MicroRNA-378: An important player in cardiovascular diseases (Review)

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Abstract. Cardiovascular disease (CVD) is a common chronic clinical condition and is the main cause of death in humans worldwide. Understanding the genetic and molecular mechanisms involved in the development of CVD is essential to develop effective prevention strategies and therapeutic measures. An increasing number of CVD-related genetic studies have been conducted, including those on the potential roles of microRNAs (miRs). These studies have demonstrated that miR-378 is involved in the pathological processes of CVD, including those of myocardial infarction, heart failure and coronary heart disease. Despite the potential importance of miR-378 CVD, a comprehensive summary of the related literature is lacking. Thus, the present review aimed to summarize the findings of previous studies on the roles and mechanisms of miR-378 in a variety of CVDs and provide an up-to date basis for further r research targeting the prevention and treatment of CVDs.

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Abbreviations: AMI, acute myocardial infarction; AS, aortic stenosis; CHD, coronary heart disease; CVD, cardiovascular disease; DCM, diabetic cardiomyopathy; DOX, doxorubicin; ER, endoplasmic reticulum; HIF, hypoxia-inducible factor; KATP, adenosine triphosphate-sensitive potassium channels; lncRNA, long non-coding RNA; LVH, left ventricular hypertrophy; miRNA/miR, microRNA; MMPs, matrix metalloproteinases; ncRNA, non-coding RNA; OPN, osteopontin; PPIA, peptidylprolyl isomerase A; GRB2, growth factor receptor-binding protein 2; KSR1, kinase inhibitor Ras 1; MAPK1, mitogen-activated protein kinase 1; HSF1, heat shock transcription factor 1

Key words: miR-378, microRNA, gene expression, cardiovascular diseases

Contents

1. Introduction

Cardiovascular disease (CVD) is, as a common chronic clinical disease characterized by high incidence, high disability and high mortality rates. The number of CVD patients in China is ~290 million and the incidence and mortality rates continue to increase worldwide (1). Treatment of CVD has become a subject of interest in modern medicine. Significant progress has been made in the treatment of CVD, the clinical application of new drugs and continuous improvements in medical advances, however, CVD still exacts a heavy toll on the health of patients, causes undue economic pressure and remains the commonest cause of mortality (2). Thus, it is necessary to understand the potential molecular mechanisms that regulate the progress of CVD to develop highly effective prevention strategies and therapeutic measures.

In the early stages of heart failure, the heart compensates for abnormal hemodynamics by promoting cardiomyocyte hypertrophy and inducing abnormal expression of genes (3,4). However, long-term myocardial hypertrophy leads to ventricular remodeling in which myocardial fibroblasts promote cardiomyocyte hypertrophy and extracellular matrix deposition through autocrine and paracrine mechanisms, leading to further reduction in cardiac function (5). MicroRNAs (miRNAs/miRs) are noncoding RNAs (ncRNAs) containing 19-22 nucleotides that exist stably in the blood and regulate posttranscriptional gene expression by binding to target mRNAs and reducing protein synthesis (6). miRNAs serve important regulatory roles in biological processes such as cell proliferation, apoptosis and differentiation (7) and are involved in the pathogenesis of numerous diseases, such as ovarian cancer, glioma, oral squamous cell carcinoma, gastric cancer and hepatocellular carcinoma (7-10). Abnormal miRNA expression is involved in the development and occurrence of CVDs (11). miRNAs may serve as a new mode of cell-to-cell communication via the regulation of gene expression in target cells and tissues and play a core role in gene regulation (12).

