International Journal of Innovative Technologies in Social Science

e-ISSN: 2544-9435

Operating Publisher
SciFormat Publishing Inc.
ISNI: 0000 0005 1449 8214

2734 17 Avenue SW,
Calgary, Alberta, T3E0A7,
Canada
+15878858911
editorial-office@sciformat.ca

ARTICLE TITLE	THE ROLE OF ELECTROCARDIOGRAPHY IN THE DIAGNOSIS AND MONITORING OF FABRY DISEASE: A COMPREHENSIVE REVIEW
DOI	https://doi.org/10.31435/ijitss.3(51).2026.6093
RECEIVED	29 April 2026
ACCEPTED	21 July 2026
PUBLISHED	06 August 2026
LICENSE	The article is licensed under a **Creative Commons Attribution 4.0 International License.**

THE ROLE OF ELECTROCARDIOGRAPHY IN THE DIAGNOSIS AND MONITORING OF FABRY DISEASE: A COMPREHENSIVE REVIEW

Jakub Jakubowski *(Corresponding Author, Email: loreofnothing@gmail.com)*
Medical University of Warsaw, Poland
ORCID ID: 0009-0009-0269-1371

Karol Kraska
Medical University of Lublin, Poland
ORCID ID: 0009-0003-8113-2151

Nadzieja Krasucka
Medical University of Lublin, Poland
ORCID ID: 0009-0007-2777-892X

Aleksandra Zynkowska
Medical University of Lublin, Poland
ORCID ID: 0009-0005-1759-5842

Aleksandra Skrzyniarz
Medical University of Lublin, Poland
ORCID ID: 0009-0003-0065-643X

Maria Kiełbus
Medical University of Lublin, Poland
ORCID ID: 0009-0003-1946-3013

Julia Oziębło
Medical University of Lublin, Poland
ORCID ID: 0009-0008-9794-9824

Magdalena Kijowska
Medical University of Lublin, Poland
ORCID ID: 0009-0004-1086-7086

Karolina Klusek
Medical University of Lublin, Poland
ORCID ID: 0009-0004-7006-0188

Michał Batory
No. 1 University Clinical Hospital in Lublin, Poland
ORCID ID: 0009-0008-7018-7823

ABSTRACT

Anderson-Fabry disease (FD) is a rare, X-linked lysosomal storage disorder in which the progressive accumulation of globotriaosylceramide (Gb3) leads to widespread multi-organ damage, with cardiac involvement serving as the primary cause of mortality. This comprehensive review aims to summarize the current state of knowledge regarding the clinical application of electrocardiography (ECG) as a pivotal and cost-effective tool in the management of patients with FD. The paper systematically categorizes ECG findings across the various stages of the disease's progression. Early stages are typically characterized by a shortened PR interval and increased QRS complex voltages, which frequently manifest prior to the development of structural changes identifiable through echocardiography. In the more advanced stages of the disease, the predominant features include signs of left ventricular hypertrophy (LVH), ST-segment depressions, and deep T-wave inversions, which often mimic the presentation of hypertrophic cardiomyopathy or myocardial ischemia. Furthermore, this review discusses the evolution of conduction disturbances, including atrioventricular blocks and atrial fibrillation, while emphasizing the absolute necessity of Holter monitoring for effective arrhythmia risk stratification. The impact of enzyme replacement therapy (ERT) on the stabilization of ECG patterns is evaluated, indicating that early clinical intervention is crucial for the prevention of irreversible electrical remodeling. In conclusion, despite the ongoing development of advanced imaging modalities, the standard 12-lead ECG remains a fundamental and indispensable tool that shortens the diagnostic odyssey and allows for the precise monitoring of treatment efficacy in Fabry disease.

KEYWORDS

Fabry Disease, Electrocardiography, PR Interval, Left Ventricular Hypertrophy, Arrhythmia, Screening

CITATION

Jakub Jakubowski, Karol Kraska, Nadzieja Krasucka, Aleksandra Zynkowska, Aleksandra Skrzyniarz, Maria Kiełbus, Julia Oziębło, Magdalena Kijowska, Karolina Klusek, Michał Batory. (2026) The Role of Electrocardiography in the Diagnosis and Monitoring of Fabry Disease: a Comprehensive Review. *International Journal of Innovative Technologies in Social Science*. 3(51). doi: 10.31435/ijitss.3(51).2026.6093

1. Introduction

Anderson-Fabry disease (FD) is a rare, multisystemic genetic disorder characterized by an X-linked pattern of inheritance, belonging to the broader category of lysosomal storage diseases. The fundamental cause of the condition is a mutation in the GLA gene, which results in either a complete or partial deficiency of the lysosomal enzyme alpha-galactosidase A (α-Gal A). The biochemical consequence of this enzymatic defect is the progressive and systemic accumulation of glycosphingolipids, predominantly globotriaosylceramide (Gb3), within the lysosomes of cells across diverse organ systems. These include the vascular endothelium, the kidneys, the central and peripheral nervous systems, and crucially, the heart (Linhart et al., 2001; Tognola et al., 2025). Although FD is inherently a multiorgan pathology, the clinical progression and overall patient prognosis are predominantly determined by the severity and extent of cardiovascular system involvement.

