM was the most common subtype of inherited cardiomyopathy (26 cases) compared to non-consanguineous marriages (only two cases).[77] Despite the relatively rare occurrence of *FLNC* mutations reported in Saudi Arabia, the significance of genetic testing cannot be overstated. It plays a pivotal role not only in confirming the diagnosis but also in guiding the clinical management and personalized treatment strategies for affected individuals.[78] Indeed, early detection through genetic screening is crucial for improving patient outcomes, particularly in complex cardiomyopathies associated with *FLNC* variants.

Diagnostic and Therapeutic Challenges

The diagnosis of cardiac filaminopathy in Saudi Arabia faces several challenges, including limited access to genetic testing, a lack of awareness among healthcare providers, and cultural factors that may influence the uptake of genetic counseling and testing. Despite these challenges, advances in genetic testing and the establishment of specialized cardiac genetic clinics have the potential to improve the diagnosis and management of *FLNC*-related cardiomyopathies. Management strategies for patients with cardiac filaminopathy include primary prevention by using ICD implantation as well as the use of beta-blockers and antiarrhythmic drugs to prevent sudden cardiac death.[79,80] In severe cases, heart transplantation may be considered.[22] Given the high risk of sudden cardiac death associated with *FLNC*-related cardiomyopathies, early disease identification and management are crucial to improving outcomes.[35]

Discussion

This paper provides a comprehensive overview of the current understanding of cardiac filaminopathy, particularly in the context of the Saudi Arabian population. It emphasizes the need for further research and improved diagnostic and management strategies to address the unique challenges posed by this condition in Saudi Arabia. Though a pathogenic mutation in the *FLNC* gene is contributing significantly to the cause of inherited cardiomyopathies, it remains insufficiently acknowledged in Saudi Arabia. The high prevalence of consanguinity in the Saudi population may contribute to a higher burden of *FLNC*-related cardiomyopathies, although more research is needed to confirm this. Genetic testing and early diagnosis are critical to preventing severe outcomes, including sudden cardiac death. There is an urgent need for large-scale epidemiological studies to determine the true prevalence of *FLNC*-related cardiomyopathies in Saudi Arabia. Additionally, establishing a national registry for inherited cardiomyopathies could help track these conditions more effectively and improve patient management.

Research into the genetic basis of inherited cardiomyopathies and the specific *FLNC* mutation spectrum in Saudi Arabia, as well as the development of targeted therapies, is crucial for advancing the care of patients with cardiac filaminopathy. These studies provide important insights into risk stratification and prognosis.[81]

Conclusion

More efforts are needed to increase awareness, improve access to genetic services, and develop further research into the genetic landscape of cardiomyopathies in Saudi Arabia. Perhaps these are essential steps toward advanced and better patient care in this nation.

Competing Interests

The authors declare that they have no competing interests.

