

**Advanced glycation end products (AGEs)**

AGEs are lipids and proteins that have become glycosylated due to increased exposure to carbohydrates (eg, hyperglycemia due to type 2 diabetes). AGEs are thought to play a key role in mediating various pathologies associated with chronic diseases, including promoting vasoconstriction, increasing arterial stiffness, and increasing oxidative stress, all of which can contribute to cardiac dysfunction.

**B-type natriuretic peptide (BNP)**

BNP is a 32-amino-acid vasoactive peptide secreted by the atria and ventricles in response to ventricular volume expansion and/or to increased wall stress (cardiomyocyte stretch) due to pressure overload. BNP elicits its biological actions—eg, natriuresis, vasodilation, diuresis, inhibition of the renin-angiotensin-aldosterone system, enhanced myocardial relaxation, inhibition of fibrosis and hypertrophy, promotion of cell survival, and inhibition of inflammation—by activating specific natriuretic peptide receptors (NPR-A)/guanylate cyclase (GC-A) that utilize cyclic guanosine monophosphate (cGMP) as an intracellular second messenger. Circulating BNP levels have been demonstrated to be a marker for prognosis and risk stratification in the setting of heart failure.

**Cardiac resynchronization therapy**

Cardiac resynchronization therapy is a treatment strategy for heart failure that involves the insertion of electrodes into the left and right ventricles of the heart (occasionally an electrode may be inserted into the right atria as well), which acts to coordinate ventricular function via pacemaker.

**Cardioprotection**

Cardioprotection represents the strategies and treatments for protecting the heart against the various pathologies that affect the myocardium (eg, ischemia/reperfusion injury, heart failure, cardiomyopathy, etc).

**Fatty acid oxidation**

Fatty acid oxidation is the series of biochemical reactions occurring in the mitochondria that results in the catabolism of a fatty acyl CoA (activated fatty acid) for subsequent energy (ATP) production. Each round of fatty acid oxidation shortens the fatty acyl CoA by 2 carbons (as acetyl CoA) and produces reducing equivalents, which donate their electrons to the

electron transport chain, producing the proton motive force that drives ATP production.

**Glucagon-like peptide-1 (GLP-1)**

GLP-1 is an incretin hormone synthesized and secreted from intestinal L cells. GLP-1 is derived from proglucagon via the action of prohormone convertase 1. Biologically active GLP-1 is generated from GLP-1(1-37) as either GLP-1(7-37) or GLP-1(7-36) amide, which represents the majority of biologically active GLP-1 in human plasma. GLP-1 exerts a variety of effects relevant to the regulation of glucose homeostasis, including enhancing glucose-stimulated insulin secretion, while inhibiting glucagon secretion. In addition, GLP-1 has been demonstrated to promote  $\beta$ -cell proliferation, inhibit  $\beta$ -cell apoptosis, decrease the rate of gastric emptying, and decrease food intake.

**Glycolysis**

Glycolysis is the series of biochemical reactions occurring in the cytosolic compartment that converts a glucose molecule into two molecules of pyruvate. In the presence of oxygen (ie, the aerobic setting), pyruvate is transported into the mitochondria, and undergoes oxidative decarboxylation yielding acetyl-CoA. In the absence of oxygen (ie, the anaerobic setting), pyruvate is reduced to lactate by the enzyme lactate dehydrogenase, which generates NAD<sup>+</sup> required to maintain flux through glycolysis.

**Glucose oxidation**

Glucose oxidation (ie, pyruvate oxidation) occurs in the mitochondrial matrix, where pyruvate undergoes oxidative decarboxylation via the pyruvate dehydrogenase complex, yielding acetyl coenzyme A (CoA) for the tricarboxylic acid cycle, and reduced nicotinamide adenine dinucleotide (NADH) for the electron transport chain.

**Heart failure with preserved ejection fraction (HFpEF)**

HFpEF is usually defined as heart failure with an ejection fraction higher than 50% and is characterized by diastolic dysfunction rather than systolic dysfunction. It is primarily accompanied by concentric remodeling and defects in left ventricular compliance. Approximately 50% of all heart failure cases are classified as HFpEF.