The characteristics of miRNAs are similar in males and females and in individuals of different ages; thus, miRNAs represent potential indicators of different diseases (13).

miR-378 (also known as miR-378a-3p) is a cardioprotective miRNA involved in the regulation of the occurrence and development of a variety of heart diseases (14,15). Several variants of miR-378 exist, including miR-378a/b/c/d/e/f/g/h/i/j, all of which are encoded by different genomic sites but possess common regulatory targets because they share the same seed sequence.

miR-378 is involved in the pathological processes of heart diseases, including myocardial infarction, heart failure and coronary heart disease (CHD). The pathological processes involve myocardial hypertrophy, myocardial cell fibrosis, myocardial remodeling, mitochondrial energy metabolism and angiogenesis (16,17).

Notably, the physiological expression of miR-378 is associated with the growth and development of individuals. For example, the expression of miR-378 gradually increases with age in mouse hearts, as shown in measurements of 16-day-old mouse fetuses and 1, 2, 4 week- and 10 month-old mice (18). This trend of increasing expression was confirmed in a second study of mouse fetuses examined at 10 and 14 days (19). Thus, the expression of miR-378 in the heart gradually increases from the fetal stage to adulthood following significant growth of the heart and continues to increase even after heart development is complete after birth.

There are no reviews involved in the function of miR-378 in CVD. Therefore, the present review summarized the current understanding of the roles and mechanisms of action of miR-378 in CVD. The aim is to provide a comprehensive review of the current state of research in support of more in-depth scientific and clinical studies.

2. miR-378 regulation in heart disease

Diabetic cardiomyopathy (DCM). DCM is a special form of CVD caused by resistance to insulin metabolism in heart tissue, compensatory hyperinsulinemia and hyperglycemia. The occurrence of DCM is independent of other cardiac risk factors (20) and an increasing number of studies have shown that oxidative stress, inflammation, mitochondrial dysfunction, renin-angiotensin system activation and myocardial cell apoptosis are involved in the pathogenesis of DCM (21-24).

In patients with diabetes, high blood glucose levels can cause an imbalance in the oxidative stress state, affecting cell apoptosis, hypertrophy, fibrosis, calcium homeostasis and contractile function, leading to DCM. However, even if blood glucose levels become relatively stable, hyperglycemia-induced myocardial damage cannot be prevented. This phenomenon is called hyperglycemia or metabolic memory (25,26). A meta-analysis found that the risk of heart failure in patients with diabetes cannot be avoided even after the effective control of coronary artery disease or hypertension (27). Costantino *et al* (28) observed that 48 miRNAs returned to normal expression levels following 3 weeks of intensive insulin treatment in diabetic mice; however, the expression of 268 miRNAs did not return to their original levels. Abnormally expressed miRNAs are involved in pathways that mediate cardiomyocyte apoptosis, fibrosis, hypertrophy, autophagy, oxidative stress and heart failure (29). miR-378 is an overexpressed miRNA that cannot be restored to its original expression level and thus is a key promoter of apoptosis (30-32). As miR-378 is involved in diabetic myocardial damage, it may serve as a therapeutic target for the prevention and treatment of DCM.

Durr *et al* (33) demonstrated that diabetes mellitus is associated with increased mitochondrial (MT) miR-378a level, which, in turn, is linked to a decrease in MT-ATP6 abundance, a protein encoded by the mitochondrial genome. Furthermore, these authors demonstrated the potential of miR-378a to bind and downregulate the expression of MT-ATP6, leading to a decrease in the function of ATP synthase. Treatment with miR-378a-antagomir improved cardiac systolic function in mice treated with streptozotocin. In addition, in a genetic mouse model of miR-378a deletion, improvement in cardiac dysfunction in patients with type 2 diabetes was observed, kcnq10t1 may interact with miR378a, affecting ATP synthase activity by regulating the expression of MT-ATP6 (33).

Myocardial damage caused by doxorubicin (DOX). DOX is a highly effective anticancer drug that is widely used in cancer treatment; however, severe cardiotoxicity greatly limits its clinical application (34). More research attention is being paid to miRNAs and their role in DOX-induced cardiotoxicity at the genetic levels, with improved prospects emerging (35,36).

