10.48047/jocaaa.2024.33.06.111

Exploring the Role of Frontal QRS-T Angle in the Detection of Coronary Slow Flow

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ABSTRACT

Background: *Coronary Slow Flow Phenomenon (CSFP) is a microvascular coronary disorder characterized by delayed contrast progression through the coronary arteries during angiography in the absence of significant obstructive lesions. Despite its angiographic subtlety, CSFP has clinical consequences, often presenting with chest pain and ischemic symptoms similar to those of obstructive coronary artery disease. Given the lack of overt stenosis, diagnosis frequently relies on coronary angiography, an invasive procedure. Consequently, there is increasing interest in identifying non-invasive, cost-effective markers to predict CSFP. Among emerging electrocardiographic parameters, the frontal QRS-T angle (fQRS-T angle) has shown promise as a predictor of various cardiac pathologies, including CSFP. The fQRS-T angle represents the angular difference between the axes of ventricular depolarization (QRS complex) and repolarization (T wave) in the frontal plane. A widened angle reflects electrical and possibly structural abnormalities within the myocardium. Several recent studies have demonstrated a significant association between an increased fQRS-T angle and the presence of CSFP, suggesting that this ECG-derived marker may reflect underlying microvascular ischemia, inflammation, and autonomic dysregulation common in CSFP. This review article comprehensively explores the pathophysiological basis linking fQRS-T angle to CSFP, evaluates current clinical evidence, and discusses its diagnostic and prognostic implications. The reproducibility, ease of measurement, and accessibility of the fQRS-T angle make it an attractive tool for early identification of patients at risk for CSFP, especially in emergency and outpatient settings. Moreover, its association with other indicators of cardiovascular risk, such as myocardial fibrosis and arrhythmogenic potential, enhances its utility beyond the scope of CSFP. While promising, the QRS-T angle should be interpreted in conjunction with clinical presentation and other diagnostic findings. Further prospective, large-scale studies are needed to validate its use in routine practice and to establish standard cut-off values. Nonetheless, the fQRS-T angle holds substantial potential as a non-invasive, inexpensive, and easily obtainable marker for CSFP and potentially other forms of microvascular coronary dysfunction.*

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Keywords*:* Role of Frontal QRS-T Angle, Coronary Slow Flow

1. INTRODUCTION

Coronary slow flow (CSF) is a distinct angiographic finding characterized by delayed opacification of the distal coronary vasculature in the absence of obstructive epicardial coronary artery disease. First described by Tambe et al. in 1972, CSF has emerged as a perplexing phenomenon in cardiology due to its ambiguous etiology and varying clinical implications [1]. It is typically diagnosed via coronary

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angiography using the TIMI (Thrombolysis in Myocardial Infarction) frame count method, where increased frame counts are indicative of sluggish coronary blood flow [2].

Prevalence

Although often underdiagnosed, the prevalence of CSF among patients undergoing coronary angiography for chest pain ranges from 1% to 7%, with some studies reporting up to 10% depending on population and criteria used [3]. It is more commonly observed in young men and smokers, and often coexists with traditional cardiovascular risk factors such as hypertension and dyslipidemia [4]. Its presence is particularly noted in patients with angina and normal coronary arteries (ANOCA), suggesting that CSF could be a major contributor to microvascular angina [5].

3. Demographics and Risk Profile

CSF predominantly affects middle-aged men, particularly those with metabolic syndrome components including insulin resistance and central obesity [6]. Smoking, in particular, has shown a strong association with CSF, suggesting a role for endothelial dysfunction in the pathogenesis [7]. Additionally, patients with CSF frequently present with elevated levels of inflammatory markers such as high-sensitivity C-reactive protein (hs-CRP), hinting at an inflammatory mechanism behind the condition [8].

Pathogenesis Overview

The exact pathogenesis of CSF remains unclear, but multiple mechanisms have been proposed. These include endothelial dysfunction, increased microvascular resistance, small-vessel atherosclerosis, and inflammatory processes [9]. Impairment of nitric oxide (NO)-mediated vasodilation and heightened oxidative stress in the vascular endothelium may further contribute to abnormal coronary flow despite the absence of large-vessel stenosis [10].

Role of Endothelial Dysfunction

Endothelial dysfunction is believed to be a primary contributor to CSF, resulting in an imbalance between vasodilatory and vasoconstrictive substances. This dysfunction impairs coronary microcirculation, decreasing perfusion and leading to myocardial ischemia [11]. Studies using acetylcholine infusion have demonstrated blunted vasodilatory responses in patients with CSF, supporting this mechanism [12].