References

1. Hespe S, Isbister JC, Duflou J, Puranik R, Bagnall RD, Semsarian C, et al. A case series of patients with filamin-C truncating variants attending a specialized cardiac genetic clinic. Eur Heart J Case Rep. 2023 Nov 17;7(12):ytad572. doi: 10.1093/ehjcr/ytad572. PMID: 38116480; PMCID: PMC10729912.
2. Mao Z, Nakamura F. Structure and Function of Filamin C in the Muscle Z-Disc. Int J Mol Sci. 2020 Apr 13;21(8):2696. doi: 10.3390/ijms21082696. PMID: 32295012; PMCID: PMC7216277.
3. Shammas I, Alhammad R, Naddaf E. Filamin C-Associated Nemaline Myopathy. Neurology. 2024 May;102(10):e209477. doi: 10.1212/WNL.0000000000209477. Epub 2024 Apr 24. PMID: 38657199.
4. Hooshmand SJ, Govindarajan R, Bostick BP. Cardiomyopathy, Proximal Myopathy, Camptocormia, and Novel Filamin C (FLNC) Variant: A Case Report. Am J Case Rep. 2021 Sep 16;22:e932648. doi: 10.12659/AJCR.932648. PMID: 34526477; PMCID: PMC8455110.
5. Alsubhi A, Aldarwish M, Agrawal PB, Al Tala SM, Eldadah O, Alghamdi AA, et al. A child with dilated cardiomyopathy and homozygous splice site variant in *FLNC* gene. Mol Genet Metab Rep. 2023 Nov 23;38:101027. doi: 10.1016/j.ymgmr.2023.101027. PMID: 38077956; PMCID: PMC10709609.
6. Almalki D, Ali A. Rare Genetic Variant of Distal Myopathy with Posterior Leg and Anterior Hand Involvement: Case Report. The Open Neurology Journal. 2020; 14(1). doi: 10.2174/1874205X02014010093.
7. Ohiri JC, Dellefave-Castillo L, Tomar G, Wilsbacher L, Choudhury L, Barefield DY, et al. Reduction of Filamin C Results in Altered Proteostasis, Cardiomyopathy, and Arrhythmias. J Am Heart Assoc. 2024 May 21;13(10):e030467. doi: 10.1161/JAHA.123.030467. Epub 2024 May 18. PMID: 38761081; PMCID: PMC11179814.
8. Zhou X, Fang X, Ithychanda SS, Wu T, Gu Y, Chen C, et al. Interaction of Filamin C With Actin Is Essential for Cardiac Development and Function. Circ Res. 2023 Aug 18;133(5):400-411. doi: 10.1161/CIRCRESAHA.123.322750. Epub 2023 Jul 26. PMID: 37492967; PMCID: PMC10529502.
9. Ortiz-Genga MF, Cuenca S, Dal Ferro M, Zorio E, Salgado-Aranda R, Climent V, et al. Truncating FLNC Mutations Are Associated With High-Risk Dilated and Arrhythmogenic Cardiomyopathies. J Am Coll Cardiol. 2016 Dec 6;68(22):2440-2451. doi: 10.1016/j.jacc.2016.09.927. PMID: 27908349.
10. Song S, Shi A, Lian H, Hu S, Nie Y. Filamin C in cardiomyopathy: from physiological roles to DNA variants. Heart Fail Rev. 2022 Jul;27(4):1373-1385. doi: 10.1007/s10741-021-10172-z. Epub 2021 Sep 17. PMID: 34535832.
11. Lazzarino M, Zanetti M, Chen SN, Gao S, Peña B, Lam CK, et al. Defective Biomechanics and Pharmacological Rescue of Human Cardiomyocytes with Filamin C Truncations. Int J Mol Sci. 2024 Mar 3;25(5):2942. doi: 10.3390/ijms25052942. PMID: 38474188; PMCID: PMC10932268.
12. Eden M, Frey N. Cardiac Filaminopathies: Illuminating the Divergent Role of Filamin C Mutations in Human Cardiomyopathy. J Clin Med. 2021 Feb 4;10(4):577. doi: 10.3390/jcm10040577. PMID: 33557094; PMCID: PMC7913873.
13. Akhtar MM, Lorenzini M, Pavlou M, Ochoa JP, O'Mahony C, Restrepo-Cordoba MA, et al.; European Genetic Cardiomyopathies Initiative Investigators. Association of Left Ventricular Systolic Dysfunction Among Carriers of Truncating Variants in Filamin C With Frequent Ventricular Arrhythmia and End-stage Heart Failure. JAMA Cardiol. 2021 Aug 1;6(8):891-901. doi: 10.1001/jamacardio.2021.1106. Erratum in: JAMA Cardiol. 2021 Aug 1;6(8):980. doi: 10.1001/jamacardio.2021.2422. PMID: 33978673.
14. Kandhari N, Khoury S, Behr ER, Miles C. Cardiac arrest as first presentation of arrhythmogenic left ventricular cardiomyopathy due to Filamin C mutation: a case report. Eur Heart J Case Rep. 2021 Nov 22;5(11):ytab422. doi: 10.1093/ehjcr/ytab422. PMID: 34993393; PMCID: PMC8728717.
15. Liebman SW, Palaganas H, Kobany H. A founder mutation in FLNC is likely a major cause of idiopathic dilated cardiomyopathy in Ashkenazi Jews. Int J Cardiol. 2021 Jan 15;323:124. doi: 10.1016/j.ijcard.2020.08.052. Epub 2020 Aug