The mechanism of DOX-induced cell damage is probably related to cell apoptosis and endoplasmic reticulum stress (ERS) can trigger an important signaling pathway leading to cell apoptosis (37). ERS generally affects the function of myocardial mitochondria, leading to mitochondrial dysfunction and energy imbalance in myocardial cells, which affect heart function and eventually lead to acute or chronic heart failure (38,39).

The miRNA profile of heart tissue in DOX-induced cardiotoxic mice or rat models was characterized after 2-8 weeks of treatment (40,41). Chen *et al* (42) observed changes in the miRNA profile of DOX-treated H9C2 cells within 24 h and identified 67 miRNAs with downregulated expression. The genes encoding theses miRNAs were mainly involved in extracellular matrix receptor interaction, focal adhesion and the PI3K-Akt signaling pathway. miR-378-3p and -5p were among the miRNAs exhibiting downregulated expression.

Wang *et al* (43) explained the mechanism of DOX-induced cardiotoxicity as occurring via the effect of miR-378 on mitochondrial energy metabolism and ERS. miR-378 mainly targets LDHA, reducing lactate dehydrogenase content and improving mitochondrial energy metabolism. LDHA can also target PPIA to regulate cell apoptosis; thus, miR-378 participates in the regulation of energy metabolism and cell apoptosis by affecting LDHA and PPIA (43). miR-378 is also involved in ERS-mediated apoptosis through its regulation of the expression of the calcium-binding endoplasmic reticulum protein calumenin (44). Calumenin serves important roles via two mechanisms: i) inhibiting the levels of GRP78, p-PERK and p-eIF2a, which reduces ERS-mediated apoptosis and eases cell apoptosis; and ii) inhibiting the activities of SERCA2 and the calcium release channel RyR2 to maintain a steady state of calcium circulation in cardiomyocytes, which then maintains the contractile and diastolic functions of cardiomyocytes (45).

Coronary heart disease

Improving hypoxia. Acute myocardial infarction (AMI) is a common type of CHD and caused by acute ischemia and hypoxia (Table I and Fig. 1). Hypoxia-inducible factor (HIF) is the main regulator of cellular responses to hypoxia (46). Under hypoxic conditions, HIF-α is activated and transferred from the cytoplasm to the nucleus, thereby activating the hypoxia adaptation pathway, which reduces oxygen consumption and improves the cell survival rate by promoting angiogenesis, erythropoiesis and iron metabolism (47,48). Continuous hypoxia eventually leads to cell apoptosis and even necrosis (49).

Previous studies have confirmed that hypoxia, called 'hypoxemia', can regulate the expression of miRNAs involved in the HIF signaling pathway (50-52). Exosomes are signaling mediators that promote cell-to-cell communication by transporting cytoplasmic components, including miRNAs, mRNAs and proteins (53). Under hypoxic conditions, miRNAs in cells and exosomes undergo certain changes and miR-378 is considered a potential biomarker of cell hypoxia (54). *In vitro* experiments have confirmed that exosomes under early hypoxic conditions can reduce hypoxia-induced apoptosis by overexpressing cardioprotective miRNAs, such as miR-378-3p (55). Hypoxia also alters the expression levels of 92 miRNAs in H9C2 cells and 62 miRNAs in exosomes. Differentially expressed exosomal miRNAs mainly participate in pathways related to cell viability, including the HIF-1, TNF, MAPK and mTOR signaling pathways (56,57).

Promoting angiogenesis. Angiogenesis is a key and complex process in the treatment of CVD and is determined by the interaction between proangiogenic and antiangiogenic factors (58,59). During the pathological process of CHD, there is an imbalance between oxygen consumption and supply in cardiomyocytes, which can damage vascular function. Therefore, angiogenesis is considered to be the primary cause of CHD (60). Thus, promoting angiogenesis and improving myocardial tissue perfusion and the recovery of myocardial function are the primary aims in treating CHD (61,62).

miRNAs have certain advantages in regulating angiogenic factors to improve vascular function in patients with CHD (63). Among these, a class of ncRNAs, such as miR-126 and miR-378, can regulate the expression of anti-angiogenic genes and promote angiogenesis. These ncRNAs can improve angiogenesis in endothelial cells and reduce the proliferation and migration of ectopic vascular smooth muscle cells, reducing the risk of CHD (64).

