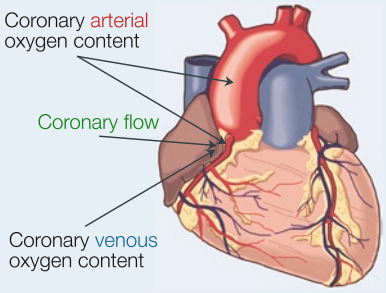
Chapter 16
Cardiac Oxygen Consumption and Hemodynamics



Cardiac oxygen consumption can be determined from the product of coronary flow, Q_{coron}, and arterio-venous oxygen content difference, ΔAVO_2. Coronary artery 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, in the periphery with microspheres, or at the venous side with thermodilution. These methods are difficult. To circumvent these preferentially simultaneous and difficult determinations, many indices for estimating oxygen consumption from mechanical 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 pressure generation. Pressure generation costs more oxygen than muscle shortening (flow). This means that systemic pressure generation rather than Cardiac Output determines oxygen consumption of the heart. Therefore almost all methods to derive oxygen consumption from hemodynamics are based on heart rate and pressure. The most used methods are the Rate Pressure Product (*RPP*), often used in biochemical studies, the Tension Time Index (*TTI*), and the Pressure Volume Area (*PVA*).

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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. 16.1). Also, it has been shown that oxygen consumption, VO_2, is almost proportional to Heart Rate. These findings imply that the main mechanical variables to estimate cardiac oxygen consumption are pressure and Heart Rate. If oxygen consumption is expressed per beat, pressure remains as major determinant.

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, especially when limited to changes in oxygen consumption. The triple product, defined as $HR \cdot P_{syst} \cdot dP_{LV}/dt$, with dP_{LV}/dt the 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 [1]. The oxygen consumption per beat is assumed to be proportional to the area under the ventricular pressure or (in absence of aorta stenosis) under the aortic pressure curve during the ejection period. Often the systolic period is used instead (Fig. 16.2). Implicitly the authors

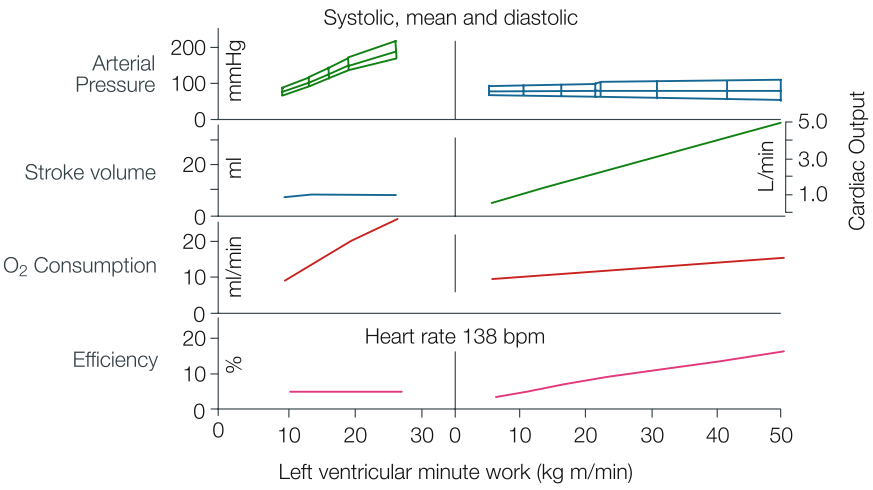

Fig. 16.1 Oxygen consumption is, at constant heart rate, primarily determined by pressure, not by flow or external work. In the *left panel* arterial pressure is increased while Stroke Volume and Cardiac Output are kept the same. The increase in pressure results in an increase in oxygen consumption. In the *right panel* Cardiac Output is increased while pressure is kept the same. Oxygen consumption changes only little. Adapted from ref. [1], used by permission

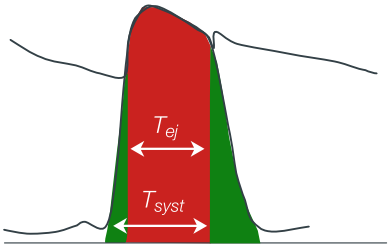

Fig. 16.2 Tension Time Index, TTI, equals the area under the pressure curve during the ejection period. Systolic and ejection periods are indicated

assumed this area to be proportional to the mean systolic left ventricular pressure times the duration of systole. However, it is better to use the total area under the *ventricular* pressure curve (red plus green in Fig. 16.2), and when we can neglect the contribution in diastole it follows that this area equals mean ventricular pressure, $P_{lv,mean}$, times heart period, T, i.e., $\mathrm{TTI} \approx P_{lv,mean}\ T$. In isolated heart studies where isovolumic contractions are studied, and the ejection period is negligible, the area under the *ventricular* pressure curve should 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.

The Pressure Volume Area

Another way to estimate oxygen consumption per beat is the Pressure Volume Area (PVA, the red area in top part of Fig. 16.3). This method requires measurement of ventricular pressure and volume for at least two, and preferably more cardiac loading conditions (Chaps. 13 and 15). The relation between oxygen consumption and PVA is shown in the bottom part of Fig. 16.3, and can be written as:

$$VO_2 = \mathrm{a}_1 \cdot \mathrm{PVA} + \mathrm{a}_2 \cdot E_{\mathrm{es}} + \mathrm{a}_3$$

where E_{es} or E_{max}, 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 or isobaric contraction, i.e., a contraction without build up of pressure. The second term is the energy cost of excitation-contraction coupling and depends on the contractile state of the cardiac muscle, expressed as E_{es}. The last term is the basal oxygen consumption, used for the maintenance of cell structure, etc. For details see Suga [2].