15. PMID: 32805325.
16. Begay RL, Tharp CA, Martin A, Graw SL, Sinagra G, Miani D, et al. *FLNC* Gene Splice Mutations Cause Dilated Cardiomyopathy. JACC Basic Transl Sci. 2016 Aug;1(5):344-359. doi: 10.1016/j.jacbts.2016.05.004. Epub 2016 Jul 27. PMID: 28008423; PMCID: PMC5166708.
17. Verdonschot JAJ, Vanhoutte EK, Claes GRF, Helderman-van den Enden ATJM, Hoeijmakers JGJ, Hellebrekers DMEI, et al. A mutation update for the FLNC gene in myopathies and cardiomyopathies. Hum Mutat. 2020 Jun;41(6):1091-1111. doi: 10.1002/humu.24004. Epub 2020 Mar 20. PMID: 32112656; PMCID: PMC7318287.
18. Kumar P, Paramasivam G, Prabhu MA, Devasia T, Rajasekhar M. A novel FLNC variation associated with restrictive cardiomyopathy with an unusually long clinical course—A case report. Gene Reports. 2023; 31:101769. doi: 10.1016/j.genrep.2023.101769.
19. Hall CL, Akhtar MM, Sabater-Molina M, Futema M, Asimaki A, Protonotarios A, et al. Filamin C variants are associated with a distinctive clinical and immunohistochemical arrhythmogenic cardiomyopathy phenotype. Int J Cardiol. 2020 May 15;307:101-108. doi: 10.1016/j.ijcard.2019.09.048. Epub 2019 Oct 8. PMID: 31627847.
20. Schoonvelde SAC, Ruijmbeek CWB, Hirsch A, van Slegtenhorst MA, Wessels MW, von der Thüsen JH, et al. Phenotypic variability of filamin C-related cardiomyopathy: Insights from a novel Dutch founder variant. Heart Rhythm. 2023 Nov;20(11):1512-1521. doi: 10.1016/j.hrthm.2023.08.003. Epub 2023 Aug 9. PMID: 37562486.
21. Wang S, Zhang Z, He J, Liu J, Guo X, Chu H, Xu H, Wang Y. Comprehensive review on gene mutations contributing to dilated cardiomyopathy. Front Cardiovasc Med. 2023 Dec 1;10:1296389. doi: 10.3389/fcvm.2023.1296389. PMID: 38107262; PMCID: PMC10722203.
22. Lian H, Song S, Chen W, Shi A, Jiang H, Hu S. Genetic characterization of dilated cardiomyopathy patients undergoing heart transplantation in the Chinese population by whole-exome sequencing. J Transl Med. 2023 Jul 17;21(1):476. doi: 10.1186/s12967-023-04282-5. PMID: 37461109; PMCID: PMC10351148.
23. Writing Committee Members; Ommen SR, Ho CY, Asif IM, Balaji S, Burke MA, Day SM, et al. 2024 AHA/ACC/AMSSM/HRS/PACES/SCMR Guideline for the Management of Hypertrophic Cardiomyopathy: A Report of the American Heart Association/American College of Cardiology Joint Committee on Clinical Practice Guidelines. J Am Coll Cardiol. 2024 Jun 11;83(23):2324-2405. doi: 10.1016/j.jacc.2024.02.014. Epub 2024 May 8. Erratum in: J Am Coll Cardiol. 2024 Oct 29;84(18):1771. doi: 10.1016/j.jacc.2024.08.055. PMID: 38727647.
24. Hutt E, Desai MY. Medical Treatment Strategies for Hypertrophic Cardiomyopathy. Am J Cardiol. 2024 Feb 1;212S:S33-S41. doi: 10.1016/j.amjcard.2023.10.074. Epub 2024 Jan 29. PMID: 38368034.
25. Lopes LR, Ho CY, Elliott PM. Genetics of hypertrophic cardiomyopathy: established and emerging implications for clinical practice. Eur Heart J. 2024 Aug 9;45(30):2727-2734. doi: 10.1093/eurheartj/ehae421. PMID: 38984491; PMCID: PMC11313585.