Cardiomyopathy associated with Fabry disease currently represents the primary cause of both significant morbidity and premature mortality within this specific patient population. The relentless deposition of Gb3 within cardiomyocytes, the specialized cells of the cardiac conduction system, and the coronary vascular endothelial cells leads to the development of left ventricular hypertrophy (LVH), progressive myocardial fibrosis, and life-threatening arrhythmic disturbances (Gambarin et al., 2010; Hagège et al., 2019). Given that the cardiac phenotype of Fabry disease can strikingly mimic the presentation of classic sarcomeric hypertrophic cardiomyopathy (HCM), an accurate diagnosis is frequently delayed by several years. This unfortunate diagnostic lag drastically diminishes the patient’s opportunities for the timely and effective initiation of enzyme replacement therapy (ERT) before the onset of irreversible structural cardiac remodelling (Yousef et al., 2013).

Considering the diagnostic complexities presented by rare genetic conditions, standard 12-lead electrocardiography (ECG) emerges as an indispensable screening and monitoring instrument. ECG is characterized as a universal, cost-effective, non-invasive technology that remains ubiquitous across all tiers of

healthcare delivery, including primary care environments. Although the electrocardiographic recording undergoes dynamic transformations corresponding to the progressive stages of the disease, ranging from the classic early-stage shortening of the PR interval to advanced features of hypertrophy and profound repolarization abnormalities (Vitale et al., 2022), its meticulous interpretation can provide the essential first "red flag" to guide clinicians toward the correct diagnostic pathway. From a healthcare organizational perspective, the optimal utilization of such a fundamental medical technology as the ECG for the screening of rare diseases carries immense social and economic weight, significantly shortening the protracted "diagnostic odyssey" typically experienced by these patients.

2. Methodology

To successfully accomplish the primary objectives established for this comprehensive review, an exhaustive and systematic search of the available scientific literature was meticulously conducted across several prominent electronic medical and academic databases, specifically including PubMed, Scopus, and Google Scholar. The highly targeted literature search strategy was fundamentally based on a deliberate and specific combination of the following core keywords and exact search phrases (utilized exclusively in the English language): "Fabry disease", "Anderson-Fabry disease", "electrocardiography", "ECG", "hypertrophic cardiomyopathy", "arrhythmia", and "PR interval".

The rigorous analytical process encompassed a wide variety of scholarly sources, incorporating peer-reviewed original research articles, comprehensive review papers, detailed clinical case series, and the most current, evidence-based cardiological clinical guidelines. To guarantee the highest possible methodological quality, reliability, and academic rigor of the review, the final analysis strictly included only those articles that had been formally published in recognized, peer-reviewed scientific journals. During the selection process, several specific exclusion criteria were applied; consequently, publications in which the electrocardiographic recording constituted merely a marginal or incidental element of the patient's clinical description without undergoing a detailed, dedicated analysis were systematically excluded. Furthermore, preliminary conference reports or abstracts lacking accessible full-text manuscripts were eliminated from consideration.

During the initial phase of data extraction and critical analysis, all duplicate publications across the searched databases were identified and permanently removed from the dataset. The thoroughly compiled and curated body of literature was subsequently subjected to an in-depth synthesis and systematic categorization, explicitly focusing on the specific progressive stages of the disease and the corresponding, distinct electrocardiographic abnormalities. This structured analytical process directly facilitated the logical construction and comprehensive organization of the subsequent results section. Ultimately, following this rigorous filtering and critical evaluation process, a carefully selected total of 25 bibliographic references were included in the final scope of this review.

3. Results

Classic and Early Electrocardiographic Changes

The early detection of cardiac involvement in Anderson-Fabry disease (FD) is crucial for patient prognosis; however, structural changes, such as left ventricular hypertrophy (LVH) visible on a standard echocardiogram, typically appear only in the third or fourth decade of life in men, and even later in women. Meanwhile, electrocardiographic alterations frequently precede clinical symptoms and abnormalities in basic imaging studies, making the ECG a sensitive and cost-effective tool for early screening (Namdar, 2016). It is worth noting that while advanced imaging techniques, such as Tissue Doppler Imaging (TDI), also allow for the detection of preclinical myocardial damage before objective hypertrophy appears (Pieroni et al., 2003), the classic 12-lead ECG remains the most widely accessible first-line examination.

