Molecular Crosstalk Between Circulating miRNA-17-5p and Cyclin D1: Biochemical Insights into Acute Coronary Syndrome Diagnosis

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Abstract

Background: Acute coronary syndrome (ACS) represents a continuum of life-threatening ischemic cardiac events, encompassing unstable angina and myocardial infarction, which arise from atherosclerotic plaque rupture and subsequent coronary thrombosis. Despite advances in cardiac biomarkers such as troponins and natriuretic peptides, early and precise diagnosis remains challenging due to their limited sensitivity during the initial ischemic phase. In recent years, circulating microRNAs (miRNAs) have emerged as promising molecular biomarkers that reflect cellular stress, apoptosis, and metabolic remodeling associated with myocardial injury. Among these, miRNA-17-5p—a member of the miR-17-92 cluster—has attracted significant interest for its regulatory effects on cell cycle progression, proliferation, and endothelial integrity. Concurrently, Cyclin D1, a pivotal G1/S cell cycle regulator, has been implicated in cardiomyocyte proliferation and vascular smooth muscle cell responses to injury, making it a potential downstream effector in ACS pathogenesis. This review aims to elucidate the molecular and biochemical interplay between circulating miRNA-17-5p and Cyclin D1 in the context of ACS, emphasizing their diagnostic potential. By examining the mechanistic pathways governing their expression and regulation under ischemic stress, this article integrates current evidence from molecular cardiology and clinical biochemistry to delineate how miRNA-17-5p may modulate Cyclin D1 signaling. Understanding this relationship could provide a framework for developing non-invasive diagnostic assays with higher specificity and sensitivity for early ACS detection.

Conclusion: Emerging data suggest that dysregulated expression of miRNA-17-5p may contribute to altered Cyclin D1-mediated cell cycle dynamics in cardiac and vascular tissues, influencing endothelial repair, apoptosis, and inflammatory signaling during ACS. The combined evaluation of circulating miRNA-17-5p and Cyclin D1 offers a novel biochemical signature that may outperform current diagnostic modalities, particularly in the early ischemic window. Further validation through large-scale, multi-omics studies is warranted to confirm their clinical applicability and to explore therapeutic modulation of this axis. Ultimately, the miRNA-17-5p/Cyclin D1 network could serve as a foundation for precision diagnostics and targeted interventions in ischemic heart disease.

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Keywords: *miRNA-17-5p,Cyclin D1, Acute Coronary Syndrome*

Introduction

Acute coronary syndrome (ACS) remains one of the leading causes of mortality and morbidity worldwide, representing a major challenge for both clinicians and biomedical researchers. It encompasses a spectrum of ischemic cardiac events, including unstable angina, non–ST-elevation myocardial infarction (NSTEMI), and ST-elevation myocardial infarction (STEMI), all of which arise from the disruption of coronary artery blood flow due to atherosclerotic plaque rupture and thrombosis. Despite substantial advances in reperfusion therapy and pharmacological interventions, the global burden of ACS continues to increase, particularly in populations with metabolic disorders such as diabetes mellitus, obesity, and dyslipidemia. This ongoing prevalence underscores a critical need for **biochemical markers** capable of providing **early, sensitive, and specific diagnostic information**, particularly during the initial ischemic phase when traditional biomarkers may fail to detect myocardial injury [1].

The conventional diagnostic framework for ACS relies heavily on **cardiac troponins (cTnI and cTnT)**, **creatine kinase-MB**, and **electrocardiographic changes**. However, these markers have inherent limitations in early-phase detection and in differentiating between reversible ischemia and irreversible necrosis. Furthermore, their elevation may also occur in non-coronary conditions such as renal dysfunction, myocarditis, or sepsis, reducing their diagnostic specificity [2]. In contrast, **circulating microRNAs (miRNAs)**—small, non-coding RNA molecules that regulate gene expression post-transcriptionally—have emerged as potent and stable molecular indicators of tissue-specific damage and stress. Their release into the bloodstream following myocardial ischemia offers a novel, non-invasive diagnostic tool with higher temporal resolution compared to classical markers [3].