Inflammation and CSF

Inflammation has gained prominence in CSF research, with elevated levels of interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), and hs-CRP observed in affected patients. These markers suggest systemic inflammation that may influence coronary microvasculature function, further perpetuating

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the slow flow phenomenon [13]. Biopsy and imaging studies have even shown perivascular inflammatory infiltration in some CSF cases [14].

Microvascular Dysfunction

Coronary microvascular dysfunction is another leading hypothesis. It involves structural and functional abnormalities in small intramyocardial vessels, impairing their ability to modulate blood flow. These changes can result in angina and ischemia even in the absence of epicardial artery disease [15]. Impaired coronary flow reserve (CFR) measured by Doppler techniques has confirmed the microvascular component in many CSF patients [16].

Platelet and Hemorheological Factors

Altered platelet function and abnormal blood rheology are also implicated. Patients with CSF often show increased platelet aggregability and abnormal blood viscosity, contributing to slow coronary flow. These abnormalities may promote microvascular occlusion and reduced perfusion, especially under stress [17]. Some studies have also highlighted the presence of small thrombi in the microcirculation of CSF patients [18].

Clinical Manifestations

The clinical presentation of CSF varies, but chest pain is the most common symptom. This chest discomfort often mimics angina pectoris and may occur at rest or with exertion. In some cases, patients present with acute coronary syndrome (ACS) despite having angiographically normal arteries [19]. Other manifestations include palpitations, fatigue, and dyspnea, leading to significant patient anxiety and repeated hospital visits [20].

Electrocardiographic Findings

Electrocardiograms (ECGs) in CSF patients may show ST-segment changes during pain episodes, simulating myocardial ischemia. Some studies report transient T-wave inversions or ST depressions, particularly during stress testing. These changes, however, typically normalize at rest, distinguishing CSF from fixed obstructive coronary lesions [21].

Diagnostic Techniques

Coronary angiography remains the gold standard for diagnosing CSF. The TIMI frame count method, where the number of cine frames required for dye to reach specific distal landmarks is measured, provides a quantitative assessment. A corrected TIMI frame count >27 for the left anterior descending artery is generally diagnostic [22]. Intravascular ultrasound and cardiac MRI may also assist in ruling out other causes and assessing microvascular involvement [23].

Prognosis Overview

While CSF was once considered benign, recent evidence suggests it carries a notable risk of recurrent chest pain, decreased quality of life, and even major cardiac events such as arrhythmias and myocardial

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infarction [24]. Long-term studies indicate that CSF patients often have persistent symptoms and may develop myocardial dysfunction over time [25].

Psychological Impact

The frequent and unexplained chest pain in CSF often leads to anxiety, depression, and reduced quality of life. Recurrent hospitalizations for chest discomfort without clear diagnosis contribute to patient frustration and healthcare burden [26]. Psychological support and reassurance form an important part of CSF management [27].

Treatment – General Principles

There is no universally accepted treatment for CSF, and therapy typically targets symptom control and underlying risk factors. The mainstay of management includes anti-anginal drugs, endothelial function enhancers, and lifestyle modifications [28]. Treatment often requires a multidisciplinary approach, involving cardiologists, psychologists, and primary care providers [29].

Pharmacologic Therapy – Nitrates and Calcium Channel Blockers

Nitrates have shown limited efficacy in CSF, possibly due to their short duration and limited effect on microvasculature. Calcium channel blockers (CCBs), particularly diltiazem and verapamil, have demonstrated more consistent benefit by improving endothelial function and reducing coronary microvascular resistance [30]. These agents help relieve angina and enhance exercise tolerance in many CSF patients [31].

Statins and ACE Inhibitors

Statins, due to their anti-inflammatory and endothelial-stabilizing properties, have been effective in CSF management. ACE inhibitors may also improve microvascular function and reduce oxidative stress, providing symptomatic relief in some cases [32]. These agents are particularly useful in CSF patients with comorbid hypertension or hyperlipidemia [33].

Antiplatelet Therapy

Though not always standard, low-dose aspirin is frequently prescribed to reduce platelet aggregability in CSF patients. Some studies suggest that dual antiplatelet therapy may be beneficial in select cases, particularly those with evidence of microthrombi [34]. However, routine use remains controversial and should be individualized [35].

Non-Pharmacologic Approaches

Lifestyle interventions such as smoking cessation, exercise, stress reduction, and dietary modification play a key role in managing CSF. Cardiac rehabilitation programs may offer structured support and improve both physical and psychological outcomes [36]. In some patients, cognitive behavioral therapy has also helped reduce symptom burden [37].