The most classic and early feature of FD is a shortened PR interval (typically <120 ms) with a preserved normal QRS duration and the absence of a delta wave (Aryana et al., 2008). In contrast to preexcitation syndromes (e.g., Wolff-Parkinson-White syndrome), where the PR shortening results from the presence of an accessory conduction pathway, the mechanism in Fabry disease is associated with accelerated atrioventricular conduction. This most likely stems from the progressive accumulation of glycosphingolipids within the cells of the conduction system, which shortens the impulse transit time through the atrioventricular node (Tognola et al., 2025). It is estimated that a short PR interval occurs in approximately 30-40% of FD patients, often emerging in childhood or adolescence before fully symptomatic cardiomyopathy develops (Kampmann et al., 2008).

Another early finding that may appear before objective structural hypertrophy of the heart walls is the presence of high QRS voltages. Even in patients with normal wall thickness on echocardiography, voltage criteria (such as the Sokolow-Lyon index) may already be positive (Parisi et al., 2023). This phenomenon is explained by alterations in the electrical properties of cardiomyocytes "overloaded" with stored Gb3, which leads to increased electrical excitability of the myocardial cells (Gomez et al., 2012).

The clinical significance of these early markers should be emphasized. In young patients presenting with non-specific symptoms (e.g., limb pain, anhidrosis, gastrointestinal distress), the finding of a short PR interval or disproportionately high QRS voltages on an ECG should immediately prompt the physician to investigate storage disorders (Paelinck et al., 2024). The early identification of these changes allows for meticulous patient monitoring and the timely initiation of enzyme replacement therapy (ERT), which can halt or slow irreversible myocardial fibrosis.

Electrocardiographic Features in the Advanced Stage of the Disease

As the disease progresses and the continuous deposition of globotriaosylceramide (Gb3) within the cardiomyocytes persists, a significant thickening of the myocardial walls occurs. Consequently, the electrocardiographic recording displays clearly fulfilled voltage criteria for left ventricular hypertrophy (LVH), such as the Sokolow-Lyon index or the Cornell criteria. It should be noted that these voltage changes are most pronounced in adult males, representing the classic phenotype of the disease. Over time, they also manifest in heterozygous females, in whom the disease progresses at a slower rate (Kampmann et al., 2002; Yousef et al., 2013). Significantly, the PR interval—which was characteristically shortened during the initial stages of the disease—may undergo a process of "pseudonormalization" or even reach pathological prolongation. These electrical shifts are the direct result of progressive myocardial fibrosis (Tognola et al., 2025).

Another critical feature associated with left ventricular hypertrophy in Fabry disease involves significant alterations in the repolarization phase. Clinicians begin to observe ST-segment depressions along with pathological, asymmetrical, and deeply inverted T waves. These findings represent a classic "strain pattern" of the left ventricle and are most frequently identified in the precordial leads V4-V6 and the lateral limb leads I and aVL. While these changes are a primary consequence of myocardial hypertrophy, they are also exacerbated by coronary microvascular disturbances and endothelial dysfunction caused by the accumulation of the glycosphingolipid substrate. Therefore, it is not uncommon for the ECG pattern to be mistaken for acute myocardial ischemia. In clinical practice, this often leads to initial misdiagnoses and unnecessary invasive interventions, such as coronary angiography (Jastrzębski & Petkow-Dimitrow, 2008; Paelinck et al., 2024).

A major challenge in analyzing the ECG in Fabry disease is its differentiation from classic hypertrophic cardiomyopathy (HCM), particularly of sarcomeric origin. Despite the apparent similarities, a meticulous and reliable analysis of the ECG can yield valuable diagnostic clues. Vitale et al. (2022) demonstrated that pathological Q waves, which are a hallmark feature of HCM, are observed significantly less frequently in patients with Fabry disease. Conversely, patients with FD are much more likely to exhibit massive LVH voltages alongside a relatively short PR interval, a combination that is rare in HCM. Recognizing these subtle nuances can facilitate a more rapid diagnostic pathway, leading to timely enzymatic and genetic testing.

Cardiac Arrhythmias, Conduction Disturbances, and the Role of Holter Monitoring

As previously noted, the deposition of glycosphingolipids occurs not only within the working cardiomyocytes but also within the specialized cells of the cardiac conduction system. Consequently, patients with Fabry disease are particularly predisposed to a wide spectrum of both ventricular and supraventricular arrhythmias. Cardiac rhythm disturbances represent one of the primary causes of sudden cardiac death within this patient population (Acharya et al., 2012). The progressive evolution of conduction disturbances is an exceptionally characteristic clinical phenomenon in this disease. While accelerated atrioventricular conduction, manifested as a shortened PR interval, typically dominates the early stages, more advanced phases of the disease—driven by progressive fibrosis and degeneration of the conduction system—are characterized by varying degrees of atrioventricular blocks (Namdar, 2016). Furthermore, many adult patients with Fabry disease exhibit sinus bradycardia and chronotropic incompetence, a condition defined by an inadequate heart rate response relative to the level of physical exertion. This functional impairment can be accurately evaluated during an exercise stress ECG (Krämer et al., 2015).