26. Gaudreault N, Ruel LJ, Henry C, Schleit J, Lagüe P, Champagne J, Sénéchal M, et al. Novel filamin C (FLNC) variant causes a severe form of familial mixed hypertrophic-restrictive cardiomyopathy. Am J Med Genet A. 2023 Jun;191(6):1508-1517. doi: 10.1002/ajmg.a.63169. Epub 2023 Mar 2. PMID: 36864778.
27. Gowda SN, Ali HJ, Hussain I. Overview of Restrictive Cardiomyopathies. Methodist Debakey Cardiovasc J. 2022 Mar 14;18(2):4-16. doi: 10.14797/mdcvj.1078. PMID: 35414858; PMCID: PMC8932380.
28. Szczygieł JA, Michałek P, Truszkowska G, Drozd-Sokołowska J, Wróbel A, Franaszczyk M, et al. Clinical features, etiology, and survival in patients with restrictive cardiomyopathy: A single-center experience. Kardiol Pol. 2023;81(12):1227-1236. doi: 10.33963/v.kp.97879. Epub 2023 Nov 8. PMID: 37937352.
29. Cimiotti D, Budde H, Hassoun R, Jaquet K. Genetic Restrictive Cardiomyopathy: Causes and Consequences-An Integrative Approach. Int J Mol Sci. 2021 Jan 8;22(2):558. doi: 10.3390/ijms22020558. PMID: 33429969; PMCID: PMC7827163.
30. Garcia Hernandez S, Ortiz-Genga M, Analia Ramos K, Ochoa J, Lamounier A, Fernandez X, et al. Novel Filamin C missense mutation associated with severe restrictive cardiomyopathy overlapping with left ventricular non-compaction. European Heart Journal. 2020; 41(Supplement_2): p. ehaa946. 3714. doi: doi.org/10.1093/ehjci/ehaa946.3714.
31. Bermúdez-Jiménez FJ, Carriel V, Santos-Mateo JJ, Fernández A, García-Hernández S, Ramos KA, et al. ROD2 domain filamin C missense mutations exhibit a distinctive cardiac phenotype with restrictive/hypertrophic cardiomyopathy and saw-tooth myocardium. Rev Esp Cardiol (Engl Ed). 2023 May;76(5):301-311. English, Spanish. doi: 10.1016/j.rec.2022.08.002. Epub 2022 Aug 8. PMID: 35952944.
32. Corrado D, Basso C. Arrhythmogenic left ventricular cardiomyopathy. Heart. 2022 May;108(9):733-743. doi: 10.1136/heartjnl-2020-316944. Epub 2021 Jul 13. PMID: 34257076; PMCID: PMC8995901.
33. Brun F, Gigli M, Graw SL, Judge DP, Merlo M, Murray B, et al. *FLNC* truncations cause arrhythmogenic right ventricular cardiomyopathy. J Med Genet. 2020 Apr;57(4):254-257. doi: 10.1136/jmedgenet-2019-106394. Epub 2020 Jan 10. PMID: 31924696; PMCID: PMC7539291.
34. Carruth ED, Qureshi M, Alsaid A, Kelly MA, Calkins H, Murray B, et al.; Regeneron Genetics Center; Baras A, Lester Kirchner H, Fornwalt BK, James CA, Haggerty CM. Loss-of-Function *FLNC* Variants Are Associated With Arrhythmogenic Cardiomyopathy Phenotypes When Identified Through Exome Sequencing of a General Clinical Population. Circ Genom Precis Med. 2022 Aug;15(4):e003645. doi: 10.1161/CIRCGEN.121.003645. Epub 2022 Jun 14. PMID: 35699965; PMCID: PMC9388603.
35. Simonit F, Da Broi U, D'Elia AV, Fabbro D, Mio C, Bussani R, Pinamonti M, Desinan L. Filamin C (FLNC) truncating mutation in a fatal arrhythmogenic left ventricular cardiomyopathy (ALVC). Leg Med (Tokyo). 2024 Jul;69:102438. doi: 10.1016/j.legalmed.2024.102438. Epub 2024 Mar 26. PMID: 38547641.
36. Bueno Marinas M, Cason M, Bariani R, Celeghin R, De Gaspari M, Pinci S, et al. A Comprehensive Analysis of Non-Desmosomal Rare Genetic Variants in Arrhythmogenic Cardiomyopathy: Integrating in Padua Cohort Literature-Derived Data. Int J Mol Sci. 2024 Jun 6;25(11):6267.

