

CARDIOVASCULAR DISEASE	EXISTING EVIDENCE OF ASSOCIATION OF OXIDATIVE STRESS AND CARDIOVASCULAR DISEASE			
Myocardial infarction and cardiac ischemia-reperfusion	<p>Reactive oxygen species (ROS) may play important roles in the pathogenesis in myocardial infarction⁷⁵.</p> <p>Evidence showed an imbalance between oxidant and antioxidant molecules in acute myocardial infarction (AMI)⁷⁶.</p> <p>Increased production of ROS, decreased endothelium-dependent relaxation and NO bio-availability have been observed in the vasculature of rats after myocardial infarction^{77,78}.</p>	<p>Significant increase in malondialdehyde and conjugated dienes in patients with acute myocardial infarction was observed⁷⁹.</p> <p>"In addition to the decrease of nonenzymatic antioxidant defenses, the increase in oxidative stress was probably a result of the elevation in ROS production due to the ischemic/reperfusion event of AMI"⁸⁰.</p>	<p>"Blood sample from patients with ischemic heart disease has been shown to contain evidence of oxidative stress"⁸¹.</p> <p>"In myocardial ischemia, hypoxia and re-oxygenation induces an increase in free radical production in cardiac tissues [which cause] reperfusion injury" and inflammation⁸².</p> <p>"Oxidative stress contributes critically to the pathogenesis of ischemia-reperfusion injury"⁸³.</p>	<p>"Myocardial ischemia/reperfusion promotes excess generation of highly ROS and causes oxidative stress"⁸⁴.</p> <p>"A consequence of ischemia-reperfusion is mitochondrial oxidative stress...harbingers to the activation of cell death apoptotic pathways"⁸⁵.</p> <p>"...increased oxidative stress, which oxidizes biological macromolecules and impairs cell functions, is a major pathogenic factor in MI/R injury"⁸⁶.</p>
Cardiac hypertrophy, cardiomyopathy & heart failure	<p>"Increase in ROS is responsible for impaired endothelial regulation of left ventricular relaxation observed in moderate pressure overload left ventricular hypertrophy"^{87,88}.</p> <p>"Myocardial remodeling in congestive heart failure has been attributed to ROS production by the mitochondrial, xanthine oxidase, nitric oxide synthetase and NADPH oxidase pathways"^{89,90}.</p> <p>"ROS activate a broad variety of hypertrophy signaling kinases and transcription factors"⁹¹.</p> <p>"ROS have potent effects on the extracellular matrix, stimulating cardiac fibroblast proliferation"⁹².</p>	<p>"Investigations aimed at prevention of hypertrophy should address reduction of oxidative stress"⁹³.</p> <p>"Treatment with the antioxidant vitamin C produced a significant inhibition of oxidative stress, an improvement in endothelial function, and a reduction of cardiac hypertrophy"⁹⁴.</p> <p>"More specific targeting of the source of oxidative stress, such as recoupling of NOS or enhancing intrinsic antioxidants, may ultimately provide more effective approaches to reversing cardiac remodeling"⁹⁵.</p> <p>"[O₂⁻] contributes to impaired endothelium-dependent relaxation in coronary arteries of...cardiomyopathic hamsters"⁹⁶.</p>	<p>"The level of oxidative stress significantly increased and was positively correlated with the degree of myocardial damage in patients with cardiomyopathy"⁹⁷.</p> <p>Hyperhomocysteinemia (HCM) is characterized by enhanced oxidative stress⁹⁸.</p> <p>"Oxidative stress was elevated in myocardia of [hypertrophic cardiomyopathy] patients and the levels were correlated with left ventricular dilatation and systolic dysfunction"⁹⁹.</p> <p>"...supplementation with antioxidants in the treatment of idiopathic dilated cardiomyopathy (IDC) may be helpful to these patients"¹⁰⁰.</p>	<p>"...heart failure under acute as well as chronic conditions is associated with reduced antioxidant reserve and increased oxidative stress"^{101,102}.</p> <p>"...oxidative stress contributes to the exaggerated muscle reflex in heart failure"¹⁰³.</p> <p>"Level and activity of xanthine oxygenase [an important cardiovascular source of ROS] increased in heart failure"¹⁰⁴.</p> <p>Levels of ROS are elevated in heart failure and cardiac protection is observed with antioxidant treatment¹⁰⁵⁻¹⁰⁷.</p>

Table 2 | Existing evidence of association of oxidative stress and cardiovascular disease