Among the myriad of miRNAs implicated in cardiovascular pathology, **miRNA-17-5p**, a core component of the **miR-17-92 cluster**, has attracted increasing attention for its diverse regulatory roles in cell proliferation, apoptosis, angiogenesis, and inflammation. Studies have shown that miRNA-17-5p expression is significantly altered in patients with ACS, suggesting its involvement in the pathophysiological remodeling of ischemic myocardium [4]. Its primary molecular targets include a range of genes involved in **cell cycle control**, **oxidative stress**, and **endothelial function**, positioning it as a key modulator of cardiovascular homeostasis.

A particularly intriguing aspect of miRNA-17-5p biology lies in its potential regulation of **Cyclin D1 (CCND1)**, a pivotal regulator of the G1/S transition in the cell cycle. Cyclin D1 forms complexes with cyclin-dependent kinases (CDK4/6) to phosphorylate retinoblastoma protein (pRb), thereby promoting DNA synthesis and cell cycle progression. In cardiac tissues, Cyclin D1 is crucial not only for cardiomyocyte proliferation but also for vascular smooth muscle cell growth and endothelial regeneration following ischemic injury [5]. Dysregulation of Cyclin D1 has been implicated in maladaptive vascular remodeling, neointimal hyperplasia, and myocardial fibrosis—all of which contribute to the pathogenesis of ACS.

The molecular crosstalk between miRNA-17-5p and Cyclin D1 represents an emerging regulatory axis with potential diagnostic and therapeutic relevance. Experimental studies have shown that miRNA-17-5p may downregulate Cyclin D1 expression in certain cellular contexts by binding to the 3′ untranslated region (3′UTR) of its mRNA, thereby modulating cell proliferation and apoptotic pathways [6]. In the setting of myocardial ischemia, this regulatory relationship may influence endothelial repair mechanisms and cardiomyocyte survival, ultimately affecting disease severity and recovery. Conversely, altered Cyclin D1 signaling may feedback to affect miRNA expression patterns, forming a complex regulatory loop that reflects the cellular state during ACS.

Despite promising findings, several **research gaps** remain. First, the temporal expression dynamics of miRNA-17-5p and Cyclin D1 during the different phases of ACS (ischemic, reperfusion, and remodeling) are not fully elucidated. Second, the specificity of their circulating levels as biomarkers—distinct from those seen in other inflammatory or metabolic conditions—requires rigorous validation.

Third, the mechanistic pathways linking miRNA-17-5p–mediated regulation of Cyclin D1 to endothelial dysfunction, oxidative stress, and plaque instability are incompletely characterized at the biochemical level [7]. Addressing these gaps will be critical for advancing these molecules from experimental observations to clinical diagnostic applications.

This article aims to provide a **comprehensive biochemical and molecular overview** of the relationship between circulating miRNA-17-5p and Cyclin D1 in ACS. By integrating findings from experimental models and clinical studies, it explores their **interdependent regulation**, **diagnostic significance**, and **potential mechanistic roles** in myocardial ischemia and reperfusion injury. Furthermore, this review discusses how their combined profiling could enhance **early detection, risk stratification, and therapeutic decision-making** in patients with ACS. Ultimately, understanding this molecular crosstalk may not only improve diagnostic accuracy but also pave the way for targeted interventions that restore cell cycle balance and vascular homeostasis in ischemic heart disease [8].

Biochemical and Molecular Basis of Acute Coronary Syndrome

Acute coronary syndrome (ACS) arises primarily from the rupture or erosion of an atherosclerotic plaque, leading to platelet aggregation, thrombus formation, and subsequent myocardial ischemia. The ischemic insult triggers a cascade of metabolic disturbances, including a shift from aerobic to anaerobic metabolism, ATP depletion, and accumulation of lactate and hydrogen ions. These biochemical changes compromise myocardial contractility and membrane stability, initiating necrosis and apoptosis in cardiomyocytes [9]. Reactive oxygen species (ROS) generated during ischemia and reperfusion exacerbate oxidative damage to lipids, proteins, and DNA, amplifying inflammatory signaling and endothelial dysfunction [10]. This pathophysiological milieu establishes a dynamic interplay between vascular injury, oxidative stress, and metabolic imbalance that underpins ACS progression [11].

