

**ATP/ADP ratio**

The ratio of adenosine triphosphate (ATP) to adenosine diphosphate (ADP) indicates cellular status and is responsible for controlling a myriad of metabolic activities, including the balance between catabolic and anabolic processes. A high ATP/ADP ratio indicates that the cell is replete with ATP, whereas a low ATP/ADP ratio is indicative of cellular energy depletion. Importantly, the ATP/ADP ratio determines the free energy change of ATP hydrolysis.

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

B-type natriuretic peptide (BNP) is a 32-amino-acid vasoactive peptide secreted by the atria and ventricles in response to increased wall stress (cardiomyocyte stretch) due to pressure overload and/or volume expansion. 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 (natriuretic peptide receptor A [NPR-A]/guanylate cyclase A [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.

**N-terminal pro-B-type natriuretic peptide (NT-proBNP)**

N-terminal pro-B-type natriuretic peptide (NT-proBNP) is a 76-amino-acid peptide generated from cleavage of the 108-amino-acid proBNP (the storage form of BNP): cleavage of proBNP generates 76-amino-acid NT-proBNP and 32-amino-acid BNP. NT-proBNP is not biologically active; however, the level of circulating NT-proBNP is a marker for prognosis and risk stratification in the setting of heart failure.

 **$\Delta G_{ATP}$** 

$\Delta G_{ATP}$  represents the free energy change of adenosine triphosphate (ATP) hydrolysis (ie,  $ATP + H_2O \rightarrow ADP + P_i$ ).  $\Delta G_{ATP}$  drives ATP-dependent reactions.  $\Delta G_{ATP}$  can be calculated from the cellular contents of ATP, adenosine diphosphate (ADP), and phosphate ( $P_i$ ) as:  $\Delta G_{ATP} = \Delta G_{ATP}^{\circ} + RT \ln [ADP] [P_i] / [ATP]$ , where  $G_{ATP}^{\circ} = 30\,500$  J/mol, and  $R = 8.315$  J/mol·K.

**Extracellular volume (ECV)**

Extracellular volume (ECV) represents the volume of the extracellular fluid compartment (ie, plasma and interstitial fluid). It is generally accepted that under normal conditions, ECV (measured in liters) is 20% of body weight (measured in kilograms).

**End-diastolic pressure-volume relationship (EDPVR)**

The end-diastolic pressure-volume relationship (EDPVR) defines the changes in ventricular pressure and volume during passive ventricular filling and can be readily discerned from invasively measured ventricular pressure-volume relationships (ie, pressure-volume loops). The inverse of the slope of the EDPVR (ie,  $\Delta V / \Delta P$ ) represents ventricular compliance, which can be altered in heart failure.

**Ejection fraction (EF)**

Ejection fraction (EF) represents the proportion of ventricular volume ejected relative to end-diastolic volume. EF can be calculated as follows:  $EF = (\text{stroke volume} / \text{end-diastolic volume}) \cdot 100$ . Under normal conditions, EF is  $\geq 60\%$ , whereas in severe heart failure, it can be  $\leq 20\%$ .

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

Heart failure with preserved ejection fraction (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.

**Heart failure with reduced ejection fraction (HFrEF)**

Heart failure with reduced ejection fraction (HFrEF) is usually defined as heart failure with an ejection fraction lower than 40% and is characterized by systolic dysfunction. It is primarily accompanied by eccentric remodeling and a decreased left ventricular wall thickness. Approximately 50% of all heart failure cases are classified as HFrEF.

**Heart failure with midrange ejection fraction (HFmrEF)**

Heart failure with midrange ejection fraction (HFmrEF) is a new category of heart failure defined as heart failure with an ejection fraction between 40% and 49%. This new class of heart failure is meant to apply to patients in a “gray zone,” where the benefits of therapies on morbidity and mortality have not been conclusively proven as they have been for patients with HFrEF.

**Global longitudinal strain (GLS)**

Global longitudinal strain (GLS) is a new technique for detecting, quantifying, and evaluating subtle disturbances/deteriorations in left ventricular systolic function via use of speckle-tracking echocardiography.

**T1 mapping**

T1 mapping is a new noninvasive cardiac magnetic resonance imaging technique that can be performed with or without contrast and is useful in characterizing myocardial tissue properties such as increased extracellular volume in conditions such as hypertrophic cardiomyopathy and aortic stenosis. It can also noninvasively detect myocardial fibrosis.

**Nitric oxide–cyclic guanosine monophosphate (NO-cGMP) axis**

The nitric oxide–cyclic guanosine monophosphate (NO-cGMP) axis refers to the signaling transduction pathway mediated by the gaseous signaling molecule NO, which activates soluble guanylyl cyclase (sGC). NO induction of sGC activity leads to massive increases in the intracellular levels of the second messenger cGMP, which leads to activation of protein kinase G–mediated signaling events.

**Wild-type transthyretin amyloid (WTTA)**

Wild-type transthyretin amyloid (WTTA) is a disease that arises from the accumulation of wild-type transthyretin (normal version of the protein) in the heart or tendons, and it primarily affects the elderly. Men are affected to a much greater degree than women. As wild-type transthyretin accumulates in the heart, it results in increased myocardial stiffness and wall thickness, precipitating symptoms often including shortness of breath and exercise intolerance.