Xing *et al* (65) confirmed that the overexpression of miR-378a-5p in mesenchymal stem cells under hypoxic conditions inhibit mesenchymal stem cell apoptosis and promote the expression of angiogenesis-related genes (VEGFA, PDGF-β and TGF-β1). The expression of $CD34^+$ progenitor cells is significantly increased in patients with ST elevated myocardial infarction and exhibit high proangiogenic activity, which is closely related to the release of paracrine factors (66), including the upregulation of miR-378 expression. miR-378 may promote angiogenesis by targeting the expression of suppressor of fused (SuFu) and Fus-1 (67). The promotion of angiogenesis by upregulating CD34 and miR-378 expression is a unique repair mechanism in patients with AMI (68).

Improving cell apoptosis. Myocardial ischemia/reperfusion resulting in cardiomyocyte apoptosis and necrosis is the main feature of AMI (69,70). This process causes a decrease in cardiomyocyte function and ventricular remodeling, eventually leading to heart failure.

A mouse model of myocardial ischemia-reperfusion injury (MI/RI) was established by ligating the left anterior descending branch of the coronary artery. The level of miR-378 in the MI/RI model mice decreased, while that of MAPK1 increased, whereas after intervention with isoproterenol (ISO), miR-378 and MAPK1 were upregulated and downregulated, respectively. This confirmed that ISO improved cardiomyocyte apoptosis by regulating miR-378 and MAPK1 in the MI/RI model (71).

Improving autophagy. Long non-coding RNAs (lncRNAs) interact with miRNAs as competitive endogenous RNAs (ceRNAs) and participate in regulating target gene expression. Zhang *et al* (72) confirmed that lncRNA NEAT1 is highly expressed in the peripheral blood of patients with myocardial infarction and in mouse cardiomyocytes. lncRNA NEAT1 binds to and inhibits the expression of miR-378a-3p, thereby promoting the proliferation and migration of cardiomyocytes. Inhibiting the expression of miR-378a-3p facilitates the expression of Atg12 and related autophagy factors, thereby enhancing the autophagy of cardiomyocytes. Therefore, the proliferation of cardiomyocytes in patients with myocardial infarction can be modulated by inhibiting the NEAT1/miR-378-3p/Atg12 axis.

Prognosis. miR-378 is considered as a marker of CHD risk and of the degree of coronary stenosis and restenosis following coronary stent intervention (64,73). The plasma level of miR-378 expression in patients with CHD is significantly downregulated and negatively correlated with the Gensini score (74). Patients with unprotected left main coronary artery disease were followed-up in the first, second and third years after coronary angiography to observe the incidence of major adverse cardiac and cerebrovascular event (MACCE) and to detect the levels of circulating miR-378 in the peripheral blood. The results showed that a high level of miR-378 expression can independently predict a low incidence of MACCE (75). The expression of osteopontin (OPN), a matrix cell protein that regulates inflammation and biomineralization, also increases under a number of pathological conditions (76). Increased OPN levels can effectively predict the mortality rate in patients with heart failure (77). Kwee *et al* (78) measured the expression of miRNAs in 186 patients in the TRILOGY-ACS trial and discovered that the expression of miR-378a-3p was closely associated with OPN levels, which are linked with cardiovascular death, myocardial infarction and stroke.

Heart failure. In patients with early heart failure, the level of miR-378 expression was relatively upregulated and gradually decreased with the aggravation of heart failure, whereas the level of NT-proBNP expression showed an upward trend with heart failure progression (Table II and Fig. 1). This may be related to the compensatory function of the heart. Therefore, it is hypothesized that the upregulation of miR-378 expression is a self-compensatory effect of the heart in the early stages of

Table I. miR-378 roles and changes in coronary heart disease.

