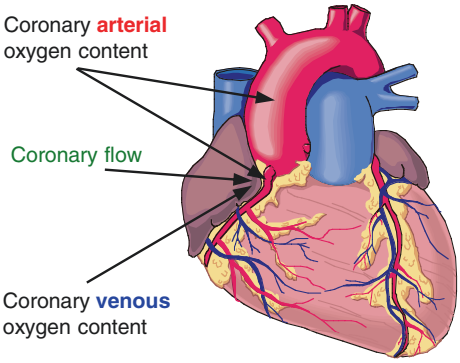
Chapter 17
Cardiac Oxygen Consumption and Hemodynamics



Cardiac oxygen consumption can be determined from the product of coronary flow, Q_{coron}, and arterio-venous oxygen content difference, ΔAVO_2. Coronary arterial oxygen content can be obtained from any arterial blood sample. Coronary venous or great cardiac vein oxygen content requires blood sampling at that location. Total coronary flow can be determined in the main stem coronary artery (ultrasound, catheter-tipped) flow meter, MRI (non-invasive), with microspheres, or at the venous side with thermodilution. To circumvent these preferentially simultaneous but difficult determinations, many indices for estimating cardiac oxygen consumption from hemodynamic variables have been proposed. It has been shown that heart rate is a primary determinant of oxygen consumption. The second major determinant is tension (stress) generation of the cardiac muscle, mostly measured as ventricular pressure. Muscle stress (pressure) generation costs more oxygen than muscle shortening (flow). Therefore many methods to derive oxygen consumption from hemodynamics are based on heart rate and pressure. The most used methods are the Rate Pressure Product (RPP, systolic pressure times Heart Rate), often used in biochemical studies, and the Tension Time Index (TTI, mean pressure during ejection). Total oxygen consumption depends two terms each consisting of two

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sub-terms. The first is the 'unloaded' contraction, consisting of 'cell maintenance' plus excitation-contraction coupling (E_{es}, the slope of the End-Systolic Pressure-Volume relation). The second is the hemodynamic part namely the Pressure-Volume Area (PVA) that is the sum of external work plus potential energy measurable from the Pressure-Volume Relation.

17.1 Description

It was shown by Sarnoff et al. [1] that the production of pressure costs much more oxygen than the production of flow or Cardiac Output (see Fig. 17.1). Also, it has been shown that oxygen consumption, VO_2, is almost proportional to Heart Rate. These findings imply that the main mechanical variables determining cardiac oxygen consumption are pressure and Heart Rate. If oxygen consumption is expressed per beat, pressure remains as major determinant.

17.1.1 Rate Pressure Product and Tension Time Index

In approximation, the product of the systolic ventricular pressure and Heart Rate can be used to estimate oxygen consumption. This so-called Rate Pressure Product, RPP, is simple to use. The triple product, defined as $HR \cdot P_{syst} \cdot dP_{lv}/dt$, with dP_{lv}/dt the

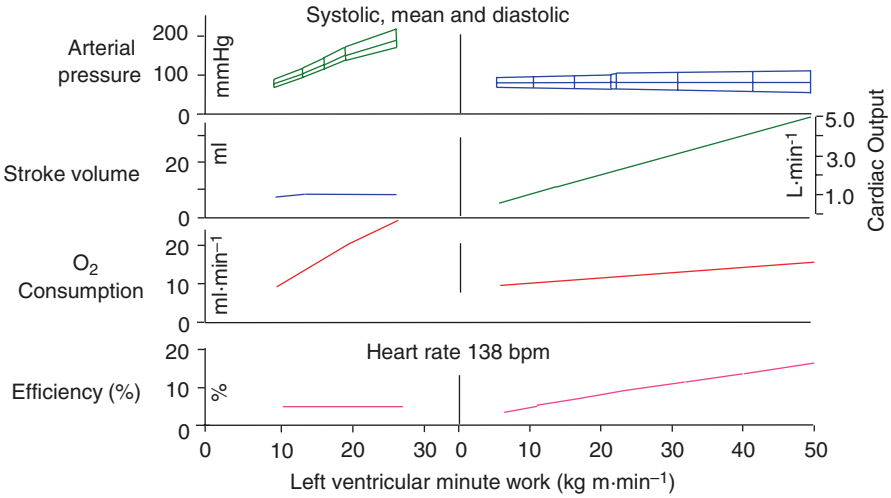

Fig. 17.1 Oxygen consumption as a function of minute work (power) was studied in experiments where Heart Rate was kept constant and cardiac filling and load were manipulated. Left panels: Arterial pressure was increased by diastolic cardiac filling while stroke volume was kept the same by a load increase. Right panels: stroke volume is increased by increased filling and decreased load while keeping pressure constant. Efficiency is the ratio of Stroke Work and oxygen consumption. Oxygen consumption changes much less with minute work during a stroke volume increases than with a pressure increase. (Adapted from Ref. [1], used by permission)