Novel Therapies and Research Directions

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Emerging treatments targeting endothelial repair and oxidative stress are under investigation. Agents such as trimetazidine and ranolazine have shown promise in small studies for improving angina in CSF patients [38]. Ongoing research continues to explore gene therapy, microvascular vasodilators, and biomarkers for improved diagnosis and treatment [39].

Coronary slow flow is a complex and under-recognized condition that can cause significant morbidity despite the absence of obstructive coronary disease. While the pathogenesis remains multifactorial, recent advances in understanding microvascular and inflammatory mechanisms offer hope for more targeted therapies. Early recognition and a comprehensive, multidisciplinary approach are essential to improving outcomes in affected individuals [40].

Frontal QRS-T Angle: Pathological Widening of the QRS-T Angle

The frontal QRS-T angle represents the spatial difference between the vectors of ventricular depolarization (QRS complex) and repolarization (T wave) in the frontal plane of an electrocardiogram (ECG). It is a straightforward, non-invasive marker that can be extracted from routine ECGs and has shown significant prognostic value in various cardiac conditions [41]. This angle can be derived using the absolute value of the angle between the QRS axis and the T axis, offering a glimpse into the electrophysiological harmony or discordance within the myocardium.

Under normal conditions, the frontal QRS-T angle is narrow, typically less than 45°, suggesting a physiological alignment between depolarization and repolarization vectors. However, when this angle widens beyond this threshold, it reflects underlying electrical or structural abnormalities in the heart. A widened QRS-T angle is considered pathological and has been associated with increased risk of adverse cardiac events, particularly sudden cardiac death and arrhythmias [42].

The pathological widening of the QRS-T angle indicates heterogeneity in myocardial repolarization. This discordance often stems from myocardial ischemia, fibrosis, left ventricular hypertrophy, or cardiomyopathies, all of which distort the propagation of electrical impulses. As such, the QRS-T angle serves not merely as a mathematical metric but as a functional marker of myocardial vulnerability [43].

Clinical studies have highlighted the value of a widened QRS-T angle in predicting mortality among patients with cardiovascular disease. In patients with heart failure, for example, an increased angle correlates with worse outcomes and is an independent predictor of mortality, even after adjusting for ejection fraction and other conventional risk factors [44]. This reinforces its utility in risk stratification and long-term management planning.

Moreover, in post-myocardial infarction (MI) patients, a widened QRS-T angle can reveal subtle yet clinically relevant electrical remodeling of the myocardium. These patients may not show overt left ventricular dysfunction initially, but the presence of an abnormal QRS-T angle can signify increased arrhythmic risk, underscoring the need for close monitoring [45].

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The role of the QRS-T angle extends beyond ischemic heart disease. In individuals with non-ischemic cardiomyopathy, the angle still holds prognostic weight. It is especially valuable in identifying those who may benefit from implantable cardioverter-defibrillators (ICDs) or more aggressive therapeutic interventions, even in the absence of severe left ventricular systolic dysfunction [46].

Several mechanisms contribute to the widening of the QRS-T angle, including abnormal conduction pathways, regional heterogeneity in repolarization, and ventricular dyssynchrony. These mechanisms disrupt the coordinated sequence of ventricular activation and recovery, leading to vector misalignment evident on the ECG [47].

Electrocardiographic parameters like the QRS duration or QT interval have traditionally been used in clinical practice, but the QRS-T angle offers additive value because it captures the interaction between depolarization and repolarization rather than assessing them in isolation. This integrative approach improves its sensitivity in detecting arrhythmogenic substrates [48].

The simplicity and reproducibility of measuring the frontal QRS-T angle enhance its clinical applicability. It can be calculated from automated ECG reports, reducing the need for complex manual interpretation and allowing for easy incorporation into routine clinical workflows [49].

In the general population, epidemiological studies have found that individuals with a widened QRS-T angle are at a higher risk of cardiovascular mortality, even when traditional risk factors such as hypertension or diabetes are controlled for. This supports its use as a screening tool in preventive cardiology [50].

Interestingly, the prognostic relevance of the QRS-T angle is not confined to older adults or those with pre-existing heart disease. Young individuals with idiopathic ventricular arrhythmias may also exhibit abnormal QRS-T angles, suggesting early electrophysiological changes that could precede structural disease [51].