First author/s, year	Effect	Types of miR-378	Trend	Model	Condition	Pathway/targets	(Refs.)
Krown *et al*, 1996; Chang and Karin, 2001	Improving hypoxia	miR-378-3p	Upregulated	H9C2 cells and exosomes	Hypoxia	HIF-1, TNF, MAPK, mTOR	(56,57)
Xing *et al*, 2014	Promoting angiogenesis	miR-378a-5p	Upregulated	MSCs	Hypoxia	SuFu and Fus-1	(65)
Lee *et al*, 2007		miR-378	Upregulated	CD34+ progenitor cells	STEMI patients		(67)
Zhou *et al*, 2021	Improving cell apoptosis	miR-378	Downregulated	MI/RI model in mice	Ligating the LAD	MAPK1	(71)
Zhang *et al*, 2020	Improving autophagy	miR-378-3p	Downregulated	Peripheral blood	Patients with UA and patients with ischemic cardiomyopathy/MI	lncRNA NEAT1/miR-378-3p/Atg12	(72)
				MI/RI injury in mice	Ligating the distal part of the left ECA		
				Myocyte isolated from the heart of the newborn rat	Hypoxia		
Li *et al*, 2019	Improved prognosis	miR-378	Downregulated	Plasma	Patients who underwent PCI with DES implantation	-	(74)
Shen *et al*, 2021			Downregulated		ULMCAD patients who underwent CABG		(75)
Kwee *et al*, 2019	Worse prognosis	miR-378a-3p	Downregulated	Plasma	NSTE-ACS	-	(78)

miR, microRNA; MSCs, mesenchymal stem cells; MI/RI, myocardial ischemia reperfusion; ECA, external carotid artery; LAD, left anterior descending; UA, unstable angina; STEMI, ST elevated myocardial infarction; MI, myocardial infarction; PCI, percutaneous coronary intervention; DES, drug-eluting stent; ULMCAD, unprotected left main coronary artery disease; CABG, coronary artery bypass graft; NSTEMI, non-ST elevated myocardial infarction; ACS, acute coronary syndrome; HIF, hypoxia-inducible factor; lncRNA, long non-coding RNA; MAPK1, mitogen-activated protein kinase 1.