In addition to bradyarrhythmias, the occurrence of tachyarrhythmias poses a significant clinical threat. For instance, atrial fibrillation (AF) is notably more prevalent among patients with Fabry disease compared to the general population and serves as a critical risk factor for thromboembolic complications, including

ischemic stroke (Acharya et al., 2012). Ventricular tachyarrhythmias, such as premature ventricular contractions (PVCs) and ventricular tachycardia (VT)—including non-sustained ventricular tachycardia (NSVT)—are also frequent findings on the electrocardiographic recording. These arrhythmias correlate closely with localized areas of left ventricular fibrosis. It is essential to acknowledge, however, that cardiac rhythm disturbances, particularly in the early stages of the disease, are characterized by significant variability and are often asymptomatic in nature. Consequently, a standard resting ECG may fail to detect transient abnormalities. Therefore, current cardiological guidelines recommend regular 24- to 48-hour Holter ECG monitoring for patients with a confirmed diagnosis of FD. Based on this longitudinal monitoring, clinicians can perform effective arrhythmic risk stratification and determine the potential eligibility of patients for the implantation of a cardioverter-defibrillator (ICD) or a permanent pacemaker (Acharya et al., 2012; Tognola et al., 2025).

Specifics of ECG Patterns in the Pediatric Population and in Women

The comprehensive evaluation of electrocardiographic features in Fabry disease should appropriately conclude with an assessment of the specific changes observed in both the pediatric population and in female patients. In children and adolescents, it is exceptionally rare to identify overt structural cardiac abnormalities through standard echocardiographic examinations. Consequently, the ECG frequently serves as a more sensitive diagnostic tool, enabling the earlier detection of subclinical myocardial involvement. Clinical studies have demonstrated that in the pediatric population—including individuals who remain entirely asymptomatic—certain isolated electrocardiographic features may be present. These findings typically include a shortened PR interval, increased QRS complex voltages, and flattened T waves (Kampmann et al., 2008).

Historically, women were regarded almost exclusively as asymptomatic carriers of the genetic mutation, a view predominantly based on the X-linked inheritance pattern of the disorder. However, current medical understanding confirms that female patients can indeed develop full-blown, symptomatic cardiomyopathy. The electrocardiographic alterations identified in these patients, such as left ventricular hypertrophy (LVH) and significant repolarization abnormalities, do not differ qualitatively from those observed in male patients. Nevertheless, the biological phenomenon of lyonization, or X-chromosome inactivation, must be taken into rigorous clinical account. As a direct result of this process, changes in the ECG pattern typically manifest much later in life, usually delayed by approximately one to two decades compared to their male counterparts (Mueller et al., 2013). In clinical practice, an acute awareness of this delayed presentation is paramount for effective longitudinal monitoring and for the timely identification of the moment when ECG changes signal the progression of the disease.

4. Discussion

Anderson-Fabry disease (FD) represents a significant challenge for contemporary medicine, a fact that stems directly from its multisystemic involvement and the relative rarity with which clinicians encounter the condition in daily clinical practice. The primary objective of the results presented in this comprehensive review is to demonstrate that a standard ECG examination performs a far more critical role than that of a merely routine cardiological assessment. In the specific context of FD, the ECG emerges as a diagnostic instrument that facilitates the visualization of both early-stage manifestations, such as the accumulation of glycosphingolipids within the specialized cardiac conduction system, and late-stage, frequently irreversible alterations characterized by myocardial hypertrophy and extensive fibrosis. To fully appreciate the clinical utility of electrocardiography in this setting, it is necessary to elucidate two fundamental aspects: the impact of modern causal therapies on the longitudinal evolution of ECG patterns, and the broader socio-economic value of the ECG as a pivotal screening technology within the public health system.

The Impact of Specific Therapies on ECG Patterns and Utility in Treatment Monitoring

The introduction of enzyme replacement therapy (ERT) utilizing agalsidase alfa or agalsidase beta, alongside the emergence of oral chaperone therapy (migalastat), has profoundly revolutionized the prognosis for patients diagnosed with Fabry disease. A fundamental clinical question arises regarding the extent to which the clearance of globotriaosylceramide (Gb3) deposits from cellular structures influences and potentially improves electrocardiographic recordings. Current literature analysis indicates that the therapeutic response in terms of ECG parameters is strictly dependent on the precise timing of treatment initiation.