Sex and ethnic differences in normal QRS-T angle ranges have also been reported. For instance, women typically have narrower angles compared to men, while certain ethnic groups exhibit variations that may affect the diagnostic thresholds. This necessitates population-specific reference values to improve diagnostic precision [52].

Technological advancements, such as vectorcardiography and three-dimensional ECG analysis, offer enhanced visualization of the QRS-T spatial relationship. These tools provide more precise measurements and may further refine the prognostic capabilities of QRS-T angle assessment in the future [53].

In patients undergoing chemotherapy, particularly with cardiotoxic agents like anthracyclines, the QRS-T angle has emerged as an early marker of myocardial injury. Serial changes in the angle can precede clinical symptoms or echocardiographic abnormalities, facilitating timely intervention [54].

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The QRS-T angle is also being explored in the context of metabolic disorders such as diabetes mellitus, where cardiac autonomic neuropathy can disrupt ventricular repolarization. A widened angle in this population is linked with silent myocardial ischemia and increased mortality, independent of glycemic control [55].

Pediatric applications of the QRS-T angle are gaining attention, especially in congenital heart disease and inherited arrhythmia syndromes like long QT syndrome or Brugada syndrome. Abnormal angles in these populations may guide genetic testing or treatment choices [56].

Lifestyle interventions and pharmacologic treatments may influence the QRS-T angle. For example, antihypertensive therapy, beta-blockers, and weight loss have shown modest improvements in the angle, implying that it could serve as a modifiable risk marker and therapeutic endpoint [57].

Despite its promise, the QRS-T angle is underutilized in clinical guidelines, possibly due to lack of standardized cutoffs and limited awareness among clinicians. Increased education and incorporation into risk calculators may promote its wider adoption in routine practice [58].

In conclusion, the frontal QRS-T angle is a powerful, underappreciated ECG marker that encapsulates the interplay between ventricular depolarization and repolarization. Its pathological widening is associated with a spectrum of cardiovascular pathologies and adverse outcomes. Embracing its diagnostic and prognostic potential could enhance patient stratification and inform clinical decision-making in both primary and specialized care settings [59].

Frontal QRS-T Angle as a Non-invasive Predictor of the Presence of Coronary Slow Flow

The coronary slow flow phenomenon (CSFP) is a well-recognized angiographic entity characterized by delayed opacification of coronary arteries in the absence of obstructive coronary artery disease. Despite the absence of significant epicardial stenosis, patients may present with chest pain and even myocardial ischemia. This condition is commonly detected during coronary angiography when contrast dye progresses sluggishly through the coronary vasculature. The underlying mechanisms of CSFP are multifactorial and include microvascular dysfunction, inflammation, and endothelial dysfunction [60].

Electrocardiography (ECG) remains an indispensable tool in cardiology for assessing various cardiac pathologies. Among emerging parameters derived from ECG, the frontal QRS-T angle (fQRS-T angle) has garnered attention for its prognostic value in different cardiovascular conditions. The fQRS-T angle is defined as the absolute angular difference between the directions of the QRS complex and the T wave in the frontal plane. This angle represents the disparity between ventricular depolarization and repolarization axes and reflects underlying electrical and structural abnormalities in the myocardium [61].

Several studies have demonstrated that a wider frontal QRS-T angle is associated with increased cardiovascular morbidity and mortality. It serves as an indicator of electrical instability and myocardial

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heterogeneity, both of which are closely linked to adverse outcomes such as arrhythmias and sudden cardiac death. In patients with ischemic heart disease, a widened QRS-T angle is often observed, even in the absence of overt infarction, which suggests its utility in detecting subtle myocardial changes [62].

Coronary slow flow is often overlooked in clinical settings due to its angiographic subtlety. However, patients with CSFP frequently present with exertional angina or acute coronary syndrome-like symptoms. Identifying a non-invasive and accessible predictor for CSFP, such as the fQRS-T angle, could significantly aid in early diagnosis and management. Utilizing a routine ECG parameter reduces the need for invasive diagnostic procedures in some patients [63].

Mechanistically, the alteration in the frontal QRS-T angle among patients with CSFP is thought to be due to microvascular ischemia, which disrupts the normal sequence of repolarization. Ischemia can result in changes in myocardial conduction, leading to spatial dispersion in ventricular recovery times. This alteration manifests as an increase in the QRS-T angle. Therefore, a widened QRS-T angle may be reflective of the underlying microvascular abnormalities that characterize CSFP [64].