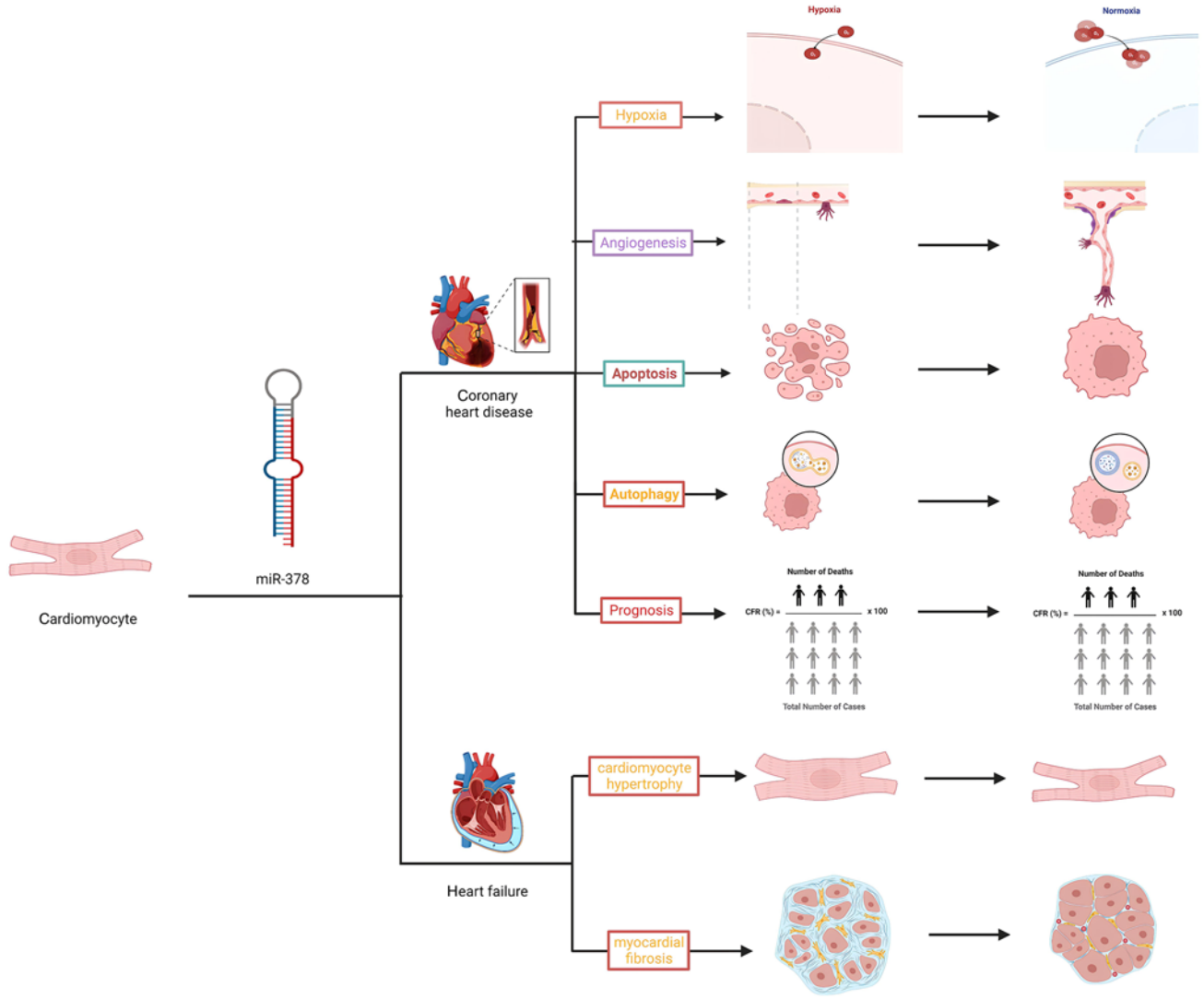

Figure 1. miRNA-378 is involved in mediating myocardial hypoxia, angiogenesis, cell apoptosis, autophagy, hypertrophy and fibrosis. miRNA/miR, microRNA.

heart failure (79). In patients with heart failure, evaluation of the expression levels of circulating miRNAs before and after acute exhaustive exercise showed that the level of miR-378 was elevated and was not significantly related to exercise endurance, muscle damage, or inflammation (80). However, with the progression of heart failure, a series of pathophysiological mechanisms, such as cardiomyocyte hypertrophy and myocardial fibrosis, cause ventricular remodeling, which further aggravates heart failure and the miR-378 expression levels vary accordingly (80).

Adenosine triphosphate sensitive potassium channels (KATP) serve as gating channels connecting vascular reactivity, metabolism and ischemic protection and are potential targets for the treatment of heart failure (81). A causal relationship exists between lower serum apolipoprotein A-I (ApoA-I) concentrations and the risk of heart failure. In one study, a total of 634 patients were retrospectively selected, including 317 patients with lo ApoA-I concentrations (<120 mg/dl) and 317 patients with high ApoA-I concentrations (≥120 mg/dl). Identification of extracellularly derived miRNA expression profiles through next-generation sequencing revealed that KATP rs41294036 was related to an increased risk of lower ApoA-I levels and an increased incidence rate of heart failure, particularly heart failure with preserved ejection fraction. Furthermore, patients carrying the rs141294036 CC genotype were associated with an increased risk of heart failure-related rehospitalization (82).

