Editorial

Cardiac work and efficiency

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1. Work output and efficiency of the heart

1.1. Pressure–volume relation and oxygen consumption

Many researchers have tried to relate cardiac energy metabolism in terms of oxygen consumption or heat production to mechanical performance. One now popular and accepted mechanical parameter is based on the pressure–volume relations found in the intact heart where pressure is plotted as a function of volume over the cardiac cycle [2]. The curve that is followed during the heartbeat consists of the following four parts (Fig. 1, top). Starting at end-diastole (right bottom corner) ventricular pressure increases while volume remains constant (isovolumic contraction), during the ejection phase volume decreases but pressure changes little, and, after closure of the aortic valves isovolumic relaxation ensues, which is followed by the filling phase. The area circumscribed is external mechanical work per beat. The triangular area between the systolic and diastolic pressure–volume relations and bounded by isovolumic relaxation is ‘potential energy’. The sum of the two areas, shaded in Fig. 1 top, is called the pressure–volume area (PVA).

It was shown that the oxygen consumption per beat \( (V_{O_2}) \) is linearly related to the PVA (Fig. 1, bottom). To derive oxygen consumption per minute, \( V_{O_2} \) may be multiplied by heart rate. The intercept with the \( V_{O_2} \) axis is the ‘unloaded’ oxygen consumption, found when the heart is not allowed to develop pressure so that the PVA is negligible. The ‘unloaded’ oxygen consumption consists of two parts, activation and basal oxygen consumption. The first depends on excitation–contraction coupling and is proportional to cardiac contractility. For the quiescent muscle the PVA and the oxygen cost of activation both are zero. The remaining part results from all other processes requiring oxygen such as ion pumps. With increased cardiac contractility the oxygen cost of activation (Fig. 1, bottom) is increased in a proportional manner but the slope of the relation between PVA and oxygen consumption is not affected.

The relation between PVA and \( V_{O_2} \) holds for all types of contractions, from isovolumic to isobaric (‘unloaded’) contractions. Isovolumic contractions correspond to the largest PVA and thus the largest oxygen consumption [3]. We see that external work is not a good measure of oxygen consumption.

Many other relations between oxygen consumption and mechanical or hemodynamic parameters have been proposed. The two best known are the rate pressure product (RPP) and the tension time index (TTI).

The RPP is the product of systolic pressure \( (P_s) \) and heart rate and is used as a measure of oxygen consumption in many biochemical studies. When these studies are performed in isolated hearts in Langendorff perfusion, i.e. no external work is performed, the PVA \( \equiv 0.5P_s(V_e - V_0) \equiv 0.5P_sV_0/E_s \), with \( V_e \) and \( V_0 \) is end-diastolic volume, and \( E_s \) the volume axis intercept and the slope of the systolic the pressure–volume relation (Fig. 1, top). In other words, for constant contractility (constant \( E_s \) the \( P_s \) relates in a quadratic way to the PVA. With an increase in contractility but constant filling (constant \( V_0 \)) the PVA increases in a linear way with \( P_s \) but the intercept of relation between PVA and oxygen consumption is altered. Thus the RPP, as a measure of cardiac metabolism should be used with care.

The use of the TTI [4], the averaged pressure over the ejection period, is also limited because for an isovolumic contraction the TTI is negligible (ejection time negligible).
When the TTI is calculated as the pressure–time integral for isovolumic beats it is a measure of cardiac economy (see below).

1.2. Efficiency and economy

External (mechanical) efficiency is defined in analogy to that of motors and equals the ratio of external work and oxygen consumption. Cardiac efficiency is normally about 20–25% [5]; the remainder of the oxygen used is converted to heat. In terms of the above diagrams (Fig. 1, bottom [3]) the myocardial conversion efficiency is defined as PVA/total $V_O$. The contractile efficiency or myofibrillar efficiency is defined the inverse of the slope of the $V_O$–PVA relation. This contractile efficiency is in the order of 40–50%. Economy of contraction is often used when no muscle shortening takes place (presumably approached in isovolumic beats) and is usually defined as the amount of energy (oxygen consumption, ATP-usage or contraction related heat rate) used for isovolumic contraction [6].

Work and efficiency depend on the load and the heart [7]. Isovolumic (isometric) contraction, i.e. no ejection (no shortening) and unloaded contractions, i.e. no pressure (force) development, do not produce mechanical work and efficiency is therefore also negligible. This means that when plotting work or efficiency as a function of pressure or cardiac output [7], at the extremes work and efficiency are negligible and that in between a maximum exists. It was shown that the heart under control resting conditions pumps at these maxima [7].

1.3. Heat production

Heat production of the heart has been measured [5]. Measurements show that heat is transported by convection by the coronary circulation and by diffusion to thorax and ventricular lumen in about equal amounts, and that convection transport increases with increasing perfusion. These measurements agree with the observation that the heart is about 25% efficient. However, accurate measurements are extremely difficult to carry out.