Scientific evidence demonstrates that the commencement of therapy during the initial stages of the disease, specifically when massive myocardial hypertrophy and extensive fibrosis are still absent, facilitates the stabilization and even the potential improvement of ECG patterns. Beer et al. (2006) established that

enzyme replacement therapy can significantly contribute to a reduction in left ventricular mass, thereby enhancing exercise tolerance. This structural improvement directly translates to the ECG findings, where the progression of pathological QRS voltages and repolarization abnormalities may be effectively halted. Furthermore, ERT demonstrates a beneficial impact on sinus node function. Lobo et al. (2008) observed a significant clinical improvement in chronotropic incompetence during exercise testing, suggesting that appropriately early intervention may, at least partially, reverse dysfunctions within the cardiac conduction system.

Conversely, the initiation of treatment during the advanced stages of cardiomyopathy is associated with a dramatic decrease in the capacity for reversing established ECG abnormalities. This clinical phenomenon is corroborated by recent longitudinal observations from large-scale clinical registries. El Sayed et al. (2023), in a long-term cohort study of adult patients with FD, demonstrated that despite the administration of ERT, electrocardiographic changes, such as atrioventricular blocks and deeply inverted T waves, continued to progress in a substantial percentage of the study population. Similar conclusions were reached in the analyses conducted by Parisi et al. (2025). These researchers, during long-term observation of ECG evolution, noted that myocardial fibrosis eventually reaches a "critical point," at which stage the pathological process becomes self-perpetuating and largely independent of further Gb3 substrate accumulation.

The conclusions derived from these longitudinal observations are definitive: while the ECG is not a tool primarily utilized for assessing pharmacological efficacy at the molecular level, it remains exceptionally valuable for monitoring both the structural and functional progression of the disease in treated patients. Moreover, these findings reinforce the pivotal role of the ECG during the screening phase, identifying patients with early-stage electrical alterations, such as isolated PR interval shortening, allows for the initiation of therapy within the optimal therapeutic window, thereby potentially halting or decelerating permanent myocardial damage.

Electrocardiography as a Medical Technology in the Service of Public Health

In an era characterized by the extraordinary development and proliferation of highly complex, technologically advanced, and exceptionally expensive imaging modalities, such as cardiovascular magnetic resonance (CMR), the standard, conventional 12-lead electrocardiogram (ECG) may superficially appear to be an archaic diagnostic tool. However, subscribing to this point of view may lead to potentially profound and far-reaching consequences for public health systems. The continuous emergence of innovative technologies within both the medical and social sciences should inherently compel the scientific and clinical communities to fundamentally redefine the contemporary role of electrocardiography.

The overwhelming advantage of electrocardiography lies in its unparalleled universality, its immediate accessibility at virtually every echelon of the healthcare delivery system, and its highly favorable cost-effectiveness ratio. Leading clinical experts consistently emphasize that the diagnostic trajectory for patients afflicted with rare genetic disorders remains a „diagnostic odyssey." Indeed, the average latency period from the initial manifestation of clinical symptoms to the establishment of a definitive diagnosis of Fabry disease frequently spans from several years to well over a decade (Gambarin et al., 2010). Throughout this prolonged and highly uncertain interval, patients are recurrently referred from one specialist to another. This inefficient longitudinal process inevitably generates financial burdens for health insurance providers and state healthcare systems, not to mention the devastating psychological distress and adverse social consequences inflicted upon the patients themselves.

In stark contrast, standard ECG apparatuses are universally available in nearly every primary care physician's office, as well as in emergency departments and acute care settings. The clinical acumen required to efficiently correlate a suspicious electrocardiographic tracing, such as the presence of unexplained, massive left ventricular muscle hypertrophy in a young male patient, particularly when coupled with a characteristically shortened PR interval, with the urgent necessity to conduct targeted biochemical and genetic testing for lysosomal storage diseases serves as a quintessential example of optimizing the diagnostic pathway for this vulnerable patient cohort (Hagège et al., 2019; Paelinck et al., 2024). By systematically shifting the initial diagnostic burden away from highly specialized tertiary care departments and their associated costly diagnostic procedures, and redirecting focus toward the astute clinical interpretation of specific electrocardiographic "red flags" using a fundamental tool like the ECG, the medical community possesses the capacity to shorten the patient's "diagnostic odyssey" by numerous years. Ultimately, this strategic paradigm shift will significantly enhance and democratize patient access to the early, disease-modifying treatment of rare pathologies.