Cardiomyocyte hypertrophy (CH). CH is an adaptive response of the heart to pressure or volume overload to maintain cardiac function during the early stages (83). However, persistent cardiac hypertrophy often leads to maladaptive cardiac remodeling and increases the risk of heart failure and sudden death (83).

CH is primarily involved in physiological and pathological hypertrophy. However, no association has been observed between physiological hypertrophy and heart failure. Physiological hypertrophy mainly occurs during postnatal development, exercise response and pregnancy and is an adaptive response that can protect the heart (84). CH is reversible and the main pathological process involves the activation of the IGF1-PI3K (p110a)-Akt pathway. Pathological hypertrophy mainly occurs during the development of heart diseases (hypertension, myocardial infarction and heart failure), manifesting as an accumulation of extracellular matrix, death or apoptosis

Table II. miR-378 roles and changes in heart failure.

First author/s, year	Effect	Types of miR-378	Trend	Model	Intervention method	Target genes/pathways	(Refs.)
Bernardo *et al*, 2010; Ganesan *et al*, 2013	Cardiomyocyte hypertrophy	miR-378	Downregulated	Isolated neonatal rat cardio-myocytes or cardiac fibroblasts	Phenylephrine	MAPK1, KSR1, GRB2 and IGF1R	(84,85)
			Downregulated	Left ventricular myocardium	Transgenic overexpression of the β1-adrenergic receptor		
			Downregulated	Left ventricular myocardium	Not discussed		
Barut *et al*, 2021	Cardiomyocyte hypertrophy	miR-378a-3p	Upregulated	Left ventricular hypertrophy	Not discussed	Not discussed	(87)
Moghiman *et al*, 2021	Myocardial fibrosis	miR-378	Upregulated	Neonatal CMs and CFs	miR-378 mimics	MKK6/p38MAPK/Smad2/3	(94)
			Upregulated	TAC	Intravenous injections of chemically modified miR-378 mimics		
Sun *et al*, 2019			Downregulated	Male C57BL/6 mice	Ligating the LAD	LncRNA PCFL/ miR-378/GRB2	(95)
			Downregulated	CFs	Transfection of lncRNA PCFL plasmids		

miR, microRNA; CMs, cardiomyocytes; CFs, cardiac fibroblasts; TAC, transverse aortic constriction; LAD, left anterior descending; lncRNA, long non-coding RNA; KSR1, kinase suppressor of ras 1; GRB2, growth factor receptor-bound protein 2; MAPK1, mitogen-activated protein kinase 1; IGF1R; insulin-like growth factor1 receptor; MKK6, mitogen-activated protein kinase kinase 6.

of cardiomyocytes and an imbalance in calcium homeostasis, leading to a decrease in contraction and diastole of cardiomyocytes. This change is irreversible and is usually related to increases in various endogenous factors (such as angiotensin II, endothelin 1 and norepinephrine) and affects cardiomyocyte hypertrophy via the RAS signaling pathway (84).

miR-378 is an endogenous protective modulator of the heart. Overexpression of miR-378 not only reduces cardiomyocyte hypertrophy during the stress-loaded heart adaptation period but also reduces cardiac hypertrophy by targeting Ras signaling pathways, such as growth factor receptor-binding protein 2 (GRB2), kinase inhibitor Ras 1 (KSR1) and mitogen-activated protein kinase (MAPK)1. miR-378 target genes are enriched in MAPK pathway, including genes encoding MAPK1, insulin-like growth factor receptor 1, GRB2 and KSR1 (85).

Chen *et al* (86) systematically studied the ceRNA regulatory network related to the circRNAs involved in CH. They used a public database of online prediction websites to predict, and screen for, differentially expressed mRNAs and miRNAs, ultimately identifying circRNAs related to CH. To the best of the authors' knowledge, this is the first study to establish a ceRNA regulatory network associated with myocardial hypertrophy. A total of three mRNAs, four miRNAs (including miR-378a-3p) and four related circRNAs may play key roles in CH. Barut *et al* (87) hypothesized that high circulating levels of miRNA-378 could serve as a new biomarker for the diagnosis of left ventricular hypertrophy (LVH).