2. Papillary muscle

Papillary muscle is used as a model of the whole heart with the main advantages that (blood) perfusion is not required and geometry is relatively simple. When a (complex) geometric model of the left ventricle is used, wall stress ($F$, tension) can be related to ventricular pressure ($P$) and muscle length ($L$) to ventricular volume ($V$). The PVA becomes force length area (FLA, see Fig. 1), which can be related to oxygen consumption per contraction.

In the tradition of the measurement of heat in skeletal muscle many studies have been performed on isolated cardiac muscles using thermopiles [8,9]. The temperature of the muscle is measured, and heat production derived. Many aspects of the heat production and their meaning have been published [8,10,11]. However, for the present discussion it is sufficient to state that the measurement of temperature and mechanical performance allows the calculation of enthalpy, a measure of oxygen consumption [1,12].

The model relating PVA and $V_O$, as suggested by Suga and coworkers [2,3], based on (isolated) blood perfused.
heart studies, did not seem to agree with the accepted concepts on (skeletal) muscle contraction. Fenn’s experiments [13], on skeletal muscle, disproved the notion that with each contraction, a predetermined amount of energy was liberated either in the form of work or heat, or their combination. This ‘all or none’ phenomenon is not supported by the model relating FLA with \( V_o \), because the PVA depends on the load. In other words the FLA concept is not supporting the long discarded ‘all or none’ behavior of muscle energetics. The major argument that appeared to disprove the concept of FLA, was also given by Fenn [13] who reported that, for skeletal muscle, a contraction with shortening (thus smaller FLA) generated more heat (used more oxygen) than an isometric contraction (with larger FLA). However, this so-called Fenn effect is difficult to show in cardiac muscle, and is only found under very special experimental conditions [11].

Most studies on isolated cardiac muscle did not use the pattern of contraction the muscle encounters in the heart and thus also did not allow for determination of the FLA. This approach was started relatively late [14,15] but makes it possible to study if the findings in the heart are based on cardiac muscle behavior. It took until 1990 [16] to show that the FLA of isolated heart muscle was a good measure of relaxation heat (oxygen consumption). This was shown also by Gibbs et al. [12]. In other words there appeared to be basic differences between skeletal muscle and heart muscle in terms of the Fenn effect. It also implies that the PVA approach to cardiac metabolism finds its basis in the behavior of the cardiac muscle.

### 3. Cardiac aging

Because of the interaction of regulatory systems in the intact human and animal, it is extremely difficult to obtain a dependable measures of intrinsic contractile and energetic behavior. Therefore studies on isolated cardiac muscle, where conditions can be accurately controlled, are required to obtain the effects of aging on cardiac muscle mechanics and energy.

The changes taking place in the cardiovascular system with age have been extensively discussed by Lakatta [17]. Although studies on the mechanics and efficiency of cardiac muscle in normal and diseased conditions have been performed [6,12], very little has been done with respect to aging. It has been reported that with age the rate of contraction is decreased, electrical performance is altered, changes take place in the isoenzymes of the contractile apparatus and calcium handling is affected [17,18].

#### 3.1. Study by Kiriazis and Gibbs

In the study of Kiriazis and Gibbs [1], mechanical performance and efficiency are studied in the isolated cardiac muscle of aging rat. The basal metabolism (Fig. 1), measured in the quiescent muscle, was found to be decreased with age. This could have resulted from fewer membrane pumps in the somewhat hypertrophied myocytes where cellular area-volume ratio is decreased. Active metabolism (Fig. 1) was not different between the muscles from young and old rats.

With senescence both shortening and force generation decreased, leading to a smaller external work. Also energy consumption was decreased, but mechanical efficiency (in terms of work over enthalpy) remained the same. Contractile efficiency and economy did not change either with age. Thus force and shortening change with age but all indicators of efficiency stay the same. The authors found similar results in muscles of the rabbit with long-term volume overload [12].

In guinea-pigs the effects of aging were found to be a shift myosin heavy chains (MHC) from the alpha to the beta type resulting in a slower but more economical myocardium [18]. The difference may result from the difference in experimental animal because in the rat mostly \( \beta \)-MHC is present. In pressure overloaded hearts [17] and in the transition to failure in the rat [12] efficiency and economy appear to be increased as well. Aging is thus in terms of contraction speed not unlike the overloaded condition but efficiency and economy seem to stay the same while in overload these parameters increase.

It is possible to study energetics in human muscle strips from biopsies [10]. This approach gives the opportunity to study patient groups in terms of mechanics and efficiency. This type of study should be encouraged.

#### 3.2. Clinical aspects

With the use of ultrasound techniques (Doppler and echo) much information on cardiac pump function can be obtained. Also magnetic resonance imaging gives much functional information. The mechanical parameters required to obtain work, in combination with oxygen consumption and the derivation of efficiency, are presently not part of the standard diagnostic procedures. This is in large part because a series of contractions with different filling is required to obtain at least some accuracy in the determination of the PVA. Also oxygen consumption is rather complex to measure in the human. The use of magnetic resonance spectroscopy and positron emission tomography may change this.

### References

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