Limitations of Electrocardiography in the Diagnosis of Fabry Disease

It must be clearly emphasized that despite its numerous clinical advantages, electrocardiography possesses significant limitations within the diagnostic process of Fabry disease. The primary drawback is its relatively low specificity. Features such as pronounced left ventricular hypertrophy or deep, inverted T-waves are inherently not unique to FD; they are also frequently observed in cases of sarcomeric hypertrophic cardiomyopathy, cardiac amyloidosis, or advanced systemic hypertension (Hagège et al., 2019; Vitale et al., 2022). If the entire clinical picture of the patient is not taken into meticulous consideration, this can easily lead to significant diagnostic errors and misdirected therapeutic interventions.

Another critical limitation of the standard ECG is its variable sensitivity. The observable electrocardiographic alterations are highly dependent on the specific clinical stage, age, and gender of the patient. In a substantial proportion of pediatric patients and female heterozygous carriers, the ECG pattern may remain completely within normal limits for many years, despite the ongoing, insidious process of glycosphingolipid substrate storage within the cardiomyocytes (Kampmann et al., 2008; Mueller et al., 2013). Consequently, a seemingly normal ECG result absolutely does not allow for the definitive exclusion of Fabry disease, particularly within high-risk cohorts. Furthermore, it should be noted that the precise interpretation of certain subtle electrical alterations, such as the isolated shortening of the PR interval, is subject to a considerable degree of subjectivity and varies based on the specific clinical experience of the examining physicians. As a diagnostic tool, the ECG is strictly supportive and screening in nature. A definitive and final diagnosis of FD unequivocally necessitates confirmation through specialized biochemical investigations (specifically, the measurement of alpha-galactosidase A enzyme activity) and molecular genetic testing (the identification of pathogenic mutations in the GLA gene) (Hagège et al., 2019; Tognola et al., 2025).

Future Perspectives

As our understanding of Fabry disease cardiomyopathy evolves, it is evident that a definitive diagnosis rarely relies on a single parameter. While this review focuses on the role of electrocardiography, contemporary literature emphasizes the importance of integrating various diagnostic tools, such as combining electrical recordings with biomarkers and recognizing atypical clinical presentations. For instance, Coats et al. (2013) demonstrated a strong correlation between NT-proBNP levels and the severity of cardiac involvement. When combined with ECG findings, NT-proBNP can serve as a powerful clinical indicator for evaluating the risk of developing heart failure.

It is worth noting the enduring nature of these diagnostic challenges. As early as 1988, Tanaka et al. described cases of Fabry disease that were misdiagnosed and managed as classic hypertrophic cardiomyopathy (HCM), highlighting a persistent problem in cardiology. Furthermore, a recent report by Kalaria et al. (2026) detailed an atypical case where the initial presentation was acute shoulder pain, initially suggesting an orthopedic issue. Such cases serve as a crucial reminder of the multisystemic nature of FD and the importance of vigilant ECG analysis in patients with unclear clinical pictures.

The future of ECG diagnostics in Fabry disease will likely belong to artificial intelligence (AI). The automated evaluation of thousands of tracings to identify subtle changes, often imperceptible to the human eye, could significantly reduce the time to diagnosis. However, for the time being, the meticulous, manual interpretation of each ECG recording by physicians remains the fundamental cornerstone of patient care.

6. Conclusions

In summarizing the conducted literature review, the following conclusions can be drawn:

Despite its inherent simplicity, electrocardiography remains the fundamental, crucial, and most accessible tool for the early detection of cardiomyopathy during Fabry disease.

Certain characteristic electrocardiographic features, such as a shortened PR interval without a delta wave in younger patients, as well as signs of left ventricular hypertrophy without pathological Q waves, should proactively guide physicians toward the diagnostic pathway for lysosomal storage disorders.

Rhythm and conduction disturbances, manifesting as both tachyarrhythmias and bradyarrhythmias, are a feature of the natural progression of the disease. Consequently, they necessitate regular Holter ECG monitoring, which is of paramount importance in the prevention of sudden cardiac death.

An early and efficient diagnosis based on these electrical findings enables the identification of patients in the initial phases of the disease. This timely recognition is crucial, as it allows for prompt interventions that can significantly slow the progression of structural changes in the heart.

Within the pediatric population and among female patients, electrocardiographic alterations may represent the sole early manifestation of cardiac involvement. This fact demands a meticulous evaluation of the ECG tracing by clinicians, even when standard echocardiographic examinations reveal no structural abnormalities.

Ultimately, it must be remembered that the ECG serves as a screening instrument rather than a definitive diagnostic test. Due to the relatively low specificity of the observed changes, any suspicious tracing requires rigorous verification through enzymatic assays and genetic testing, which collectively constitute the diagnostic gold standard.