doi: 10.3390/ijms25116267. PMID: 38892455; PMCID: PMC11173278.
37. Carrier L. Targeting the population for gene therapy with MYBPC3. J Mol Cell Cardiol. 2021 Jan;150:101-108. doi: 10.1016/j.yjmcc.2020.10.003. Epub 2020 Oct 11. PMID: 33049255.
38. Beltrami M, Fedele E, Fumagalli C, Mazzarotto F, Girolami F, Ferrantini C, et al. Long-Term Prevalence of Systolic Dysfunction in MYBPC3 Versus MYH7-Related Hypertrophic Cardiomyopathy. Circ Genom Precis Med. 2023 Aug;16(4):363-371. doi: 10.1161/CIRCGEN.122.003832. Epub 2023 Jul 6. PMID: 37409452.
39. Lorenzini M, Norrish G, Field E, Ochoa JP, Cicerchia M, Akhtar MM, et al. Penetrance of Hypertrophic Cardiomyopathy in Sarcomere Protein Mutation Carriers. J Am Coll Cardiol. 2020 Aug 4;76(5):550-559. doi: 10.1016/j.jacc.2020.06.011. PMID: 32731933; PMCID: PMC7397507.
40. Tikunova SB, Thuma J, Davis JP. Mouse Models of Cardiomyopathies Caused by Mutations in Troponin C. Int J Mol Sci. 2023 Aug 2;24(15):12349. doi: 10.3390/ijms241512349. PMID: 37569724; PMCID: PMC10419064.
41. Tudurachi BS, Zăvoi A, Leonte A, Țăpoi L, Ureche C, Bîrgoan SG, et al. An Update on MYBPC3 Gene Mutation in Hypertrophic Cardiomyopathy. Int J Mol Sci. 2023 Jun 22;24(13):10510. doi: 10.3390/ijms241310510. PMID: 37445689; PMCID: PMC10341819.
42. Osborn DPS, Emrahi L, Clayton J, Tabrizi MT, Wan AYB, Maroofian R, et al. Autosomal recessive cardiomyopathy and sudden cardiac death associated with variants in MYL3. Genet Med. 2021 Apr;23(4):787-792. doi: 10.1038/s41436-020-01028-2. Epub 2020 Dec 8. PMID: 33288880; PMCID: PMC8026398.
43. Velicki L, Jakovljevic DG, Preveden A, Golubovic M, Bjelobrk M, Ilic A, et al. Genetic determinants of clinical phenotype in hypertrophic cardiomyopathy. BMC Cardiovasc Disord. 2020 Dec 9;20(1):516. doi: 10.1186/s12872-020-01807-4. PMID: 33297970; PMCID: PMC7727200.
44. Bourfiss M, van Vugt M, Alasiri AI, Ruijsink B, van Setten J, Schmidt AF, et al. Prevalence and Disease Expression of Pathogenic and Likely Pathogenic Variants Associated With Inherited Cardiomyopathies in the General Population. Circ Genom Precis Med. 2022 Dec;15(6):e003704. doi: 10.1161/CIRCGEN.122.003704. Epub 2022 Oct 20. PMID: 36264615; PMCID: PMC9770140.
45. Stroeks SLVM, Lunde IG, Hellebrekers DMEI, Claes GRF, Wakimoto H, Gorham J, et al. Prevalence and Clinical Consequences of Multiple Pathogenic Variants in Dilated Cardiomyopathy. Circ Genom Precis Med. 2023 Apr;16(2):e003788. doi: 10.1161/CIRCGEN.122.003788. Epub 2023 Mar 27. PMID: 36971006.
46. Pua CJ, Tham N, Chin CWL, Walsh R, Khor CC, Toepfer CN, et al. Genetic Studies of Hypertrophic Cardiomyopathy in Singaporeans Identify Variants in *TNNI3* and *TNNT2* That Are Common in Chinese Patients. Circ Genom Precis Med. 2020 Oct;13(5):424-434. doi: 10.1161/CIRCGEN.119.002823. Epub 2020 Aug 20. PMID: 32815737; PMCID: PMC7676617.
47. Sorrentino U, Gabbiato I, Canciani C, Calosci D, Rigon C, Zuccarello D, Cassina M. Homozygous *TNNI3* Mutations and Severe Early Onset Dilated Cardiomyopathy: Patient Report and Review of the Literature. Genes (Basel). 2023 Mar 19;14(3):748. doi: 10.3390/genes14030748. PMID: 36981019; PMCID: PMC10048074.