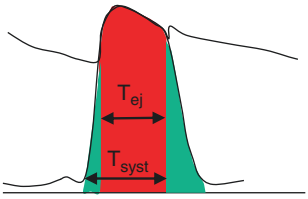

Fig. 17.2 TENSION TIME INDEX equals the area under the pressure curve during ejection (red), and is a simple method to estimate cardiac oxygen consumption per beat

maximal rate of rise of ventricular pressure, has also been suggested as a measure of cardiac oxygen consumption.

Sarnoff introduced the Tension Time Index, TTI, based on the results presented in Fig. 17.1 [1]. The oxygen consumption per beat is assumed to be proportional to the area under the ventricular (or aortic pressure when no stenosis is present) during the ejection period (red area Fig. 17.2). Often the whole contraction period is used instead, thus the green plus red area (Fig. 17.2). When we can neglect the contribution in diastole this area equals mean ventricular pressure, $P_{lv,mean}$ times heart period, T, i.e., TTI $\approx P_{lv,mean} \cdot T$. In isolated heart studies where isovolumic contractions are studied, and the ejection period is negligible, the total area under the *ventricular* pressure curve, thus $P_{lv,mean} \cdot T$ can be used as a measure of cardiac oxygen consumption. The TTI is a global measure of cardiac oxygen consumption, and the term tension is not meant to be local stress, but is pressure. The TTI is more difficult to measure than the RPP.

17.1.2 Cardiac Oxygen Consumption and the Pressure Volume Area

Another way to estimate oxygen consumption per beat is the Pressure Volume Area (PVA, the red area in the top part of Fig. 17.3) is the sum of external work (EW, Chap. 16) and Potential Energy, PE [2]. This method requires measurement of ventricular pressure and volume for at least two, and preferably more cardiac filling conditions to obtain the End-Systolic Pressure-Volume Relation (Chap. 14). The relation between oxygen consumption, VO_2 per beat and 100 ml muscle, and PVA is shown in the bottom part of Fig. 17.3, and can be written as:

$$VO_2 = a_1 \cdot \mathrm{PVA} + a_2 \cdot E_{es} + a_3$$

where E_{es}, is the slope of the End-Systolic Pressure-Volume Relation (ESPVR), giving a measure of contractile state. The first term is the relation between mechanics and oxygen consumption. The two other terms together give the oxygen consumption for the unloaded contraction or isobaric contraction, i.e., a contraction without buildup of pressure. The second term, $a_2 \cdot E_{es}$, is the energy cost of excitation-contraction coupling, mainly Calcium handling, and depends on the contractile state of the cardiac muscle, expressed as *Ees*. The last term is the basal oxygen consumption, used for the maintenance of cell structure, etc. For details see Suga [2].

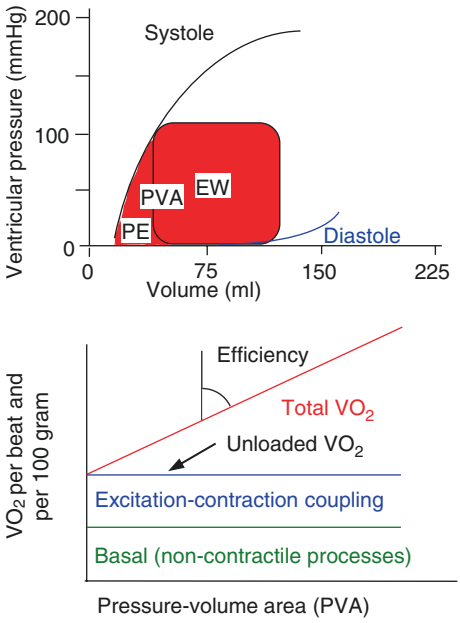

Fig. 17.3 The pressure-volume area (PVA) is the sum of external work (EW) and Potential Energy (PE). PVA relates to cardiac oxygen consumption. Oxygen consumption is also determined by basal (non-contractile) processes such as cell integrity and ion pumps, and by excitation-contraction coupling (activation energy, Calcium handling). Increased contractility increases activation energy. The PVA determines the third part of the energy. The inverse slope of the relation between PVA and VO_2 (red line) is the contractile efficiency. Overall efficiency equals EW/VO_2. (Adapted from Ref. [2], used by permission)

Ventricular efficiency is EW/VO_2. The PVA – VO_2 relation shows that pressure contributes more to VO_2 than flow for similar changes in EW, but the difference is smaller than suggested by Sarnoff et al. [3]. Increased contractility does not change the a_1 and a_3 but increases *Ees* implying that with similar PVA and similar External Work more oxygen is used due to increased energy utilization associated with excitation-contraction coupling and efficiency is lowered [4]. This may be called oxygen wasting by enhanced contractility.