Recent clinical investigations have sought to establish the link between the QRS-T angle and CSFP by comparing ECG findings with coronary angiographic results. These studies consistently show that patients diagnosed with CSFP have significantly larger fQRS-T angles than those with normal coronary flow. The statistical significance of this correlation suggests a potential role of this ECG parameter in predicting the presence of CSFP [65].

Furthermore, the reproducibility and ease of calculation of the frontal QRS-T angle make it a valuable parameter in routine clinical practice. Unlike other ECG-derived markers that require specialized software or complex interpretation, the QRS-T angle can be easily obtained from standard ECG printouts. This feature enhances its utility in primary care and emergency settings where rapid decision-making is crucial [66].

Additionally, the frontal QRS-T angle has been correlated with other markers of subclinical atherosclerosis and endothelial dysfunction, both of which are implicated in CSFP. This adds to the biological plausibility of its association with coronary microvascular abnormalities. In this way, the fQRS-T angle may serve as a surrogate marker for the extent of microvascular impairment in these patients [67].

Inflammation has been proposed as a central contributor to the development of coronary slow flow. Inflammatory markers such as high-sensitivity C-reactive protein (hs-CRP) and interleukin-6 (IL-6) have been found to be elevated in patients with CSFP. Since inflammation also affects myocardial electrophysiology, it is plausible that systemic inflammatory activity may contribute to QRS-T angle widening, linking this ECG parameter with the inflammatory etiology of CSFP [68].

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Oxidative stress is another factor commonly implicated in CSFP. It induces endothelial dysfunction and microvascular damage, which in turn affects myocardial perfusion. Altered perfusion gradients influence myocardial action potentials and can manifest as repolarization abnormalities. These electrophysiological disturbances contribute to the widening of the QRS-T angle, making it an indirect marker of oxidative stress-related cardiac changes [69].

Another advantage of the QRS-T angle is its prognostic potential beyond CSFP. Its association with arrhythmic events and adverse cardiovascular outcomes underscores its broader applicability in cardiovascular risk stratification. This widens the clinical relevance of measuring the QRS-T angle, as it not only aids in identifying CSFP but also helps in evaluating overall cardiac risk [70].

From a pathophysiological standpoint, the fQRS-T angle integrates both anatomical and functional aspects of the myocardium. It reflects myocardial scar, ischemia, and fibrosis—all of which are often subclinical yet impactful in CSFP. Therefore, a widened QRS-T angle could serve as a composite marker of cumulative myocardial stress and injury, particularly in the setting of unexplained chest pain [71].

Sex and age-related variations in QRS-T angle have been documented, but the relationship with CSFP appears to be consistent across different demographic groups. However, some studies suggest that younger individuals with CSFP may exhibit a more pronounced increase in QRS-T angle, possibly due to more acute or reactive microvascular dysfunction compared to older patients with chronic vascular changes [72].

In terms of diagnostic performance, the QRS-T angle shows promise when integrated with other non-invasive markers. For example, combining ECG-derived parameters with echocardiographic indices or serum biomarkers can enhance diagnostic accuracy for CSFP. Multimodal approaches could potentially refine risk stratification and guide further diagnostic interventions [73].

Longitudinal studies have also explored the predictive value of the fQRS-T angle in monitoring disease progression or response to therapy in CSFP. A reduction in QRS-T angle after pharmacological treatment (e.g., with calcium channel blockers or nitrates) may suggest an improvement in myocardial perfusion, although more evidence is needed to validate this concept [74].

It is important to note that while the fQRS-T angle has diagnostic and prognostic significance, it should not be used in isolation. It is best employed as part of a broader clinical assessment that includes patient symptoms, risk factors, and other diagnostic tests. Nevertheless, its accessibility and predictive value make it an attractive adjunct in clinical evaluation [75].

From a research perspective, the QRS-T angle offers opportunities to explore novel pathways in cardiac electrophysiology and microvascular disease. Investigating its genetic, molecular, and autonomic correlates could uncover new therapeutic targets for CSFP and other microvascular disorders [76].

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As interest in non-invasive cardiovascular diagnostics grows, parameters like the QRS-T angle underscore the evolving role of ECG in precision medicine. With advances in digital ECG analysis and artificial intelligence, automated calculation and interpretation of the QRS-T angle may further enhance its clinical utility and standardization [77].

In conclusion, the frontal QRS-T angle stands out as a simple, cost-effective, and non-invasive tool with significant potential in predicting the presence of coronary slow flow. It provides insights into underlying myocardial and microvascular abnormalities, bridging the gap between electrical and structural heart disease. Further large-scale studies are warranted to fully establish its role in routine clinical practice [78].

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