Myocardial fibrosis. Excessive myocardial fibrosis is the main pathological process underlying heart remodeling and failure (88,89). Myocardial fibrosis is characterized by the accumulation of fibroblasts, excessive deposition of extracellular matrix proteins and increased levels of collagen and matrix metalloproteinases (MMPs) (90,91). Abnormal expression of numerous miRNAs during excessive hemodynamic pressure is a key component of heart remodeling (92,93).

miR-378 can reduce the expression of collagen and MMP9 by inhibiting the p38MAPK and Smad2/3 signaling pathways, thereby inhibiting myocardial fibrosis. miR-378 mimics reduced myocardial fibrosis in rats with transverse aortic constriction (TAC) (94). A possible mechanism involves miR-378 inhibition of the p38MAPK and Smad2/3 signaling pathways by directly targeting MAPK6 in an extracellular vesicle-dependent manner. Therefore, the expression of collagen and MMP in cardiac fibroblasts cells (CFs) is regulated and that in myocardial fibrosis is inhibited (79). miR-378 also exerts an anti-myocardial fibrotic effect through a ceRNA mechanism. The combination of the pro-cardiac fibrotic lncRNA and miR-378 relieves the inhibition of GRB2, resulting in elevated expression of TGF-β1, which promotes myocardial fibrosis (95). In addition, heat shock transcription factor 1 (HSF1) is a protective factor in the heart and the level of miR-378 expression in TAC mice with HSF1 knock out was significantly reduced, resulting in increased myocardial fibrosis (96).

Aortic stenosis. Aortic stenosis is a common heart valve disease that accounts for 43% of adult patients with valvular heart diseases (97). The most common complication is LVH, which is closely related to the occurrence of cardiovascular events in patients with aortic stenosis (AS) and is an independent predictor of an adverse prognosis for these patients (98-101). miR-378 mediates the pathological process of LVH through the MAPK signaling pathway (85,102). Plasma miR-378 levels in patients with AS were significantly reduced and negatively correlated with left ventricular mass index. The plasma level of miR-378 is an independent predictor of LVH in patients with AS and to a certain extent reflects heart remodeling caused by pressure overload (103).

3. Conclusions

As a cardioprotective miRNA, miR-378 regulates the development of various CVDs. In doing so, miR-378 participates in numerous processes, including myocardial hypertrophy, myocardial cell fibrosis, myocardial remodeling, mitochondrial energy metabolism and angiogenesis, among other processes waiting to be discovered. For example, Fig. 1 shows that miRNA-378 plays a significant role in the pathogenesis of CHD and heart failure. The main manifestation is that in terms of CHD, miRNA-378 is involved in mediating myocardial cell hypoxia, promoting angiogenesis, promoting cell apoptosis and autophagy and has certain value for the prognosis of CHD; In terms of heart failure, miRNA-378 is involved in mediating myocardial cell hypertrophy and myocardial fibrosis levels. Thus, regulating the level of miRNA-378 has certain value in the treatment of CHD and heart failure and miR-378 may be a vital regulator of CVDs.

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Availability of data and materials

Data sharing is not applicable to this article, as no data sets were generated or analyzed during the current study.

Authors' contributions

HW retrieved literature and drafted the manuscript. JS and JW read and classified the literature based on the different types of diseases. YH supervised the study and offered advice. HW, JS, JW and YH reviewed and classified the literature based on the different types of diseases, and wrote and revised the manuscript. All authors read and approved the final manuscript. Data authentication is not applicable.

Ethics approval and consent to participate

Not applicable.

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Not applicable.

Competing interests

The authors declare that they have no competing interests.

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