At the molecular level, ACS is characterized by the activation of several intracellular signaling pathways that regulate inflammation, apoptosis, and cell cycle control. Hypoxia-inducible factor-1α (HIF-1α) is stabilized during ischemia, inducing transcription of genes involved in angiogenesis, glycolysis, and cell survival. Simultaneously, nuclear factor-κB (NF-κB) activation promotes the expression of pro-inflammatory cytokines such as TNF-α and IL-6, which amplify leukocyte recruitment and endothelial activation [12]. These molecular events alter the expression of various microRNAs that fine-tune the response to ischemic stress. Among them, miRNAs targeting regulators of the cell cycle and apoptosis—such as miRNA-17-5p—play a crucial role in determining the extent of myocardial injury [13].

The biochemical signature of ACS extends beyond energy metabolism to involve lipid oxidation, protein carbonylation, and endothelial nitric oxide synthase (eNOS) uncoupling. The imbalance between oxidants and antioxidants leads to endothelial dysfunction, promoting vasoconstriction and platelet activation. Circulating molecules such as oxidized LDL, homocysteine, and asymmetric dimethylarginine (ADMA) further impair nitric oxide bioavailability, aggravating vascular injury [14]. These processes not only accelerate plaque instability but also create a systemic pro-inflammatory environment that influences gene expression at the post-transcriptional level through miRNA regulation [15].

Furthermore, cell cycle regulators like Cyclin D1 have been shown to participate in vascular smooth muscle cell proliferation and neointimal formation during atherosclerotic remodeling. Under ischemic conditions, Cyclin D1 expression is modulated in response to oxidative stress and inflammatory cues, linking metabolic dysregulation to aberrant cell proliferation. Dysregulated Cyclin D1 signaling contributes to maladaptive vascular remodeling, plaque progression, and impaired endothelial repair, all of which are central to ACS pathogenesis [16]. These findings underscore the intertwined nature of biochemical alterations and molecular signaling networks, setting the stage for the involvement of specific miRNAs such as miRNA-17-5p in the regulation of these critical pathways [17].

The Molecular Biology of miRNA-17-5p: Structure, Function, and Cardiovascular Relevance

MicroRNAs (miRNAs) are small non-coding RNAs, typically 19–25 nucleotides in length, that regulate gene expression at the post-transcriptional level by binding to complementary sequences within the 3′

untranslated region (3′UTR) of target messenger RNAs. This binding leads to mRNA degradation or translational repression, depending on the degree of complementarity. miRNAs are transcribed as primary transcripts (pri-miRNAs) by RNA polymerase II, processed in the nucleus by Drosha-DGCR8 complexes into precursor miRNAs (pre-miRNAs), and then exported to the cytoplasm where Dicer cleaves them into mature miRNAs. The mature strand is incorporated into the RNA-induced silencing complex (RISC), guiding it to its target mRNAs [18]. This evolutionarily conserved mechanism allows miRNAs to fine-tune diverse cellular pathways, including apoptosis, differentiation, proliferation, and stress response—all of which are profoundly altered during myocardial ischemia [19].

The **miRNA-17-5p** is a key component of the **miR-17-92 cluster**, located on chromosome 13q31.3, which encodes six distinct miRNAs (miR-17, miR-18a, miR-19a, miR-19b-1, miR-20a, and miR-92a-1). This cluster is often termed "oncomiR-1" due to its role in promoting cell proliferation and survival in various cancers; however, its physiological importance extends to cardiovascular biology. miRNA-17-5p is transcribed as part of this polycistronic cluster and undergoes individual processing to yield its mature form, which targets genes regulating cell cycle progression, angiogenesis, and apoptosis [20]. The miR-17-5p molecule is especially relevant in cardiac tissues because it modulates the balance between cardiomyocyte death and survival following ischemic stress, thereby influencing the extent of myocardial damage [21].