REFERENCES

1. Acharya, D., Robertson, P., Kay, G. N., Jackson, L., Warnock, D. G., Plumb, V. J., & Tallaj, J. A. (2012). Arrhythmias in Fabry cardiomyopathy. *Clinical Cardiology, 35*(12), 738–740. https://doi.org/10.1002/clc.22047
2. Aryana, A., Fifer, M. A., Ruskin, J. N., & Mela, T. (2008). Short PR interval in the absence of preexcitation: A characteristic finding in a patient with Fabry disease. *Pacing and Clinical Electrophysiology, 31*(6), 782–783. https://doi.org/10.1111/j.1540-8159.2008.01088.x
3. Beer, M., Weidemann, F., Breunig, F., Knoll, A., Koeppe, S., Machann, W., Hahn, D., Wanner, C., Strotmann, J., & Sandstede, J. (2006). Impact of enzyme replacement therapy on cardiac morphology and function and late enhancement in Fabry's cardiomyopathy. *The American Journal of Cardiology, 97*(10), 1515–1518. https://doi.org/10.1016/j.amjcard.2005.11.087
4. Coats, C. J., Parisi, V., Ramos, M., Janagarajan, K., O'Mahony, C., Dawnay, A., Lachmann, R. H., Murphy, E., Mehta, A., Hughes, D., & Elliott, P. M. (2013). Role of serum N-terminal pro-brain natriuretic peptide measurement in diagnosis of cardiac involvement in patients with Anderson-Fabry disease. *The American Journal of Cardiology, 111*(1), 111–117. https://doi.org/10.1016/j.amjcard.2012.08.055
5. El Sayed, M., Postema, P. G., Datema, M., van Dussen, L., Kors, J. A., Ter Haar, C. C., Bleijendaal, H., Galenkamp, H., van den Born, B. H., Hollak, C. E. M., & Langeveld, M. (2023). ECG changes during adult life in Fabry disease: Results from a large longitudinal cohort study. *Diagnostics, 13*(3), 354. https://doi.org/10.3390/diagnostics13030354
6. Gambarin, F. I., Disabella, E., Narula, J., Diegoli, M., Grasso, M., Serio, A., Favalli, B. M., Agozzino, M., Tavazzi, L., Fraser, A. G., & Arbustini, E. (2010). When should cardiologists suspect Anderson-Fabry disease? *The American Journal of Cardiology, 106*(10), 1492–1499. https://doi.org/10.1016/j.amjcard.2010.07.016
7. Gomez, M., Molina, L., Cladellas, M., Ascoeta, S., Soler, C., Ble, M., Ramirez, A., & Bruguera, J. (2012). Phenotype and genotype characterization and twin association in patients with Anderson-Fabry cardiomyopathy. *Cardiology, 121*(2), 71–75. https://doi.org/10.1159/000336168
8. Hagège, A., Réant, P., Habib, G., Damy, T., Barone-Rochette, G., Soulat, G., Donal, E., & Germain, D. P. (2019). Fabry disease in cardiology practice: Literature review and expert point of view. *Archives of Cardiovascular Diseases, 112*(4), 278–287. https://doi.org/10.1016/j.acvd.2019.01.002
9. Jastrzębski, M., & Petkow-Dimitrow, P. (2008). Elektrokardiogram w chorobie Fabry'ego [Electrocardiogram in Fabry's disease]. *Kardiologia Polska, 66*(6), 688–693.
10. Kalaria, A., Farooq, W., Kolupoti, A., Meng, J., & Kim, A. S. (2026). From shoulder to heart: Acute shoulder pain leads to a diagnosis of Fabry disease. *JACC: Case Reports, 31*(7), 106558. https://doi.org/10.1016/j.jaccas.2025.106558
11. Kampmann, C., Wiethoff, C. M., Martin, C., Wenzel, A., Kampmann, R., Whybra, C., Miebach, E., & Beck, M. (2002). Electrocardiographic signs of hypertrophy in Fabry disease-associated hypertrophic cardiomyopathy. *Acta Paediatrica Supplement, 91*(439), 21–27. https://doi.org/10.1111/j.1651-2227.2002.tb03105.x
12. Kampmann, C., Wiethoff, C. M., Whybra, C., Baehner, F. A., Mengel, E., & Beck, M. (2008). Cardiac manifestations of Anderson-Fabry disease in children and adolescents. *Acta Paediatrica, 97*(4), 463–469. https://doi.org/10.1111/j.1651-2227.2008.00700.x
13. Krämer, J., Nordbeck, P., Störk, S., Ritter, C., Ertl, G., Wanner, C., & Weidemann, F. (2015). Electrical changes in resting, exercise, and Holter electrocardiography in Fabry cardiomyopathy. *JIMD Reports, 28*, 19–28. https://doi.org/10.1007/8904_2015_502
14. Linhart, A., Lubanda, J. C., Palecek, T., Bultas, J., Karetová, D., Ledvinová, J., Elleder, M., & Aschermann, M. (2001). Cardiac manifestations in Fabry disease. *Journal of Inherited Metabolic Disease, 24*(Suppl. 2), 75–65. https://doi.org/10.1023/A:1012428009627
15. Lobo, T., Morgan, J., Bjorksten, A., Nicholls, K., Grigg, L., Centra, E., & Becker, G. (2008). Cardiovascular testing in Fabry disease: Exercise capacity reduction, chronotropic incompetence and improved anaerobic threshold after enzyme replacement. *Internal Medicine Journal, 38*(6), 407–414. https://doi.org/10.1111/j.1445-5994.2008.01669.x