48. Voinescu OR, Ionac A, Sosdean R, Ionac I, Ana LS, Kundnani NR, et al. Genotype-Phenotype Insights of Inherited Cardiomyopathies-A Review. Medicina (Kaunas). 2024 Mar 27;60(4):543. doi: 10.3390/medicina60040543. PMID: 38674189; PMCID: PMC11052121.
49. Yogasundaram H, Alhumaid W, Dzwiniel T, Christian S, Oudit GY. Cardiomyopathies and Genetic Testing in Heart Failure: Role in Defining Phenotype-Targeted Approaches and Management. Can J Cardiol. 2021 Apr;37(4):547-559. doi: 10.1016/j.cjca.2021.01.016. Epub 2021 Jan 22. PMID: 33493662.
50. Noureddine M, Gehmlich K. Structural and signaling proteins in the Z-disk and their role in cardiomyopathies. Front Physiol. 2023 Mar 2;14:1143858. doi: 10.3389/fphys.2023.1143858. PMID: 36935760; PMCID: PMC10017460.
51. Eldemire R, Mestroni L, Taylor MRG. Genetics of Dilated Cardiomyopathy. Annu Rev Med. 2024 Jan 29;75:417-426. doi: 10.1146/annurev-med-052422-020535. Epub 2023 Oct 3. PMID: 37788487; PMCID: PMC10842880.
52. Celeghin R, Cipriani A, Bariani R, Bueno Marinas M, Cason M, Bevilacqua M, et al. Filamin-C variant-associated cardiomyopathy: A pooled analysis of individual patient data to evaluate the clinical profile and risk of sudden cardiac death. Heart Rhythm. 2022 Feb;19(2):235-243. doi: 10.1016/j.hrthm.2021.09.029. Epub 2021 Oct 1. PMID: 34601126.
53. Broadway-Stringer S, Jiang H, Wadmore K, Hooper C, Douglas G, Steeples V, et al. Insights into the Role of a Cardiomyopathy-Causing Genetic Variant in *ACTN2*. Cells. 2023 Feb 24;12(5):721. doi: 10.3390/cells12050721. PMID: 36899856; PMCID: PMC10001372.
54. Lipari M, Wypasek E, Karpiński M, Tomkiewicz-Pajak L, Laino L, Binni F, Giannarelli D, et al. Identification of a variant hotspot in MYBPC3 and of a novel CSRP3 autosomal recessive alteration in a cohort of Polish patients with hypertrophic cardiomyopathy. Pol Arch Intern Med. 2020 Feb 27;130(2):89-99. doi: 10.20452/pamw.15130. Epub 2020 Jan 9. PMID: 31919335.
55. Toste A, Perrot A, Özcelik C, Cardim N. Identification of a novel titin-cap/telethonin mutation in a Portuguese family with hypertrophic cardiomyopathy. Rev Port Cardiol (Engl Ed). 2020 Jun;39(6):317-327. English, Portuguese. doi: 10.1016/j.repc.2019.12.007. Epub 2020 Jun 18. PMID: 32565061.
56. Liu C, Spinozzi S, Feng W, Chen Z, Zhang L, Zhu S, et al. Homozygous G650del nexilin variant causes cardiomyopathy in mice. JCI Insight. 2020 Aug 20;5(16):e138780. doi: 10.1172/jci.insight.138780. PMID: 32814711; PMCID: PMC7455123.
57. Marston S, Montgiraud C, Munster AB, Copeland O, Choi O, Dos Remedios C, et al. OBSCN Mutations Associated with Dilated Cardiomyopathy and Haploinsufficiency. PLoS One. 2015 Sep 25;10(9):e0138568. doi: 10.1371/journal.pone.0138568. PMID: 26406308; PMCID: PMC4583186.
58. Fujino N, Ino H, Hayashi K, Uchiyama K, Nagata M, Konno T, et al., Abstract 915: A Novel Missense Mutation in Cardiac Ryanodine Receptor Gene as a Possible Cause of Hypertrophic Cardiomyopathy: Evidence From Familial Analysis. Circulation. 2006; 114(suppl_18): p. II_165-II_165. doi:10.1161/circ.114.suppl_18.II_165-b.
59. Sleiman Y, Lacampagne A, Meli AC. "Ryanopathies" and RyR2 dysfunctions: can we further decipher them using in vitro human disease models? Cell Death Dis. 2021 Nov 1;12(11):1041.