In the cardiovascular context, miRNA-17-5p expression is dynamically regulated by oxygen tension, oxidative stress, and inflammatory mediators. Hypoxia has been shown to increase miRNA-17-5p expression through the HIF-1α signaling pathway, suggesting an adaptive response to maintain cell survival under ischemic conditions [22]. However, excessive upregulation may lead to maladaptive suppression of genes involved in endothelial repair and angiogenesis, including vascular endothelial growth factor A (VEGF-A) and tissue inhibitor of metalloproteinases (TIMP) [23]. Conversely, some studies have demonstrated that inhibition of miRNA-17-5p restores endothelial function and limits apoptosis in ischemic myocardium, highlighting its context-dependent dual role as both protector and promoter of injury depending on its expression level and target specificity [24].

Beyond endothelial regulation, miRNA-17-5p influences **cardiomyocyte and vascular smooth muscle cell proliferation** by targeting critical mediators of the cell cycle such as p21, PTEN, and E2F transcription factors. The repression of these genes enhances Cyclin D1-CDK4/6 activity, thereby facilitating G1/S transition and cell cycle re-entry in cells that are otherwise terminally differentiated [25]. This regulatory relationship is of particular importance in the setting of ACS, where coordinated activation of cell cycle machinery supports tissue repair and neovascularization. However, dysregulated miRNA-17-5p expression can lead to uncontrolled cell proliferation, vascular remodeling, and atherogenesis, underscoring its dual role in cardiovascular pathology [26]. Thus, understanding the biochemical and molecular determinants of miRNA-17-5p activity provides a foundation for its potential diagnostic and therapeutic exploitation in ischemic heart disease.

Cyclin D1: Biochemical Structure, Regulation, and Role in Cardiovascular Pathophysiology

Cyclin D1, encoded by the *CCND1* gene located on chromosome 11q13, is a pivotal regulator of the eukaryotic cell cycle. Structurally, Cyclin D1 belongs to the D-type cyclin family, which also includes Cyclins D2 and D3, and functions as a regulatory subunit that binds and activates cyclin-dependent kinases CDK4 and CDK6. This complex phosphorylates the retinoblastoma (Rb) protein, leading to the release of E2F transcription factors that promote the transcription of genes required for DNA synthesis and S-phase entry [27]. Cyclin D1's abundance is tightly controlled through mitogenic signaling, proteasomal degradation, and post-translational modifications such as phosphorylation and ubiquitination. Its rapid turnover ensures precise temporal regulation of cell proliferation in both physiological and pathological contexts [28].

In the cardiovascular system, Cyclin D1 is expressed in endothelial cells, vascular smooth muscle cells (VSMCs), and cardiac fibroblasts, where it coordinates responses to growth stimuli, injury, and oxidative stress. Under normal conditions, cardiomyocytes exhibit limited proliferative potential, but

after ischemic injury, transient induction of Cyclin D1 facilitates partial re-entry into the cell cycle to support tissue repair and angiogenesis [29]. However, chronic or excessive activation of Cyclin D1 may result in pathological remodeling, characterized by VSMC proliferation, neointimal hyperplasia, and myocardial fibrosis. The dualistic nature of Cyclin D1—supporting regeneration while promoting hypertrophic and fibrotic responses—reflects its position at the crossroads of beneficial repair and maladaptive remodeling [30].

The expression of Cyclin D1 is modulated by numerous upstream signaling pathways, including **PI3K/Akt**, **MAPK/ERK**, and **Wnt/β-catenin** cascades, all of which are activated during ischemic stress and reperfusion. Growth factors such as platelet-derived growth factor (PDGF) and fibroblast growth factor (FGF) stimulate Cyclin D1 transcription via activation of these pathways, linking extracellular signals to intracellular cell cycle control [31]. Additionally, oxidative stress and inflammatory mediators can alter Cyclin D1 expression through modulation of NF-κB and STAT3 transcriptional activity. In endothelial cells, such regulation determines the balance between proliferation and apoptosis, influencing vascular stability during and after ischemic events [32]. Thus, Cyclin D1 serves as both a sensor and an effector of cellular stress in the cardiovascular milieu.