In hypertrophy, with increased *Ees* due to wall thickening, the intercept and the slope of the VO_2-PVA relation is not affected [2]. Comparing a shortening contraction where PVA = PE + EW and an isovolumic contraction with the same systolic pressure where PVA = PE shows that the shortening contraction costs more oxygen in agreement with the Fenn-effect shown in muscle studies.

Local measures of oxygen consumption have been suggested as well. The Stress Time Index, i.e., mean wall stress, derived from left ventricular pressure, times heart period, is the local formulation of the TTI. In analogy with the PVA the local Force (Tension or Stress) Length Area (FLA) has been suggested in analogy with Fig. 17.3.

Most hemodynamic indices predict oxygen consumption per beat, oxygen consumption per second or minute is found by multiplication with Heart Rate. If we assume the TTI to be equal to the mean ventricular pressure times heart period, multiplying with Heart Rate results in mean pressure as a measure of oxygen consumption.

An overview of other, more complex hemodynamic indicators of cardiac oxygen consumption can be found in Rooke and Feigl's report [5].

17.1.3 Heterogeneity of Metabolism

Not only local perfusion (Chap. 19), but also local myocardial oxygen consumption is heterogeneously distributed in the myocardium [6]. Thus perfusion and metabolism seem related [7] but the reason for the heterogeneity is still disputed.

17.2 Physiological and Clinical Relevance

Cardiac oxygen consumption, or oxygen demand, and cardiac oxygen supply, are in equilibrium in the normal healthy heart. The above indices give hemodynamic measures of oxygen demand. Oxygen supply depends on coronary perfusion. Perfusion, especially to the subendocardial layers, mainly takes place in diastole when the cardiac muscle is relaxed. Thus, aortic pressure in diastole and the duration of diastole, together, quantified by the area under the diastolic aortic pressure curve, and called the diastolic pressure-time index, gives a measure of oxygen supply. The Tension Time Index, the area under the systolic pressure, is a simple measure of oxygen demand. It has therefore been proposed that the ratio of areas under the diastolic aortic pressure curve and the area under the systolic pressure curve, gives an estimate of the supply-demand ratio of the subendocardial layers of the heart [8].

With increasing age systolic pressure increases and diastolic pressure decreases a little (Chap. 25), resulting in an increase in mean systolic pressure see Fig. 17.4. This means that with age the supply-demand ratio decreases, which may result in ischemia in subendocardial layers. A similar reasoning can be applied to aortic valvular disease and tachycardia.

17.2.1 Limitations

The hemodynamic determinants of oxygen consumption, discussed above, can be used in individual hearts in situ and isolated hearts during acute experiments, such a pharmacological or loading interventions. The use of the hemodynamic parameters in different hearts, animals or in disease, should be done with care. When a dilated heart is compared with a normal heart, pressures and Heart Rates may be

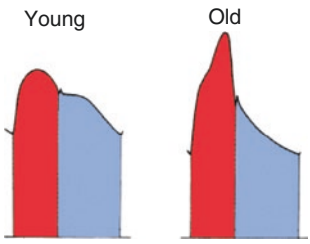

Fig. 17.4 The oxygen demand and supply relate to the areas under the systolic (red) and diastolic part (blue) of the pressure curve, respectively. The supply-demand ratio may be unfavorably influenced with increasing age

similar, but with more muscle mass, and different wall stress, oxygen consumption is not. In compensated concentric hypertrophy ventricular pressure is increased and wall thickness is increased in proportion while lumen radius is hardly changed, thereby keeping wall stress the same (Chap. 9). The Pressure Volume Area, PVA, as measure of oxygen per beat and per 100 g muscle allows for comparison of normal and hypertrophied hearts [2]. In the formula for the Pressure Volume Area the coefficients in the equation depend on animal size.

By applying the Rate Pressure Product to mouse and man, where systolic ventricular pressure and wall stress are similar but Heart Rate differs by a factor ten, it cannot be concluded that cardiac metabolism in the mouse heart is ten times that of the human heart (Chap. 32).

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