doi: 10.1038/s41419-021-04337-9. Erratum in: Cell Death Dis. 2022 Nov 30;13(12):1014. doi: 10.1038/s41419-022-05468-3. PMID: 34725342; PMCID: PMC8560800.
60. Costa S, Medeiros-Domingo A, Gasperetti A, Breitenstein A, Steffel J, Guidetti F, et al. Familial dilated cardiomyopathy associated with a novel heterozygous RYR2 early truncating variant. Cardiol J. 2021;28(1):173-175. doi: 10.5603/CJ.a2020.0099. Epub 2020 Aug 4. PMID: 32748945; PMCID: PMC8105062.
61. Zahavich L, Tarnopolsky M, Yao R, Mital S. Novel Association of a De Novo CALM2 Mutation With Long QT Syndrome and Hypertrophic Cardiomyopathy. Circ Genom Precis Med. 2018 Oct;11(10):e002255. doi: 10.1161/CIRCGEN.118.002255. PMID: 30354306.
62. Haghighi K, Kolokathis F, Pater L, Lynch RA, Asahi M, Gramolini AO, et al. Human phospholamban null results in lethal dilated cardiomyopathy revealing a critical difference between mouse and human. J Clin Invest. 2003 Mar;111(6):869-76. doi: 10.1172/JCI17892. PMID: 12639993; PMCID: PMC153772.
63. Zaffran S, Kraoua L, Jaouadi H. Calcium Handling in Inherited Cardiac Diseases: A Focus on Catecholaminergic Polymorphic Ventricular Tachycardia and Hypertrophic Cardiomyopathy. Int J Mol Sci. 2023 Feb 8;24(4):3365. doi: 10.3390/ijms24043365. PMID: 36834774; PMCID: PMC9963263.
64. Heymans S, Lakdawala NK, Tschöpe C, Klingel K. Dilated cardiomyopathy: causes, mechanisms, and current and future treatment approaches. Lancet. 2023 Sep 16;402(10406):998-1011. doi: 10.1016/S0140-6736(23)01241-2. PMID: 37716772.
65. Serpa F, Finn CM, Tahir UA. Navigating the penetrance and phenotypic spectrum of inherited cardiomyopathies. Heart Fail Rev. 2024 Sep;29(5):873-881. doi: 10.1007/s10741-024-10405-x. Epub 2024 Jun 19. PMID: 38898187.
66. Gasperetti A, Carrick RT, Protonotarios A, Murray B, Laredo M, van der Schaaf I, et al. Clinical features and outcomes in carriers of pathogenic desmoplakin variants. Eur Heart J. 2025 Jan 21;46(4):362-376. doi: 10.1093/eurheartj/ehae571. PMID: 39288222; PMCID: PMC11745529.
67. Bos TA, Piers SRD, Wessels MW, Houweling AC, Bökenkamp R, Bootsma M, et al.; European Reference Network for rare, low prevalence and complex diseases of the heart: ERN GUARD-Heart. The arrhythmogenic cardiomyopathy phenotype associated with PKP2 c.1211dup variant. Neth Heart J. 2023 Aug;31(7-8):315-323. doi: 10.1007/s12471-023-01791-2. Epub 2023 Jul 28. PMID: 37505369; PMCID: PMC10400759.
68. Zathar Z, Shah N, Desai N, Patel PA. Arrhythmogenic Cardiomyopathy: Current Updates and Future Challenges. Rev Cardiovasc Med. 2024 Jun 4;25(6):208. doi: 10.31083/j.rcm2506208. PMID: 39076315; PMCID: PMC11270059.
69. Hespe S, Gray B, Puranik R, Peters S, Sweeting J, Ingles J. The role of genetic testing in management and prognosis of individuals with inherited cardiomyopathies. Trends Cardiovasc Med. 2025 Jan;35(1):34-44. doi: 10.1016/j.tcm.2024.06.002. Epub 2024 Jul 14. PMID: 39004295.
70. Santoro F, Vitale E, Ragnatela I, Cetera R, Leopzzi A, Mallardi A,et al. Multidisciplinary approach in cardiomyopathies: From genetics to advanced imaging. Heart Fail Rev. 2024 Mar;29(2):445-462. doi: 10.1007/s10741-023-10373-8. Epub 2023 Dec 2. PMID: 38041702.