Importantly, emerging evidence suggests that Cyclin D1 is also subject to **post-transcriptional control by microRNAs**, including miRNA-17-5p, miRNA-15a, and miRNA-195, which directly bind to the 3′UTR of *CCND1* mRNA. This regulatory mechanism provides a rapid and reversible means of fine-tuning Cyclin D1 levels in response to changing metabolic and environmental conditions [33]. During acute myocardial ischemia, reduced perfusion and hypoxia alter miRNA expression profiles, resulting in modified Cyclin D1 synthesis and cell cycle arrest. Such modulation may serve as a protective adaptation to limit necrotic expansion or, conversely, contribute to impaired repair if dysregulated. Understanding this biochemical regulation provides crucial insight into how Cyclin D1 integrates metabolic, inflammatory, and epigenetic signals to determine cardiovascular outcomes [34].

Collectively, Cyclin D1 plays a multifaceted role in the pathophysiology of ACS, orchestrating cellular proliferation, vascular remodeling, and tissue regeneration. While transient activation promotes beneficial repair, sustained upregulation can accelerate atherosclerosis and post-infarction fibrosis. This delicate balance, governed by both intracellular signaling and miRNA-mediated control, underscores the importance of Cyclin D1 as a molecular nexus in cardiac biochemistry. Its interplay with miRNA-17-5p forms the foundation of an emerging diagnostic paradigm that links cell cycle dysregulation to ischemic cardiac pathology [35].

The miRNA-17-5p/Cyclin D1 Axis: Molecular Mechanisms and Regulatory Crosstalk in Acute Coronary Syndrome

The regulatory interaction between miRNA-17-5p and Cyclin D1 represents a key molecular link between post-transcriptional control and cell cycle regulation in cardiovascular pathology. miRNA-17-5p binds directly to the 3′ untranslated region (3′UTR) of *CCND1* mRNA, resulting in translational repression or mRNA degradation, depending on cellular context and expression dynamics [36]. This interaction effectively fine-tunes Cyclin D1 levels, modulating cell proliferation, differentiation, and survival during myocardial ischemia. In cardiomyocytes and endothelial cells exposed to hypoxia, miRNA-17-5p expression increases, leading to partial suppression of Cyclin D1, thereby preventing uncontrolled cell cycle re-entry and apoptosis [37]. Such modulation provides an adaptive biochemical mechanism to balance cell survival with repair following ischemic injury.

However, the relationship between miRNA-17-5p and Cyclin D1 is **not strictly inhibitory**; rather, it exhibits a bidirectional regulatory feedback. Under oxidative and inflammatory stress, Cyclin D1 can influence transcriptional networks that affect miRNA processing and expression, including components of the Drosha-DGCR8 and Dicer complexes [38]. This suggests a dynamic feedback loop wherein Cyclin D1 and miRNA-17-5p mutually regulate each other to maintain homeostasis. In acute coronary syndrome (ACS), disruption of this equilibrium—either via excessive miRNA-17-5p upregulation or Cyclin D1 overexpression—can lead to maladaptive outcomes such as endothelial dysfunction,

increased apoptosis, or pathological remodeling [39]. Thus, the miRNA-17-5p/Cyclin D1 axis functions as a sensitive molecular rheostat governing cardiac response to stress.

Experimental studies have revealed that ischemia and reperfusion alter the expression of both miRNA-17-5p and Cyclin D1 in circulating plasma and cardiac tissue. In a murine model of myocardial infarction, upregulated miRNA-17-5p expression coincided with decreased Cyclin D1 levels and reduced cardiomyocyte proliferation [40]. Conversely, inhibition of miRNA-17-5p restored Cyclin D1 expression, enhanced endothelial repair, and reduced infarct size. In clinical studies, plasma miRNA-17-5p levels have been found to correlate inversely with left ventricular ejection fraction (LVEF) and positively with serum troponin levels, indicating that its dysregulation mirrors myocardial injury severity [41]. These findings support the concept that miRNA-17-5p and Cyclin D1 co-regulation provides diagnostic insight into ischemic damage and subsequent tissue remodeling.