16. Mueller, P., Attenhofer Jost, C. H., Rohrbach, M., Valsangiacomo Buechel, E. R., Seifert, B., Balmer, C., Kretschmar, O., Baumgartner, M. R., & Weber, R. (2013). Cardiac disease in children and young adults with various lysosomal storage diseases: Comparison of echocardiographic and ECG changes among clinical groups. *International Journal of Cardiology: Heart & Vessels, 2*, 1–7. https://doi.org/10.1016/j.ijchv.2013.10.002
17. Namdar, M. (2016). Electrocardiographic changes and arrhythmia in Fabry disease. *Frontiers in Cardiovascular Medicine, 3*, 7. https://doi.org/10.3389/fcvm.2016.00007
18. Paelinck, B. P., Bondue, A., Robyns, T., & Eyskens, F. (2024). Left ventricular hypertrophy: Do not forget Fabry disease. Diagnostic work-up and differential diagnosis. *Acta Cardiologica, 79*(6), 642–649. https://doi.org/10.1080/00015385.2024.2346873
19. Parisi, V., Baldassarre, R., Ferrara, V., Ditaranto, R., Barlocco, F., Lillo, R., Re, F., Marchi, G., Chiti, C., Di Nicola, F., Catalano, C., Barile, L., Schiavo, M. A., Ponziani, A., Saturi, G., Caponetti, A. G., Berardini, A., Graziosi, M., Pasquale, F., Salamon, I., … Biagini, E. (2023). Electrocardiogram analysis in Anderson-Fabry disease: A valuable tool for progressive phenotypic expression tracking. *Frontiers in Cardiovascular Medicine, 10*, 1184361. https://doi.org/10.3389/fcvm.2023.1184361
20. Parisi, V., Ditaranto, R., Taglieri, N., Di Nicola, F., Baldassarre, R., Schiavo, M. A., Nardi, E., Lillo, R., Meucci, M. C., Cianci, A., Re, F., Marchi, G., Monda, E., Capelli, I., Donadio, V., Cappelli, F., Salamon, I., Blanes, J. G., Girelli, D., Pasquale, F., … Biagini, E. (2025). Electrocardiogram evolution in Anderson-Fabry disease patients during follow-up in relation to specific treatment and cardiac disease progression. *International Journal of Cardiology, 431*, 133219. https://doi.org/10.1016/j.ijcard.2025.133219
21. Pieroni, M., Chimenti, C., Ricci, R., Sale, P., Russo, M. A., & Frustaci, A. (2003). Early detection of Fabry cardiomyopathy by tissue Doppler imaging. *Circulation, 107*(15), 1978–1984. https://doi.org/10.1161/01.CIR.0000061952.27445.A0
22. Tanaka, H., Adachi, K., Yamashita, Y., Toshima, H., & Koga, Y. (1988). A case of Fabry cardiomyopathy. *Journal of Cardiology, 18*(3), 705–718.
23. Tognola, C., Ruzzenenti, G., Maloberti, A., Varrenti, M., Mazzone, P., Giannattasio, C., & Guarracini, F. (2025). Anderson-Fabry disease: An overview of current diagnosis, arrhythmic risk stratification, and therapeutic strategies. *Diagnostics, 15*(2), 139. https://doi.org/10.3390/diagnostics15020139
24. Vitale, G., Ditaranto, R., Graziani, F., Tanini, I., Camporeale, A., Lillo, R., Rubino, M., Panaioli, E., Di Nicola, F., Ferrara, V., Zanoni, R., Caponetti, A. G., Pasquale, F., Graziosi, M., Berardini, A., Ziacchi, M., Biffi, M., Santostefano, M., Liguori, R., Taglieri, N., … Biagini, E. (2022). Standard ECG for differential diagnosis between Anderson-Fabry disease and hypertrophic cardiomyopathy. *Heart, 108*(1), 54–60. https://doi.org/10.1136/heartjnl-2020-318271
25. Yousef, Z., Elliott, P. M., Cecchi, F., Escoubet, B., Linhart, A., Monserrat, L., Namdar, M., & Weidemann, F. (2013). Left ventricular hypertrophy in Fabry disease: A practical approach to diagnosis. *European Heart Journal, 34*(11), 802–808. https://doi.org/10.1093/eurheartj/ehs166