71. Göz M, Pohl G, Steinecker SM, Walhorn V, Milting H, Anselmetti D. Arrhythmogenic cardiomyopathy-related cadherin variants affect desmosomal binding kinetics. J Mol Cell Cardiol. 2024 Oct;195:36-44. doi: 10.1016/j.yjmcc.2024.07.009. Epub 2024 Jul 28. PMID: 39079569.
72. Landstrom AP, Kim JJ, Gelb BD, Helm BM, Kannankeril PJ, Semsarian C, et al.; American Heart Association Council on Genomic and Precision Medicine; Council on Lifelong Congenital Heart Disease and Heart Health in the Young; Council on Arteriosclerosis, Thrombosis and Vascular Biology; and Council on Lifestyle and Cardiometabolic Health. Genetic Testing for Heritable Cardiovascular Diseases in Pediatric Patients: A Scientific Statement From the American Heart Association. Circ Genom Precis Med. 2021 Oct;14(5):e000086. doi: 10.1161/HCG.0000000000000086. Epub 2021 Aug 20. PMID: 34412507; PMCID: PMC8546375.
73. Remme CA. *SCN5A* channelopathy: arrhythmia, cardiomyopathy, epilepsy and beyond. Philos Trans R Soc Lond B Biol Sci. 2023 Jun 19;378(1879):20220164. doi: 10.1098/rstb.2022.0164. Epub 2023 May 1. PMID: 37122208; PMCID: PMC10150216.
74. Allen KY, Vetter VL, Shah MJ, O'Connor MJ. Familial long QT syndrome and late development of dilated cardiomyopathy in a child with a KCNQ1 mutation: A case report. HeartRhythm Case Rep. 2015 Dec 18;2(2):128-131. doi: 10.1016/j.hrcr.2015.10.011. PMID: 28491650; PMCID: PMC5412615.
75. Marian AJ, Asatryan B, Wehrens XHT. Genetic basis and molecular biology of cardiac arrhythmias in cardiomyopathies. Cardiovasc Res. 2020 Jul 15;116(9):1600-1619. doi: 10.1093/cvr/cvaa116. PMID: 32348453; PMCID: PMC7341170.
76. El Goundali K, Chebabe M, Zahra Laamiri F, Hilali A. The Determinants of Consanguineous Marriages among the Arab Population: A Systematic Review. Iran J Public Health. 2022 Feb;51(2):253-265. doi: 10.18502/ijph.v51i2.8679. PMID: 35866117; PMCID: PMC9273505.
77. Khayat AM, Alshareef BG, Alharbi SF, AlZahrani MM, Alshangity BA, Tashkandi NF. Consanguineous Marriage and Its Association With Genetic Disorders in Saudi Arabia: A Review. Cureus. 2024 Feb 9;16(2):e53888. doi: 10.7759/cureus.53888. PMID: 38465157; PMCID: PMC10924896.
78. Albesher N, Massadeh S, Hassan SM, Alaamery M. Consanguinity and Congenital Heart Disease Susceptibility: Insights into Rare Genetic Variations in Saudi Arabia. Genes (Basel). 2022 Feb 16;13(2):354. doi: 10.3390/genes13020354. PMID: 35205398; PMCID: PMC8871910.
79. Abela M, Grech N, Debattista J, Felice T. Genetic testing in the management of inherited cardiac disorders: two cases of Filamin-C arrhythmogenic left ventricular cardiomyopathy. Eur Heart J Case Rep. 2023 Oct 18;7(11):ytad515. doi: 10.1093/ehjcr/ytad515. PMID: 37954562; PMCID: PMC10635578.
80. Liu MB, Parikh VN. Toward Precision Medicine in the Treatment of Arrhythmogenic Cardiomyopathy. Curr Treat Options Cardio Med. 2024; **26**, 317–330. doi: 10.1007/s11936-024-01052-4
81. Chiswell K, Zaininger L, Semsarian C. Evolution of genetic testing and gene therapy in hypertrophic cardiomyopathy. Prog Cardiovasc Dis. 2023 Sep-Oct;80:38-45. doi: 10.1016/j.pcad.2023.04.009. Epub 2023 May 1. PMID: 37137376.

***Corresponding author**: Dr. Yaqob Taleb, PhD, Department of Basic Sciences, College of Applied Medical Sciences (CoAMS-A), King Saud Bin Abdulaziz University for Health Sciences, Al-Ahsa, Kingdom of Saudi Arabia. E-mail: yagoob9696@hotmail.com*