At the biochemical level, the crosstalk between miRNA-17-5p and Cyclin D1 is mediated by multiple upstream pathways including **PI3K/Akt**, **MAPK/ERK**, and **TGF-β/Smad** signaling. During ischemic stress, activation of PI3K/Akt promotes miRNA-17-5p transcription through c-Myc induction, while simultaneously stimulating Cyclin D1 synthesis for cell survival [42]. The resulting transient co-activation serves to initiate repair, but sustained or imbalanced signaling may lead to cell cycle arrest or apoptosis. Additionally, oxidative stress modulates this axis via redox-sensitive transcription factors such as NF-κB and AP-1, which regulate miRNA promoter activity and Cyclin D1 transcription. This intricate biochemical network enables cells to rapidly adapt to the metabolic and oxidative fluctuations characteristic of ACS [43].

Furthermore, epigenetic modifications play a central role in governing the miRNA-17-5p/Cyclin D1 axis. DNA methylation and histone acetylation within the *MIR17HG* promoter region influence miRNA expression under ischemic conditions, while Cyclin D1 can indirectly affect chromatin structure through interactions with transcriptional co-regulators such as p300/CBP [44]. This mutual regulation extends the axis beyond simple post-transcriptional control, embedding it within broader epigenetic and signaling landscapes. Such complexity highlights why dysregulation of this pathway can contribute to divergent outcomes in ACS—ranging from adaptive repair to detrimental remodeling and plaque destabilization [45].

Taken together, the miRNA-17-5p/Cyclin D1 axis integrates multiple layers of biochemical regulation—transcriptional, post-transcriptional, and epigenetic—to orchestrate cellular responses to ischemic stress. Its modulation influences cardiomyocyte survival, endothelial regeneration, and vascular smooth muscle proliferation, all of which are critical determinants of ACS progression and recovery. These insights emphasize the potential of targeting this molecular crosstalk for diagnostic and therapeutic purposes, offering a novel window into the biochemical dynamics of ischemic heart disease [46].

Diagnostic Significance of Circulating miRNA-17-5p and Cyclin D1 in Acute Coronary Syndrome

The clinical diagnosis of acute coronary syndrome (ACS) relies heavily on cardiac troponins, electrocardiographic changes, and imaging modalities. However, these traditional markers often lack sensitivity during the early ischemic phase, when intervention is most beneficial. This limitation has prompted extensive exploration into circulating microRNAs as novel biomarkers that reflect real-time molecular and cellular changes during myocardial injury. Among them, **miRNA-17-5p** has emerged as a particularly promising candidate due to its stability in plasma, reproducibility of detection, and strong association with myocardial ischemia and reperfusion injury [47]. Circulating miRNA-17-5p levels are significantly elevated in patients presenting with ACS compared to healthy controls, and their temporal changes correlate with infarct size, left ventricular ejection fraction (LVEF), and peak troponin levels, suggesting diagnostic and prognostic value [48].

The diagnostic power of circulating miRNA-17-5p lies in its biochemical resilience. Unlike proteins such as troponin or CK-MB, miRNAs are encapsulated within exosomes, microvesicles, or bound to Argonaute2 complexes, rendering them resistant to RNase degradation and fluctuations due to pre-

analytical conditions [49]. This stability allows for reliable quantification in plasma or serum samples using RT-qPCR or next-generation sequencing platforms. Studies have demonstrated that miRNA-17-5p exhibits rapid elevation within the first 2–4 hours of myocardial ischemia, preceding the rise of cardiac troponins. Such early upregulation reflects the immediate cellular response to ischemic stress, positioning miRNA-17-5p as a potential **early-phase biomarker** for ACS diagnosis [50]. Moreover, combining miRNA-17-5p assessment with conventional biomarkers enhances sensitivity and specificity, improving early diagnostic accuracy [51].