The following local measure of oxygen consumption has 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 Tension (or Stress) Area and Force Length Area have been suggested also (Fig. 16.3 with local area and stress or local length and stress on the axes).

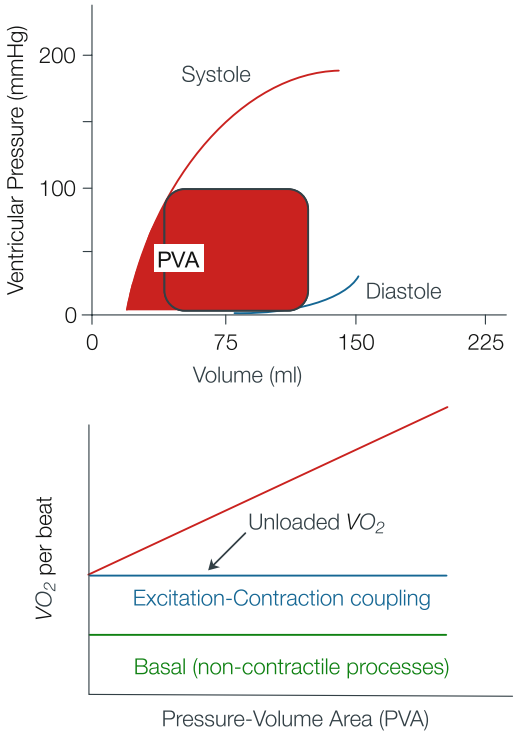

Fig. 16.3 The Pressure-Volume Area, PVA relates to cardiac oxygen consumption. Oxygen consumption is also determined by basal processes such as cell integrity and ion pumps, and by excitation-contraction coupling (activation energy). Increased contractility increases activation energy. The PVA is the third factor that determines the oxygen consumption. This is the oxygen consumption that is related to hemodynamics. The inverse slope of the relation is the so-called contractile efficiency. Adapted from ref. [2], used by permission

Since the TTI and the PVA predict oxygen consumption per beat, oxygen consumption per 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 [3].

Heterogeneity of Metabolism

Not only local perfusion (Chap. 18), but also local myocardial oxygen consumption is heterogeneously distributed in the myocardium [4]. Thus perfusion and metabolism seem [5] related but the reason for this is still disputed.

Physiological and Clinical Relevance

Cardiac oxygen consumption, or oxygen demand, and cardiac oxygen supply, are in equilibrium in the normal healthy heart. The Tension Time Index (TTI) gives a measure 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. It has therefore been proposed that the ratio of areas under the diastolic aortic pressure and the area under the systolic pressure curve, gives an estimate of the supply-demand ratio of the subendocardial layers of the heart (see Fig. 16.4).

With increasing age wave reflections become more prominent in systole (Chaps. 21 and 22), resulting in an increase in mean systolic pressure and a decrease in mean diastolic pressure. 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.

Limitations

The mechanical determinants of oxygen consumption, discussed above, can be used in individual hearts where pharmacological or other interventions are performed. The use of these determinants in different hearts should be done with care. When a dilated and hypertrophied heart is compared with a normal heart, pressures and Heart Rates may be similar, but with more muscle mass, oxygen consumption is not. In compensated concentric hypertrophy pressure is increased and wall thickness is increased in similar proportion while lumen radius is hardly changed, thereby keeping wall stresses the same (Chap. 9). This means that the Stress Volume

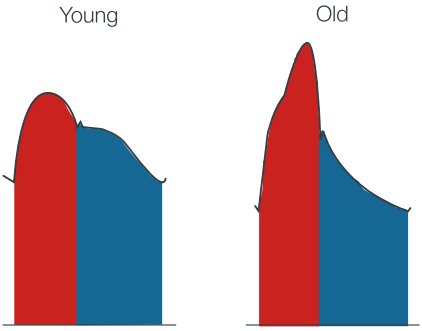

Fig. 16.4 The oxygen demand and supply. The areas under the systolic and diastolic part of the pressure curve, respectively. The ratio may be unfavorably influenced with increasing age

Area is similar in normal and hypertrophied hearts, while wall mass is increased and therefore oxygen consumption of the whole ventricle is increased. Therefore, correction for wall mass is required. Assuming wall stress to be the major determinant of oxygen consumption, total oxygen consumption would be proportional to wall mass.

Also by applying the Rate Pressure Product to mouse and man, where systolic ventricular pressure is similar but Heart Rate differs by a factor of ten, it can not be concluded that cardiac metabolism in the mouse heart is ten times that of the human heart. Even after normalizing for heart mass a difference remains because cardiac metabolism per gram of heart tissue is higher in the mouse than in the human (Chap. 30). The Pressure Volume Area, PVA, method also falls short when comparing different animals. Since the PVA predicts oxygen consumption per beat Heart Rate drops out of the equation. When normalized with respect to heart mass or body mass mouse and man would be more comparable but metabolism is not proportional to cardiac mass and body mass as will be discussed in Chap. 30.

References

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