Parallel to miRNA-17-5p, **Cyclin D1** has also shown potential as a biochemical indicator of myocardial stress and remodeling. Circulating levels of Cyclin D1, either as free protein or within endothelial-derived vesicles, have been reported to fluctuate in response to ischemia and oxidative stress. In ACS patients, downregulation of circulating Cyclin D1 correlates with increased infarct size and impaired endothelial recovery, suggesting that its plasma concentration mirrors the integrity of vascular repair mechanisms [52]. Although Cyclin D1 is not yet established as an independent diagnostic biomarker, its integration with miRNA-17-5p measurement could provide a multi-layered biochemical profile that captures both the transcriptional and post-transcriptional aspects of ischemic injury [53].

Comparative analyses have indicated that circulating miRNA-17-5p exhibits diagnostic sensitivity comparable to cardiac troponin I but with superior early detection capability. Receiver operating characteristic (ROC) curve analyses across several cohorts reveal an area under the curve (AUC) exceeding 0.90 for miRNA-17-5p when distinguishing ACS patients from healthy controls [53]. Moreover, the combined measurement of miRNA-17-5p and Cyclin D1 enhances predictive accuracy for adverse cardiac events during follow-up, reflecting the integrated contribution of cell cycle dysregulation and ischemic stress response [54]. Such findings suggest that dual assessment could refine diagnostic algorithms, enabling more precise risk stratification and timely therapeutic intervention.

Importantly, circulating miRNA-17-5p and Cyclin D1 are not only diagnostic markers but also **pathophysiological indicators**, offering mechanistic insights into myocardial and vascular responses. The miRNA-17-5p/Cyclin D1 ratio could potentially serve as a composite biomarker reflecting the balance between proliferative repair and apoptotic injury. Elevated miRNA-17-5p with suppressed Cyclin D1 expression may signify active ischemic damage and endothelial dysfunction, while normalization of this axis during recovery could indicate reparative progression [53]. Therefore, beyond diagnosis, longitudinal monitoring of this molecular pair could aid in assessing therapeutic response and predicting long-term outcomes in ACS patients [54].

Clinical Correlation and Prognostic Implications of the miRNA-17-5p/Cyclin D1 Axis in Acute Coronary Syndrome

Clinical evidence increasingly supports the prognostic significance of circulating miRNA-17-5p and Cyclin D1 as biomarkers reflecting not only acute myocardial injury but also long-term cardiovascular outcomes. Elevated plasma levels of miRNA-17-5p at hospital admission have been associated with higher peak troponin I concentrations, larger infarct sizes, and greater impairment of left ventricular ejection fraction (LVEF) in patients with acute myocardial infarction (AMI) [58]. Conversely, reduced Cyclin D1 expression correlates with impaired endothelial repair and adverse ventricular remodeling, both of which contribute to poor prognosis following ACS [59]. These findings suggest that the **miRNA-17-5p/Cyclin D1 ratio** may serve as a dynamic biochemical indicator of disease severity and myocardial recovery potential.

In prospective cohort studies, patients with persistently elevated miRNA-17-5p levels during the first week post-ACS demonstrated higher rates of recurrent ischemic events, heart failure development, and all-cause mortality during follow-up [50]. Such persistence implies ongoing myocardial stress and maladaptive remodeling. Interestingly, normalization of Cyclin D1 expression during recovery has been linked to improved endothelial function and decreased risk of reinfarction, emphasizing the importance of cell cycle regulation in tissue repair . When both biomarkers were assessed longitudinally, an inverse correlation between miRNA-17-5p and Cyclin D1 levels was noted—patients showing early restoration

of Cyclin D1 tended to experience better clinical recovery, while those with sustained suppression exhibited higher rates of adverse cardiac remodeling [52].

Incorporating these molecular markers into clinical evaluation could refine risk stratification beyond conventional tools. For instance, combining circulating miRNA-17-5p and Cyclin D1 levels with established clinical scores such as the GRACE or TIMI risk score significantly improved predictive accuracy for major adverse cardiac events (MACE) [52]. Additionally, multi-marker models integrating miRNA-17-5p with inflammatory cytokines (IL-6, hs-CRP) and metabolic markers (BNP, NT-proBNP) yielded enhanced discrimination of high-risk ACS phenotypes [51]. This integrative diagnostic approach aligns with the emerging paradigm of precision cardiology, wherein molecular signatures guide individualized prognostication and management.

The prognostic relevance of the miRNA-17-5p/Cyclin D1 axis also extends to therapeutic response monitoring. In patients undergoing percutaneous coronary intervention (PCI), those exhibiting rapid post-procedural decline in miRNA-17-5p and concurrent recovery of Cyclin D1 expression demonstrated reduced rates of restenosis and better functional outcomes [54]. Conversely, sustained miRNA-17-5p elevation predicted recurrent ischemia and late stent thrombosis, highlighting its potential as a real-time indicator of endothelial repair efficiency [53]. These dynamic molecular changes may reflect ongoing crosstalk between ischemia-induced signaling and vascular remodeling, providing clinicians with biochemical tools for tracking therapy effectiveness.

Taken together, the clinical and prognostic data underscore that the **miRNA-17-5p/Cyclin D1 axis functions as both a biomarker and a mechanistic driver** of cardiac remodeling. Its assessment provides a multidimensional view of ACS progression—capturing early ischemic injury, reparative processes, and long-term remodeling outcomes. Harnessing this molecular signature may not only improve diagnostic precision but also enable tailored interventions that optimize myocardial recovery and prevent recurrent ischemic events [52].

Conclusion

The exploration of circulating miRNA-17-5p and Cyclin D1 as diagnostic and mechanistic biomarkers in acute coronary syndrome (ACS) highlights a transformative shift in cardiovascular molecular diagnostics. The intricate biochemical crosstalk between these two molecules bridges the gap between ischemic cellular stress and the molecular machinery of cell cycle control. miRNA-17-5p, through its ability to modulate Cyclin D1 expression, represents a dynamic regulator of endothelial function, cardiomyocyte survival, and vascular remodeling. Conversely, Cyclin D1 reflects the cellular capacity for proliferation and repair following ischemic injury, serving as a mirror of the myocardium's biochemical and structural integrity. Together, their interaction offers a multidimensional understanding of the ischemic response—spanning transcriptional regulation, post-transcriptional control, and metabolic adaptation.

From a diagnostic standpoint, the combined assessment of miRNA-17-5p and Cyclin D1 provides earlier and more specific detection of myocardial injury compared with conventional biomarkers such as troponins. Their expression profiles evolve dynamically throughout the course of ACS, allowing not only early diagnosis but also continuous monitoring of disease progression and therapeutic response. Integrating these biomarkers into clinical algorithms may enhance risk stratification and improve the precision of acute management strategies, particularly in patients presenting during the early ischemic phase or with atypical symptomatology.

Beyond diagnostics, the miRNA-17-5p/Cyclin D1 axis represents a potential therapeutic target. Modulating miRNA-17-5p expression could restore Cyclin D1-dependent endothelial repair and attenuate post-infarction fibrosis, offering molecular avenues for cardioprotection. The development of miRNA-targeted therapies, including antisense oligonucleotides and small-molecule modulators, underscores the feasibility of manipulating these regulatory pathways for clinical benefit. Additionally, pharmacological agents that indirectly influence this axis—such as statins or antioxidant therapies—may further optimize cardiac remodeling outcomes when used in combination with molecular

approaches.

In summary, understanding the biochemical interplay between circulating miRNA-17-5p and Cyclin D1 unveils a novel diagnostic and therapeutic paradigm for ACS. Their coordinated regulation embodies the convergence of molecular biochemistry and clinical cardiology, illustrating how cellular signaling networks can be translated into actionable clinical tools. As research progresses toward multi-omics integration and large-scale validation, this molecular axis stands poised to redefine precision diagnostics and targeted treatment in ischemic heart disease—ushering in a new era of molecularly guided cardiology.

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